XLIX Annual Meeting
Chilean Society for Biochemistry and Molecular Biology

ABSTRACTS BOOK
2026

5th-8th October
Hotel Club La Serena, Región de Coquimbo

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CONFERENCE ABSTRACTS

Opening Lecture

How Mitochondria Respond to Changes in Caloric Intake

Alicia J. Kowaltowski 1 (alicia@iq.usp.br). Departamento de Bioquímica, Instituto de Química, Universidade de São Paulo.

In humans, obesity is associated with increased incidence of a variety of age-related diseases. Similarly, laboratory rodent lifespans are limited by obesity, including overeating promoted by ad libitum access to standard chow diets. Indeed, a daily limitation of caloric intake (calorie restriction) has been widely shown to enhance lifespans and prevent age-related diseases in rodents. We will discuss the metabolic effects of caloric restriction, and show that mitochondrial bioenergetics, redox state, and calcium homeostasis are regulated by caloric restriction, with an impact on tissue stress responses.

Protein Society Lecture

Allosteric Connections Across the Ras/Raf Dimer

Dra. Carla Mattos, Northeastern University, USA

The Ras/Raf interaction is central to activation of the MAPK signaling pathway in the cell, and it occurs through two Ras binding domains of Raf: RBD and CRD. While the molecular mechanisms through which Ras-GTP activates Raf kinase are still under investigation, we have found that binding Raf promotes dimerization of Ras leading to extensive allosteric connections across the Ras/Raf dimer. These connections link binding sites, at the extremity of the two Raf-RBD molecules in the dimer, for the scaffold protein Galectin, which is itself a dimer. In our model, this leads to a signaling platform composed of Ras/Raf and Galectin dimers for coordinated signal amplification. While much of the work on the Ras/Raf interaction has been done with CRaf, BRaf is known to be of major importance in the MAPK pathway. Here we present the crystal structures of KRas/BRaf-RBD and KRas/BRaf-RBD_CRD, and combine them with molecular dynamics simulations to investigate isoform-specific differences in intermolecular contacts and allosteric communication within Ras/Raf dimers. Overall, we observe enhanced allosteric communication in the presence of BRaf relative to CRaf and we mechanistically link this to isoform-specific residues. The presence of the CRD diminishes overall allosteric connections while diversifying the pathways that link the putative galectin binding pockets on RBD. Key residues previously shown when mutated to decrease signaling through MAPK are located on paths of allosteric connections on the Ras/Raf dimer complex, correlating these pathways to functional outcomes.

Severo Ochoa Lecture

Advancing Neurometabolic Disease Research Through iPSC-Derived Cellular Models and Genetic Therapies

Dra. Lourdes Ruiz Desviat. Centro de Biología Molecular Severo Ochoa, Universidad Autónoma de Madrid, Spain.

Rare neurometabolic diseases such as propionic acidemia (PA), caused by mutations in the PCCA or PCCB genes, and phenylketonuria (PKU), caused by defects in the PAH gene, are characterised by severe neurological and systemic complications, yet current treatments are mainly supportive or suboptimal, highlighting an unmet need for effective therapies. Our research aims to advance precision molecular medicine for these inherited metabolic disorders by combining cutting-edge disease models with next-generation RNA- and DNA-based therapeutic strategies. We have recently generated iPSCs from PA patients-derived fibroblasts and subsequently differentiated them into relevant cellular lineages (cardiomyocytes, neuronal precursors, astrocytes), allowing the characterization of molecular and cellular pathological mechanisms. We have also obtained isogenic gene edited knockout PCCA and PCCB iPSCs with subsequent differentiation to brain organoids. For PKU, we have generated humanized mouse models of PKU with splicing mutation c.1166-11G>A, the second most frequent PKU variant worldwide, as well as gene edited HepG2 cells with patient-specific PAH mutations. The disease models provide a powerful platform for preclinical testing of novel precision therapies. In this context, we have developed antisense oligonucleotide (SSO) strategies and gene-editing approaches. We have used SSO to correct aberrant pseudoexon inclusion caused by a deep-intronic variant in the PCCA gene causing PA. We have demonstrated that blocking an enhancer motif with SSO restores normal splicing and rescues protein and enzyme activity. To explore a potential one-time durable genetic therapy, we have also used CRISPR/Cas to abrogate PCCA pseudoexon inclusion in the mRNA. For PKU, we have used SSO to correct clustered PAH splicing defects in splicing vulnerable exon 11. SSO were designed to cover a silencer motif bound by hnRNAPA1/2, that in minigenes corrected the splicing alteration of different variants, and which in edited HepG2 resulted in the restoration of PAH protein and activity.

Osvaldo Cori Lecture

CoREST: a modular architecture, many functions

María Estela Andrés. Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile.

In the late 1990s, a central question in molecular neurobiology was how neuronal genes are silenced outside the nervous system. The transcription factor REST represses these genes, but the machinery acting through its repression domains was unknown. In searching for the answer, we identified CoREST, a corepressor that turned out to be much more than an adaptor. This discovery, made during my postdoctoral training in Gail Mandel's laboratory, became the starting point of a research program that I have developed in Chile for more than two decades, together with the students and collaborators who shaped it. CoREST organizes a complex with HDAC1/2 and the demethylase LSD1 to act on nucleosomes. In other words, it is a platform that enables enzymatic activities on chromatin.

In this lecture, I will present how our work has revealed the functional diversification of the CoREST/RCOR family. We showed that the three vertebrate paralogs, despite sharing a common domain architecture (ELM2, SANT1, linker, SANT2), form complexes with distinct properties. We also found that their roles extend beyond classical repression: RCOR1 modulates active transcription, and RCOR2 operates outside chromatin, in nuclear speckles and in the dividing cell. Finally, our evolutionary analysis showed that these paralogs arose through gene duplication, providing a framework for understanding how a single architecture gave rise to divergent functions.

Funding: ANID/Fondecyt.

NEW MEMBERS SESSION

NM1. Intrinsic Resistance Mechanism of Squamous Cell Lung Carcinomas to the multi-angiokinase inhibitor Nintedanib: CXCL-1 Upregulation in Tumor-Associated Fibroblasts.

Natalia Díaz-Valdivia[1,2], Paula Duch[1], Alejandro Bernardo[1], Marselina Arshakyan[1], Noemí Reguart[3,4], Derek C. Radisky[5], Oriol Casanovas[6], Jordi Alcaraz1,4.1Unit of Biophysics and Bioengineering, Department of Biomedicine, School of Medicine and Health Sciences, Universitat de Barcelona, Barcelona, Spain. [2] Núcleo Interdisciplinario de Biología y Genética (NiBG), Instituto de Ciencias Biomédicas (ICBM), Facultad de Medicina, Universidad de Chile, Santiago, Chile. [3]Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain. [4]Thoracic Oncology Unit, Hospital Clinic Barcelona, Barcelona 08036, Spain. [5]Department of Cancer Biology, Mayo Clinic, Jacksonville, FL 32224, US. [6]Tumor Angiogenesis Group. ProCURE, Catalan Institute of Oncology, Oncobell, IDIBELL, Barcelona, Spain.

Introduction: Lung adenocarcinoma (ADC) and squamous cell carcinoma (SCC) are the most common lung cancer subtypes. SCC is intrinsically resistant to anti-angiogenic therapies, but the underlying mechanisms remain unclear. Nintedanib, a multi-angiokinase inhibitor approved for ADC in combination with docetaxel, also exhibits antifibrotic activity. We previously reported stronger antifibrotic effects of Nintedanib on ADC-derived tumor-associated fibroblasts (TAFs) than on SCC-TAFs. Here, we investigated whether these differential responses extend to the angiogenic properties of TAFs.

Methods: TAFs derived from ADC and SCC patients were stimulated with TGF-β1 to mimic their activated phenotype, with or without Nintedanib. Conditioned media were used to assess endothelial cell migration and vascular network formation *in vitro*. Pro-angiogenic factors were analyzed using an angiogenesis antibody array, and selected candidates were functionally validated using genetic approaches *in vitro* and *in vivo*.

Results: Nintedanib inhibited the pro-angiogenic activity of ADC-TAFs but not SCC-TAFs. Unexpectedly, Nintedanib-treated SCC-TAFs increased endothelial cell migration and angiogenesis *in vitro* and *in vivo*. Among 20 pro-angiogenic factors analyzed, Nintedanib selectively increased CXCL-1 expression and secretion in SCC-TAFs compared with ADC-TAFs. CXCL1 silencing by siRNA was sufficient to abrogate Nintedanib-induced angiogenesis, identifying CXCL-1 as a key mediator of this paradoxical response.

Discussion: SCC-TAFs are resistant to the anti-angiogenic effects of Nintedanib and instead promote angiogenesis through CXCL-1 upregulation. These findings provide mechanistic insight into the selective resistance of SCC to anti-angiogenic therapies and underscore the role of TAFs in modulating responses to multi-angiokinase inhibitors, identifying the CXCL-1 axis as a potential target to overcome resistance.

NM2. Gene-environment interactions in Parkinson's disease: insights from flies and diverse populations exposed to pesticides.

Patricio Olguín. Núcleo Interdisciplinario de Biología y Genética, Instituto de Ciencias Biomédicas y Departamento de Neurociencia, Facultad de Medicina, Universidad de Chile.

Parkinson's disease is the most prevalent neurodegenerative movement disorder, affecting 1% of the population over 60 years old. Near 90% of people living with Parkinson's disease present the idiopathic form (iPD), which is of unknown cause. Genetic risk factors explain only about 33% of heritability, and environmental factors increase the risk by only 10%. Thus, it has been proposed that gene-environment interaction (GEI) may play a significant role in the etiopathology of iPD. Pesticide exposure has been described as a strong risk factor for increased ROS, neuroinflammation, mitochondrial dysfunction, and epigenetic effects, among others. Nevertheless, Gene-pesticide exposure interaction studies in PD are limited by small cohort sizes and a lack of detailed exposure data across the lifespan, including exposure amounts and pesticide classes. Here, we present a summary of our current work using a Drosophila model of iPD induced by pesticide exposure and human populations to uncover the genetic basis of gene-pesticide exposure interactions and the molecular mechanisms underlying it.

Acknowledgment: Fondecyt 1251006

NM3. Cryo-EM structure of a brown algal Photosystem I-FCP supercomplex reveals conservation and divergence of antenna architecture in the red lineage.

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Introduction: Brown algae such as *Macrocystis pyrifera* are the most net-productive marine primary producers per unit area. Photosystem I (PSI) drives photosynthetic electron transfer and, in red-lineage algae, associates with fucoxanthin-chlorophyll a/c protein (FCP) antennae. PSI-antenna structures have been determined for red algae, cryptophytes, haptophytes, dinoflagellates, and diatoms, but not for brown algae. This work aimed to determine the first structure of the brown algal PSI-FCP supercomplex and to identify drivers of antenna evolution across the red lineage.
Materials and Methods: Chloroplasts from fresh *M. pyrifera* blades were isolated using alginate lyase. Thylakoids were solubilized with digitonin, and PSI-FCP was purified by sucrose-gradient ultracentrifugation. The structure was solved by single-particle cryo-electron microscopy. FCP subfamilies were assigned by phylogeny and by map-model Q-scores.
Results: The structure (PDB 9YGV) contains 11 PSI subunits and 18 FCPs arranged in two belts. Seven subfamilies were identified: the first belt retains an Lhcr majority, whereas the second belt is Lhcf-dominated, unlike diatoms and haptophytes. FCP1 and FCP3 show subfamily switches and a ~135° rotation correlated with PsaO loss, plus two novel positions (FCPA/B). Subfamily identity and orientation generate membrane rippling, with thickness differences up to 17 Å. Chlorophyll losses and gains reorganize excitation energy transfer, including migration of a chlorophyll from FCP8 to a Chrysista-restricted PsaR histidine.
Discussion: Contingent PSI:FCP interactions conserve the first belt, whereas gene loss, hydrophobic-mismatch minimization, and constructive neutral evolution explain outer-belt diversification. Chrysista- and Diatomista-specific energy-transfer features may underlie photosynthetic differences between kelps and diatoms, with implications for kelp productivity.
Acknowledgment: UC Davis (CBS, CAMPOS, Boomerang Award, Hellman Fellowship); FONDECYT Postdoctorado 3260629.

NM4. A GRN strategy to unveil hubs regulating *Trichoderma atroviride* mycoparasitism progression.

Karla Vargas-Menares[1,2], Thomas Aguilera[1,2,3], José David Fernández[1,2,4], Gabriel Pérez- Lara[2,4,5], Nicolas Arias[2,5], Elena Vidal[1,2,3,4,5], Paulo Canessa[2,5], Consuelo Olivares-Yáñez[1,2,3] (consuelo.olivares@umayor.cl). [1]Centro de Genómica y Bioinformática, Universidad Mayor, 8580745 Santiago, Chile. [2]Millennium Institute for Integrative Biology (iBio), 8331150 Santiago, Chile. [3] Escuela de Biotecnología Universidad Mayor. [4]Millennium Nucleus in Data Science for Plant Resilience (Phytolearning), Santiago, Chile. [5]Centro de Biotecnología Vegetal, Facultad de Ciencias de la Vida, Universidad Andres Bello, 8370186 Santiago, Chile.

Introduction: *Trichoderma atroviride* is a mycoparasitic fungus widely used for the biocontrol of phytopathogens such as *Botrytis cinerea* and *Rhizoctonia solani*. Although the stages of mycoparasitism have been described, the transcriptional regulation underlying this interaction, and its modulation by nutrient availability, remain largely unexplored. Here, we characterized the transcriptional dynamics and gene regulatory networks (GRN) governing the *T. atroviride–B. cinerea* interaction and evaluated the functional relevance of candidate transcription factors (TFs).
Materials and Methods A dual-culture assay between *T. atroviride* and *B. cinerea* was performed over seven days, with samples collected at days three, four, and seven across three culture media to assess how nutrients modulate transcriptional responses. RNA-seq data were integrate into gene regulatory networks (FIMO-GENIE3) and visualized using Cytoscape. Key TFs linked to critical mycoparasitism process were selected. *T. atroviride* knockout and overexpression strains for selected TFs were generated and evaluated in dual-culture assays and supernatant inhibition assays against four phytopathogenic fungi to validate their functional relevance.

Results: Network inference and TFs selection identified candidate regulators associated with the *T. atroviride–B. cinerea* mycoparasitic interaction. Knockout and overexpression strains for these TFs were generated. Dual-culture and supernatant inhibition assays against the four phytopathogenic fungi showed that overexpression strains exhibited enhanced inhibitory activity compared to the wild-type strain, whereas knockout strains showed reduced biocontrol capacity in dual assays, confirming the functional relevance of these TFs in modulating *T. atroviride* mycoparasitic potential.
Discussion: These results demonstrate that the candidate TFs identified through GRN inference are functionally involved in regulating *T. atroviride* mycoparasitism, and that their manipulation can enhance biocontrol performance beyond that of the wild-type strain. This supports the use of network-based approaches to prioritize regulatory targets in *Trichoderma* and highlights these TFs as promising candidates for improving the efficacy and consistency of *T. atroviride*-based biocontrol strategies against multiple phytopathogenic fungi.

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NM5. A SINE-derived RNA as a stress-responsive epigenetic ribozyme.
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[2] Harvard Medical School.

Introduction: Cells respond to macromolecular damage through rapid transcriptional reprogramming: non-essential RNA polymerase II–derived transcripts are downregulated through RNA-mediated epigenetic silencing, while transcription of cytoprotective genes is selectively enhanced. SINE-derived B2 RNAs are strongly upregulated under environmental stress. B2 RNA binds to and inhibits RNA polymerase II, leading to broad transcriptional downregulation. B2 also has self-cleaving ribozyme activity, which helps permit cytoprotective gene expression during stress and restore steady-state transcription after stress resolution. Here, we investigate the structural determinants of the B2 ribozyme both *in vitro* and *in vivo*.
Materials and Methods: We performed mutational screening to assess how specific structural features of the B2 ribozyme contribute to its biochemical functions *in vitro*. We also used a heat-shock stress model to examine the role of B2 *in vivo*, focusing on RNA polymerase II inhibition and B2 RNA abundance.
Results: We identified structural determinants that are critical for B2 interaction dynamics, RNA polymerase II inhibition, and RNA abundance under stress response.
Discussion: Our findings reveal non-canonical roles for the B2 ribozyme and support its function as a central regulator of the cellular stress response.

Acknowledgment: Pew Latin American Fellows Program.

NM6. From Sexual Recombination to Nuclear Cooperation: Experimental Evolution in Two Fungal Models.
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Introduction: Fungi deploy diverse mechanisms to withstand environmental fluctuations, making them valuable models for studying adaptation. We investigated how reproductive mode and multicellular organization influence evolutionary responses to stress in the yeast *Saccharomyces eubayanus* and the filamentous fungus *Neurospora crassa*.
Materials and Methods: Genetically diverse *S. eubayanus* populations with high or low sporulation rates were experimentally evolved for approximately 120 generations under 9% ethanol stress using sexual and asexual reproduction regimes. Growth, ethanol tolerance, fermentative performance, cellular morphology, and genomic variation were evaluated in evolved isolates. In parallel, *N. crassa* populations were evolved under elevated-temperature regimes. Isolates were characterized for circadian rhythmicity, heat-shock responses, carbohydrate utilization, and interactions among genetically distinct nuclei within their syncytial mycelia.
Results: Adaptation in *S. eubayanus* was primarily associated with a significant reduction in lag phase under ethanol stress. Sexual reproduction generated the best-performing phenotype, which displayed ethanol tolerance and fermentative capacity comparable to the industrial reference strain *S. pastorianus* W-34/70. One sexually evolved lineage developed an ethanol-inducible pseudohyphal phenotype. Genomic analysis of the most adapted isolate identified mutations in *UBR2* and *CSN9*, implicating the ubiquitin–proteasome pathway in adaptation to alcohol-induced proteotoxicity. Temperature-evolved *N. crassa* populations exhibited substantial phenotypic diversity in circadian behavior, thermal-stress responses, and carbohydrate metabolism. Isolates from evolved lineages also displayed coordinated cellular behavior despite their nuclear heterogeneity.
Discussion: These findings show that sexual reproduction can accelerate the emergence of beneficial trait combinations in yeast, whereas the syncytial organization of filamentous fungi may facilitate cooperation among genetically distinct nuclei.

Together, both models reveal how reproductive strategy and cellular organization shape fungal adaptation and generate phenotypes with ecological and biotechnological relevance.

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NM7. Unraveling metabolic functions of glucose transporter 8, GLUT8

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Introduction: GLUT8 is a class III glucose transporter, traditionally considered intracellular and linked to fructose uptake and lipid metabolism. We explored the expression and potential functions of GLUT8 in obesity and diabetic retinopathy (DR).
Methods: Two experimental models were used. Model 1: Gonadal white adipose tissue (gWAT) of male BalB/c mice fed a high fructose diet (HFrD, 30 and 50% w/v) for 4 months. Modelo 2: retina from C57BL/6 diabetic mice. DR was induced by neonatal injection of streptozotocin (90 mg/Kg body weight i.p.), three months of a standard diet and one month of high fat diet (HFD, 30% of total Kcal from fat). GLUT8 expression was analyzed by immunocytochemistry and qPCR, together with GLUT1, GLUT4, GLUT5, GLUT12, cell- and organelle-specific markers. In adipose tissue, the expression of key metabolic enzymes was also assessed by qPCR.
Results: A dose-dependent increased GLUT8 expression in gWAT was observed, accompained by a partially shift in its subcelular localization towared the cell membrane. A marked increase in GLUT4 and GLUT5 was observed, reaching aproximately 40 fold at the mRNA level. In addition, mRNA expression of ketohexokinase (KHK), lipoprotein lipase (LPL) and acetyl-CoA-carboxylase 1 (ACC1) was increased by 10, 2 and 2 folds, respectively. In the retina, GLUT8 was detected in the membrane of retinal photoreceptors and glial cells, with its expression increasing by 80 to 100% in RD. A similar pattern was observed for GLUT1. Reactive gliosis, together with morphologic and vascular abnormalities was also observed.
Discussion: We found that GLUT8 was associated with fructolysis and lipogenesis induced by HFrD in gWAT, as well as with retinal neurovascular alterations associated with DR. Together, these findings suggest that GLUT8 may contribute to glucose/fructose uptake in both tissues, supporting its potential as a pharmacological target in metabolic diseases such obesity and diabetes.

Acknowledgment: FONDECYT 111251393, DI-REG13/2022, FGII03/2024

NM8. Alternative polyadenylation and the circadian clock: Uncovering a bidirectional regulatory network in the *Drosophila* nervous system.

Íñigo Genúa[1], Sofia Paredes[1], Franco Núñez-Villegas[1], Analía Foncea-Bitrán[1,2], Camilo Villamán[3,4], Mariana Labarca[1], Gonzalo H. Olivares[1,5,6] (gonzalo.olivares@umayor.cl). [1]Center for Integrative Biology (CIB), Universidad Mayor, Santiago, Chile. [2]Programa Doctorado Genómica Integrativa, Universidad Mayor, Santiago, Chile. [3]Centro de Investigación en Ciencias de la Salud, Departamento de Procesos Diagnósticos y Evaluación, Facultad de Ciencias de la Salud, Universidad Católica de Temuco, Chile. [4]Centro de Investigación, Innovación y Creación (CIIC), Vicerrectoría de Investigación y Posgrado, Universidad Católica de Temuco, Chile. [5]Escuela de Kinesiología, Facultad de Medicina y Ciencias de la Salud, Universidad Mayor, Santiago, Chile. [6]Departamento de Neurociencia, Facultad de Medicina, Universidad de Chile, Santiago, Chile.

Introduction: Circadian rhythms arise from core transcription-translation feedback loops operating within specialized neuronal networks. However, how post-transcriptional RNA processing contributes to biological timing regulation remains poorly understood. Alternative polyadenylation (APA) generates mRNA isoforms with different 3′ untranslated regions (3′UTRs), modifying the regulatory landscape that governs mRNA stability, localization, and translation. We hypothesize that a bidirectional regulatory network between the molecular clock and APA in circadian neurons fine-tunes circadian physiology and behavior in *Drosophila melanogaster*.
Materials and Methods: We combined bioinformatic, transcriptomic, functional genetic, and behavioral approaches to investigate this regulatory network. Available RNA-seq datasets from defined circadian neuronal populations were analyzed to map global temporal dynamics of APA and the expression of cleavage and polyadenylation (CPA) factors. Potential transcription factors (TFs) regulating CPA genes were identified by integrating ChIP-seq, regulatory motif, and gene expression data. In parallel, CPA factors were knocked down in clock neurons using RNAi to evaluate their requirement for circadian locomotor behavior. Additional functional outputs will include eclosion rhythms and circadian neuronal plasticity.

Results: Bioinformatic and transcriptomic analyses revealed that CPA machinery components undergo circadian regulation and identify candidate TFs, including core clock components, linking the molecular clock to CPA expression. Conversely, neuronal knockdown of the CPA factor *CPSF6* reduced locomotor rhythmicity under constant darkness and impaired light-dark phase anticipation. Together, these findings support functional interplay between the circadian system and mRNA 3′-end processing.
Discussion: Our work investigates APA across multiple levels of circadian regulation, from transcriptional control of the CPA machinery and rhythmic APA to neuronal and behavioral outputs. This integrative approach will establish how the molecular clock regulates mRNA 3′-end processing and, reciprocally, how APA contributes to circadian network function, providing a framework for understanding post-transcriptional regulation of biological timing.

Acknowledgment: Financiado por la Agencia Nacional de Investigación y Desarrollo, ANID / Concurso FONDECYT Regular #1251851

SYMPOSIUM ABSTRACTS

SYMPOSIUM 1
Single-Cell genomics: emerging frontiers in gene regulation

Organizers: Dra. Elena Vidal, Universidad Mayor y Dr. José Miguel Alvárez, Universidad Andres Bello

S1.1. A cellular map of LATAM diversity reveals ancestry-specific gene regulatory patterns
Dr. Carlos Ortiz Ramírez, CINVESTAV UGA, México

Human genetic variation within Latin America influences population architecture and disease risk, but its impact on single-cell immune gene expression remains unexplored. To address this, we introduce LatinCells, the first extensive, single-cell immune map centered on Indigenous American diversity, created by a regional Latin American initiative. We characterized 2,596,370 PBMCs from 652 healthy participants across eight nations. Our findings show that while adaptive T cells remain conserved, innate and myeloid lineages display notable ancestry-linked deviations. Genetic origin appeared as the primary source of transcriptomic differences following biological sex, resolving fine-scale gradients among Andean, Mesoamerican, and Orinoquian-Caribbean populations. Crucially, by crossing local ancestry with cell-type-specific eQTLs, we demonstrate that ancestry-specific genomic backgrounds modulate the regulatory strength of specific loci, such as the immune regulator UTS2. LatinCells provides the foundation for equitable, locally led genomics research, enabling more representative precision medicine for diverse and admixed populations.

S1.2. Hidden complexity: single-cell approaches to immune regulation and disease risk
Marcela K. Sjöberg-Herrera[1,1] Laboratorio de Regulación Epigenética, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Chile.

The immune system comprises highly specialized circulating and tissue-resident immune cells that collectively maintain immune homeostasis across diverse physiological environments. The functional diversity of these cells emerges from the interplay between genetic background, environmental exposures, and evolutionary processes, generating substantial interindividual variation in immune responses and disease susceptibility. Despite major advances in human genetics, most studies have focused on populations of European ancestry, limiting our understanding of immune regulation across globally diverse populations.
Emerging single-cell and multimodal technologies are now uncovering previously hidden cellular states and regulatory programs, providing unprecedented opportunities to dissect how genetic variation and cellular context influence immune function and disease risk. To address these questions, we use single-cell and multimodal genomic approaches to investigate immune regulation across populations and disease contexts.
As part of the international JAGUAR consortium within the Human Cell Atlas, we contribute to the generation of immune reference maps from peripheral blood samples of admixed Latin American populations using scRNA-seq and CITE-seq. In parallel, we investigate how obesity, a major public health challenge in Chile, reshapes gene regulatory programs in immune cell populations involved in tissue homeostasis and inflammation.
Our analyses highlight the importance of studying diverse populations to capture the full spectrum of human immune variation. In parallel, single-cell approaches identify disease-associated cellular states and transcriptional programs linked to chronic inflammation, revealing regulatory mechanisms that may contribute to immune dysfunction. Together, these studies demonstrate how genetic background, cellular context, and gene regulation interact to shape immune phenotypes in both health and disease.

These studies highlight the power of single-cell genomics to uncover immune complexity, from population-level variation to disease-associated cellular reprogramming. Together, they provide new opportunities to better understand human immunity and disease mechanisms.

Acknowledgments: This work is funded by the Chan Zuckerberg Initiative (CZI), Ancestry Networks of the Human Cell Atlas and by the Agencia Nacional de Investigación y Desarrollo de Chile, ANID FONDECYT Regular 1241935.

S1.3. Non-invasive sampling and single-cell profiling to understand wound healing in a rare skin disease.

Ignacia Fuentes[1,2] (mifuente@uc.cl), Nicole Koplow[1], Pilar Morandé[2], Evelyng Catalan[1], Patricio Tapia[1], Claudio Meneses[1], Jian Ge[3], Andrew South[3], Francis Palisson[2,4]. [1]Pontificia Universidad Católica de Chile, Santiago, Chile. [2]DEBRA Chile, Santiago, Chile. [3]University of Wisconsin-Madison, Madison, USA. [4]Servicio de Dermatología, Facultad de Medicina Clínica Alemana, Universidad del Desarrollo, Santiago, Chile.

Introduction: Wound healing is a complex, multi-stage process, and understanding why some wounds fail to close remains a major clinical challenge. Recessive Dystrophic Epidermolysis Bullosa (RDEB) is a rare hereditary skin fragility disorder characterized by recurrent blistering and chronic, difficult-to-heal wounds, making it a valuable model to study the cellular basis of impaired wound closure. However, the invasive nature of conventional skin biopsies limits longitudinal sampling in these fragile patients. To overcome this, we developed a non-invasive method to collect wound-derived cells directly from discarded wound dressings.
The aim of this work was to characterize, at single-cell resolution, the cellular composition and transcriptional states associated with healing versus non-healing wounds in RDEB patients.
Materials and Methods: Cells were recovered from discarded wound dressings of RDEB patients, isolated, and cryopreserved for downstream processing. Samples were obtained from wounds that subsequently closed and from wounds that failed to close. Single-cell RNA sequencing (scRNA-seq) was performed to profile the cellular composition and gene expression profiles.
Results: scRNA-seq of more than 7,500 single cells recovered from wound dressings identified predominantly immune populations (T cells, B cells, macrophages and neutrophils), together with smaller cell populations (fibroblasts and keratinocytes). Neutrophils and macrophages were present abundantly in both healing and non-healing wounds but displayed distinct transcriptional profiles and pathway activation depending on wound outcome. Bulk RNA sequencing of wound-derived fibroblasts further revealed a role for cellular senescence in wound closure in RDEB.
Discussion: These results show that non-invasive sampling of wound dressings is a feasible strategy to obtain viable cells, at single-cell and bulk resolution. Distinct immune cell states and fibroblast senescence suggest complementary drivers of impaired wound closure. Ongoing analysis will help define wound healing stages and relevant cell types, with implications beyond RDEB for other chronic wounds.

Acknowledgment: ANID/FONDECYT Regular 1220704.

S1.4. Plant stem cell dynamics rewire differentiation and cell identity.

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Stem cells generate the cellular diversity required to build multicellular tissues. Unlike most animals, plants maintain active stem cell niches throughout their lives, continuously producing new organs. Yet how the dynamics of these stem cell populations influence the identities of the cells they generate remains poorly understood. We address this process in the *Arabidopsis* shoot stem cell niche, where a small population of undifferentiated cells continuously generates the cells that form stems, leaves and flowers. Using single-nucleus RNA sequencing, we established a transcriptional map at single-cell resolution, capturing the shoot stem cell niche together its differentiation pathways, including early floral primordia, cortex and vascular tissues. This analysis uncovered previously unresolved transcriptional states and developmental patterns such as the early specification of cortex identity during organ formation. By reconstructing cell-cycle dynamics, we resolved transcriptional landmarks associated with specialised cell identities. Profiling stem cell-related mutants with excessive cell proliferation, we then observed that expansion of the stem cell population was accompanied by a broad reorganisation of the differentiation landscape. This "cell identity shuffle" suggests that altered stem cell dynamics can propagate through the developing tissue and that cell differentiation and the organisation of cell identities are highly intertwined with upstream stem cell dynamics. Altogether, this work provides a framework for understanding how perturbations in stem cell regulation can reshape cell differentiation.

SYMPOSIUM 2
Cancer beyond individual cells: Microbial signals, lipid metabolism and tumor ecosystems

Organizers: Dra. Lorena Lobos y Dr. Andrew Quest, Universidad de Chile

S2.1. Helicobacter pylori induces senescence through non-coding RNA networks in gastric cancer.

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Introduction: Helicobacter pylori (H. pylori) infection induces a cascade of well-defined lesions (atrophy and intestinal metaplasia) collectively known as gastric premalignant conditions (GPMCs). Senescence, a cell cycle arrest phenomenon, has been recently associated with H. pylori infection, mostly through the upregulation of inflammatory protein-coding genes. We explored the role of non-coding RNA networks in the senescence induced by H. pylori. **Materials and Methods**: Forty-nine H. pylori-infected clinical samples from the Gastric Cancer Precursor Lesions (GCPL) cohort (NCT03188406) were tested for senescence by Sudan Black B (SBB) staining. Three cell lines were experimentally infected with the oncogenic H. pylori strain 26695 and evaluated for senescence. The role of non-coding RNA networks and their interactions with the senescence machinery was evaluated *in vitro.* **Results:** Among 49 GPMC H. pylori infected clinical samples, 15 (30.6%) tested positive for senescence by SBB staining. In cell lines, an increase in percentage of senescent cells was observed after infection. In addition, phosphorylated protein Retinoblastoma 1 (RB1) and protein phosphatase 1 (PP1) were found to be downregulated and upregulated, respectively. H. *pylori* infection also upregulated the expression of the long-coding (lnc) RNA KCNQ1OT1, a relevant non-coding RNA in gastric cancer (Sandoval-Borquez 2026). Silencing of the expression of KCNQ1OT1 by DsiRNA resulted in the downregulation of the PP1 transcript (PPP1CA). *In silico* screening for microRNA candidates for KCNQ1OT1 and PPP1CA simultaneous binding resulted in the identification of microRNA-4319. Further validation by Luciferase assays is being performed. **Discussion:** These experiments suggest that H. pylori might induce senescence in the human gastric mucosa through non-coding RNA networks. Upregulation of the lncRNA KCNQ1OT1 potentially binds microRNA-4319, which allows the upregulation of PP1, inducing senescence through the dephosphorylation of RB1.

Acknowledgment: FONDECYT 1231773

S2.2. The adipose tissue-cancer connection

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In recent years obesity has emerged as a major public health concern increasing as of 2021 to a staggering 39% of the population world-wide. Given the magnitude of the problem, and considering that this disease is associated with a chronic low-grade systemic inflammatory state, obesity is now considered one of the major risk factors associated with the development of several chronic diseases, including cancer. Adipose tissue dysfunction in obesity has taken center stage in attempts to understand how changes in the biology of its components, particularly adipocytes, participate in such processes. In this talk, I will initially focus on how changes that occur in adipose tissue upon excess fat accumulation generate endocrine signals that promote cancer development and subsequently dedicate attention to the role of signaling via extracellular vesicles (EVs) derived from adipocyte cells in this context. Specifically, evidence will be discussed showing that the scaffolding protein Caveolin-1 (CAV1), a prevalent protein component in adipocytes and EVs derived from such cells, plays an important role in determining EV protein composition. Moreover, experiments will be described showing that specific proteins, identified by mass spectrometry, that accumulate in EVs from adipocytes expressing CAV1, are required to trigger vascular network formation by endothelial cells in vitro and angiogenesis in vivo in chick-cam assays. Thus, beyond promoting systemic inflammation, an excess of fat tissue can favor cancer growth by enhancing angiogenesis of tumors in a CAV1-dependent manner.

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S2.3. Metformin: a protective tool in gynecological cancer therapy.

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Introduction. Metformin, a first-line treatment for type 2 diabetes mellitus, has emerged as a promising candidate for drug repurposing in oncology. Its antitumor effects involve systemic reduction of insulin-related growth signalling and direct actions on tumour cells, including mitochondrial complex I inhibition, AMPK activation, metabolic reprogramming, and modulation of proliferative and survival pathways. These effects may contribute to reduced tumour growth, altered redox homeostasis, and decreased tumour aggressiveness. Although clinical evidence remains heterogeneous, observational studies and meta-analyses suggest potential benefits in several malignancies, including breast and ovarian cancer. Its well-established safety profile, extensive clinical use, and low cost make metformin an attractive candidate for pharmacological repositioning as an adjuvant anticancer therapy, particularly in molecularly defined patient subgroups.
Methods. Metformin was evaluated in complementary *in vitro*, 3D, and *in vivo* breast and ovarian cancer models. MCF-7 and MDA-MB-231 breast cancer cells were assessed by migration assays and 3D tumoroid formation after exposure to different metformin concentrations. In parallel, SKOV-3 ovarian cancer xenografts were established by subcutaneous implantation in NOD/SCID mice and treated with different metformin regimens. Tumor growth was monitored over time, followed by tumor weight determination, histopathological analysis, and necropsy to assess metastatic dissemination. Metformin-treated tumours were compared with untreated controls.
Results. Although the experimental study is ongoing, indicate an antitumor effect of metformin across breast and ovarian cancer models. Metformin treatment reduced tumour aggressiveness in the ovarian cancer xenograft model and was associated with delayed tumour progression. In cellular models, metformin reduced the migratory capacity of both breast and ovarian cancer cells. Furthermore, metformin impaired 3D tumoroid formation, suggesting a reduction in cancer stem cell-associated tumorigenic potential.
Discussion: Further mechanistic and translational studies will be required to identify the tumour phenotypes most responsive to metformin and to define biomarkers capable of guiding its potential incorporation into precision-oriented adjuvant therapeutic strategies.

Acknowledgments. This work was supported by PIP 2022-927 (DNA) and FONDECYT 1261118 (LLG). We acknowledge the scientific collaboration of Dr. Patricia Burgos, Universidad San Sebastián (USS), and Dr. Carmen Romero, Universidad de Chile.

S2.4 Lipidomics Analysis in Cancer: EVs and Lipid Signaling to Identify Targets for Intervention.
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Lipids are essential bioactive mediators that regulate key pathways involved in carcinogenesis, including tumor initiation, progression, and metastasis. Among these, oxylipins—the enzymatic and non-enzymatic oxygenation products of polyunsaturated fatty acids (PUFAs)—are critical signaling molecules that participate in complex biological networks within the tumor microenvironment. Although liquid chromatography–tandem mass spectrometry (LC-MS/MS) platforms have been successfully optimized for high-throughput oxylipidomic profiling in clinical biofluids and chronic inflammatory disease models, characterizing these lipid signaling signatures during cancer progression remains a critical frontier for the identification of novel therapeutic targets.
This study describes the application of a robust targeted HPLC-MS/MS method for oxylipid detection and quantification, designed to characterize lipidomic signatures associated with cancer metastasis. Using a solid-phase extraction protocol coupled with reversed-phase chromatography and multiple reaction monitoring (MRM) mass spectrometry, we successfully extracted, identified, and quantified a broad range of eicosanoids and octadecanoids from diverse lipid matrices. To evaluate the platform's ability to detect metabolic reprogramming and assess therapeutic efficacy, we employed a highly aggressive murine melanoma model based on B16-F10 cells. Because metabolic reprogramming and enhanced migratory capacity are frequently associated with increased expression of Caveolin-1 (CAV1), B16-F10 cells were genetically engineered to overexpress CAV1, providing a specialized model of advanced metastatic disease. Using this system, we investigated the pharmacological effects of a bioactive natural extract from brown seaweed on altered cellular processes and lipid-mediated signaling pathways.
Our quantitative oxylipidomic platform effectively tracked changes in key bioactive lipid mediators and pathway-specific biomarkers, generating a detailed molecular map of how the intervention modulates tumor-associated lipid signaling. Notably, our findings reveal that the natural extract effectively prevents metastasis by inhibiting glycolysis while concurrently driving a marked increase in cellular oxidative stress and the accumulation of oxidized lipids. These results highlight the versatility and analytical sensitivity of mass spectrometry-based oxylipidomics as a powerful approach for cancer biomarker discovery and therapeutic monitoring. Furthermore, integrating precise lipid quantification with established models of metabolic

reprogramming provides new opportunities for target identification and the characterization of bioactive lipid signaling networks. In particular, previous studies in other pathological models have demonstrated significant alterations in extracellular vesicle-associated lysophospholipid signaling, underscoring the broader potential of lipidomic approaches to uncover mechanisms of intercellular communication and support the development of personalized, non-toxic therapeutic strategies aimed at preventing cancer metastasis.

SYMPOSIUM 3
Ciencia con Enfoque de Género

Organizers: Dra. Valentina Parra, Universidad de Chile y Dra. Roxana Pincheira, Universidad de Concepción

S3.1. Ciencia, Mujeres y Territorialidad.

María José Gallardo Nelson[1].[1]Vicerrectora de Investigación y Postgrado Universidad de Atacama. Presidenta de la comisión asesora de investigación del CRUCH.

El vínculo entre ciencia, mujeres y territorialidad constituye un espacio relevante para reflexionar sobre las condiciones en que se desarrolla la actividad científica y sobre las brechas y oportunidades que persisten en el sistema de Ciencia, Tecnología, Conocimiento e Innovación (CTCI).
La perspectiva territorial permite reconocer que las trayectorias de las mujeres en ciencia no se desarrollan bajo condiciones homogéneas, sino que están influenciadas por las características, capacidades y oportunidades propias de cada territorio. En este contexto, las universidades regionales cumplen un rol fundamental en la generación de conocimiento pertinente, la formación de capital humano avanzado y la ampliación de las oportunidades de participación y liderazgo de las mujeres en investigación, innovación y desarrollo científico.
Abordar la ciencia desde una perspectiva de género implica no solo aumentar la participación de mujeres, sino también avanzar en la transformación de las condiciones institucionales y culturales en que se produce conocimiento. Esto supone reconocer las particularidades territoriales, fortalecer capacidades locales y promover ecosistemas científicos más diversos, inclusivos y conectados con las necesidades y desafíos de sus comunidades.
Desde esta perspectiva, se plantea la necesidad de avanzar hacia una ciencia que incorpore el enfoque de género y la dimensión territorial como elementos sustantivos para construir un sistema de CTCI más equitativo, pertinente y capaz de contribuir al desarrollo de los territorios.

S3.2. Building a University with a Gender Perspective.

Vania Figueroa Ipinza (vania.figueroa@uautonoma.cl). CTGénero I+D+i+e, Universidad Autónoma de Chile.

There is broad consensus that incorporating a gender perspective can contribute to improving the quality of science. We also know that gender biases can affect not only the career trajectories of researchers, but also the research questions we formulate, the production and analysis of data, and the processes through which knowledge is evaluated, published, and disseminated. Why, then, is it so difficult to achieve meaningful changes in the way we conduct science?
At Universidad Autónoma de Chile, we have addressed this challenge by progressively modifying the rules and conditions that shape research activity, while developing tools to integrate sex, gender, and intersectionality into both scientific content and the processes through which knowledge is evaluated, published, and disseminated. We have also created mechanisms for public participation in defining research problems and developing solutions. Each step produced tangible progress; at the same time, however, it revealed a new dimension of the challenge.
This presentation will examine five years of efforts, challenges, and achievements in translating gender perspective from policy into scientific practice. It will consider which strategies succeeded in producing change, where the greatest resistance emerged, and why some transformations progressed considerably faster than others.
One of the principal conclusions from this process is that the effective integration of a gender perspective requires simultaneous action across all key decisions throughout the scientific cycle: who conducts research and which questions are formulated; how evidence is produced, and which forms of knowledge are recognized and legitimized; with whom knowledge is created; and which institutional structures are necessary to sustain these changes.
Rather than offering definitive solutions, this experience is an invitation to reflect collectively on how to ensure that gender perspective is no longer treated as an exceptional dimension of scientific practice, but becomes, quite simply, part of how we conduct better science.

S3.3. Rol de las sociedades científicas en la construcción de una ciencia con perspectiva de género.

Roxana Pincheira Barrera. Expresidenta SBBMCh, Profesora Titular Depto Bioquímica y Biología Molecular, Universidad de Concepción.

Las sociedades científicas desempeñan un papel que trasciende la promoción y difusión del conocimiento disciplinar. Como espacios de representación, colaboración y formación de comunidades, contribuyen a construir la cultura científica y pueden actuar como agentes de cambio hacia una ciencia más equitativa e inclusiva.Incorporar una perspectiva de género implica reconocer que las trayectorias científicas no siempre se desarrollan bajo las mismas oportunidades y condiciones, y que persisten brechas en ámbitos como participación, liderazgo, reconocimiento, acceso a redes y espacios de toma de decisiones. En este contexto, las sociedades científicas se encuentran en una posición privilegiada para visibilizar estas brechas, revisar sus propias prácticas y promover transformaciones en el ecosistema científico.Esta presentación abordará el rol de las sociedades científicas en este proceso, considerando acciones relacionadas con la representación en directorios y comités, participación en congresos y actividades científicas, acceso a posiciones de liderazgo, reconocimiento de trayectorias diversas y generación de oportunidades para nuevas generaciones. Asimismo, se analizarán experiencias y estrategias desarrolladas por sociedades científicas nacionales e internacionales, identificando avances, desafíos y oportunidades de colaboración.El desafío, sin embargo, va más allá de alcanzar una representación numérica equilibrada. Requiere avanzar hacia una cultura científica que reconozca y valore la diversidad, identifique barreras y genere condiciones equitativas para la participación, el desarrollo y el liderazgo científico. Las sociedades científicas, como organizaciones construidas por y para sus comunidades, tienen la oportunidad y responsabilidad de contribuir activamente a esta transformación.

S3.4. Ciencia Transdisciplinar: Colectivo de Mujeres Ernestina Pérez Barahona

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Background: Despite the growing participation of women in science, structural, geographical, and collaborative barriers continue to limit leadership opportunities, interdisciplinary interaction, and access to scientific networks in Chile. To address these challenges, the *Colectivo de Mujeres Ernestina Pérez Barahona (Las Ernestinas)* was established as a multidisciplinary and transdisciplinary network designed to strengthen collaboration, visibility, mutual support, and collective scientific development among women researchers.
Methods: *Las Ernestinas* originated in March 2024, when 13 women scientists met in Catapilco to discuss shared experiences, challenges, and critical events throughout their scientific careers. These discussions identified common barriers and motivated the creation of a collaborative network based on effective scientific and personal support. In May 2025, 32 women scientists participated as blood donors in a collaborative study on obesity and metabolism, consolidating the network's research-oriented activities. Subsequent meetings formally established its transdisciplinary identity. In august 2026 we are 131 members. Currently, Las Ernestinas connects researchers from diverse disciplines, institutions, career stages, and Chilean regions. Social media platforms, particularly Instagram, support scientific communication, dissemination, networking, methodological assistance, infrastructure sharing, student mobility, and collaborative research initiatives.
Results: The collaborative blood-donation initiative contributed to the completion of the LO-Ernestina project and preparation of a scientific manuscript. The network has also increased thesis supervision and co-supervision opportunities, student mobility among laboratories, and access to specialized methodologies, reagents, equipment, biological samples, infrastructure, and scientific expertise.
Discussion: A major strength of *Las Ernestinas* is its horizontal, multidisciplinary, and geographically transversal organization. Researchers from biomedical sciences, biochemistry, molecular biology, Physics, Mathematica's, Sociology, Anthropology, Design, Networks, engineering, and clinical sciences interact independently of institutional affiliation or academic seniority, facilitating complementary expertise and new scientific collaborations.
Conclusion: *Las Ernestinas* represents a scalable model for strengthening women's participation and leadership while promoting a more collaborative, and Solidary decentralized, interdisciplinary, and interconnected scientific ecosystem in Chile.

Funding: we are.

SYMPOSIUM 4
Integration of plant signalling, hormones and stress in challenging environments

Organizers: Dr. Rodrigo A. Gutiérrez Pontificia Universidad Católica y Dr. José M. Estevez, Universidad Andres Bello.

S4.1 Identification of a novel link connecting indole-3-acetamide with abscisic acid biosynthesis and signaling.

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Plants regulate their developmental programs and their responses to environmental changes through a complex network of small signaling compounds, known as phytohormones. The role of auxins in promoting plant growth has been extensively investigated. Furthermore, previous studies have demonstrated that the accumulation of indole-3-acetamide (IAM), an auxin precursor, results in the suppression of plant growth, particularly primary root elongation. This observation led to the hypothesis that IAM or an IAM derivative exerts negative growth regulatory effects. However, the molecular mechanism by which IAM inhibits plant growth remains largely unelucidated. To gain deeper insight into the molecular mode of action of IAM, we conducted a comprehensive genome-wide association study (GWAS) using a highly diverse collection of 166 wild Arabidopsis accessions from the Iberian Peninsula. Consequently, we identified several genomic regions associated with a reduced response to IAM under controlled *in vitro* conditions, which included *ABA3* and *GA2ox2* as candidate genes. Sequence analyses, transcriptomics studies, and comparison of three-dimensional models generated for *ABA3* proteins encoded by the reference and identified minor frequence allele for the gene identified in the collection of wild accessions suggested that IAM-triggered inhibition of primary root elongation is closely associated with the formation of abscisic acid (ABA) in *Arabidopsis thaliana* seedlings. Finally, physiological characterization of mutants for those candidate genes further corroborated that IAM activates ABA signaling. Our findings indicate that IAM is intricately associated with ABA biosynthesis and signaling, implying an independent function for IAM as a signaling molecule in the crosstalk of plant hormones.

S4.2 Nitrate-induced Endoreduplication Reprograms the Transcriptome for Cell Differentiation and Expansion in *Arabidopsis thaliana* Cotyledons.

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Introduction: Nitrate is a nutrient and a potent signal that induces cell expansion to promote plant growth. Leaf organ growth relies on a highly coordinated balance between cell number and cell expansion. While cell number is governed by the mitotic cell cycle, cell expansion and differentiation are linked to endoreduplication -a modified cell cycle without division that increases nuclear DNA content- increasing cell size and ploidy levels. However, how endoreduplication reprograms genome-wide gene expression and how it relates to cell differentiation and nutrient availability remains poorly understood.

Materials and Methods: To address these questions, we generated a ploidy-resolved transcriptome from growing cotyledons using a flow cytometry (FANS) strategy coupled to RNA-seq.

Results: Our transcriptome profile data revealed a developmental trajectory for epidermal cells transitioning from a proliferative state at lower ploidies (2C/4C) towards an endoreduplicated and differentiated population at higher ploidies (8C/16C). Within this trajectory, we identified key transcription factors (TF) that regulate epidermal cell differentiation, particularly driving the transition of stomatal-lineage ground cells (SLGCs) into pavement cells. Reporter lines showed that these TFs accumulate in SLGCs and developing pavement cells. Genetic analyses further showed that these TFs are necessary for cotyledon growth, orchestrating a fine-tuned regulation of SLGCs proliferation and expansion.

Discussion: These phenotypes align with the bimodal identity of SLGCs, which can either divide to increase stomata number or differentiate into pavement cells. Our results identified a regulatory module that integrates the cell cycle and endoreduplication with nutrient availability and epidermal developmental fate.

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S4.3. Photoreceptors and plant immunity

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Under high density conditions plants prioritize elongation growth and reduce the investment in chemical defense. These responses increase plant competitive ability but may have negative consequences for crop production, reducing the harvest index and increasing susceptibility to pests and pathogens. Jasmonates play a key role in the signaling mechanisms that plants use to adjust their morphology and defense strategies. In turn, jasmonate metabolism and signaling are finely regulated by the photoreceptors phyB and UVR8. phyB is a positive regulator of jasmonate signaling and plant antiherbivore defense. Our studies have shown that inactivation of phyB by competition signals in dense canopies (low ratios of red to far-red radiation,

R:FR) promotes the catabolism of jasmonates and reduces plant defense. In contrast, ultraviolet (UV) radiation, which is associated with open canopies and a low risk of competition for light, promotes jasmonate responses that increase plant resistance to insect herbivores and certain pathogens. I will discuss advances in our understanding of the mechanisms that connect photoreceptors with jasmonate signaling and discuss the benefits that may result from modifying these connections to increase crop yield and health.

S4.4. Redox networks driven by gasotransmitters regulate plant nitrate responses.

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Introduction: Improving nitrogen use efficiency (NUE) is a major challenge for sustainable agriculture. Beyond its nutritional role, nitrate acts as a signaling molecule that triggers the Primary Nitrate Response (PNR), a rapid transcriptional and metabolic reprogramming that enables plants to adjust to changes in nitrogen availability. Increasing evidence indicates that redox signaling constitutes a key regulatory layer in this process. Nitric oxide (NO) and hydrogen sulfide (H_2S) are important gasotransmitters that can modulate protein function through S-nitrosation and persulfidation, respectively, suggesting interconnected cysteine-based redox switches in cell signaling. The aim of this work was to investigate the role of H_2S-dependent persulfidation in the nitrate response and determine whether this redox regulation is spatially organized between roots and shoots.
Materials and Methods: *Arabidopsis thaliana* seedlings were treated with nitrate, and persulfidated proteins were enriched using a dimedone-switch approach followed by quantitative proteomic analysis. Nitrate-responsive persulfidation patterns were analyzed separately in roots and shoots to identify differential and tissue-specific targets and associated biological processes.
Results: Nitrate induced extensive remodeling of the persulfidome, with distinct responses in roots and shoots. Differentially persulfidated proteins were associated with nitrogen assimilation, carbon and energy metabolism, redox homeostasis, and proteostasis. Although a subset of nitrate-responsive proteins was shared between tissues, a substantial fraction showed root- or shoot-specific regulation, revealing a strongly compartmentalized persulfidation response.
Discussion: These results support a model in which H_2S-dependent persulfidation contributes to the spatial coordination of nitrate-induced metabolic reprogramming. Together with the established role of NO, our findings suggest that NO and H_2S may form an integrated cysteine-based redox network linking nitrate perception with metabolic adaptation across plant tissues, providing new insights into redox regulation of nitrate responses and NUE.

Acknowledgment: ANID-FONDECYT 1261744

ORAL SESSION 1

OS1.1 FchDOF1 transactivates the *FchPL* promoter and contributes to cell wall disassembly required for softening of *Fragaria chiloensis* fruit.

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Introduction: Transcription factors (TFs) play central roles as master regulators of biological events. Fruit softening, due to cell wall (CW) disassembly, needs the coordinated spatiotemporal action of CW modifying enzymes and therefore transcriptional regulation is required. *Fragaria chiloensis* is a native fruit that softens fastly during ripening and the participation of *FchPL FchPG, FchEXP2/5* and *FchXTH1* has been reported. Dof (DNA-binding with one finger) TFs recognize AAAG cis-elements in target promoters. DOFs have been functionally linked to softening in other fruits, but not in *F. chiloensis*. This study characterizes FchDOF1 and examines its regulatory role on softening-related genes.
Materials and Methods: Phylogenetic studies, domain analysis and protein modeling were performed. *Cis*-regulatory elements were searched in CW-related gene promoters using PlantPAN. Transactivation activity of FchDOF1 on CW promoters was evaluated using dual-luciferase assays. Recombinant FchDOF1-His-tag protein was purified for EMSA. To confirm functionality, *FchDOF1* was transiently overexpressed (OE) or silenced (RNAi) in C2-stage *F. chiloensis* fruit using pK7WG2 and pRNAi-GG vectors, respectively. The expression of CW genes was analyzed in transformed fruit by RT-qPCR.
Results: FchDOF1 belongs to group C2.2 and clusters with FaDOF2, a TF reported to be involved in aroma biosynthesis, color development and sugar metabolism in *F. x ananassa*, but not in softening. Its Dof domain contains all key features for functionality and closely matches that structure of CDF1 crystal (RMSD 0.52 Å). Dof *cis*-elements were identified in the five CW gene promoters tested, but only *FchPL* was significantly transactivated; EMSA confirmed sequence-specific binding.

FchDOF1 overexpression increased *FchPL*, *FchPG, FchEXP5* and *FchXTH1* transcripts; and silencing reduced *FchPL*, *FchPG* and *FchEXP5*, meanwhile *FchEXP2* and *FchRGL* were unaffected.
Discussion: The results confirm FchDOF1 as a structurally conserved transcriptional regulator that directly targets *FchPL* and modulates a subset of CW-related genes during softening of *F. chiloensis* fruit.

Acknowledgment: FONDECYT 1251538

OS1.2 PHR1-dependent transcriptional control of root hair growth under concurrent phosphate limitation and salinity in Arabidopsis.
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Introduction: Plants often encounter multiple abiotic constraints simultaneously, yet the regulatory mechanisms integrating nutrient limitation with salinity remain poorly resolved. In Arabidopsis thaliana, root hairs contribute to nutrient acquisition and rapidly adjust to changing soil conditions.
The aim of this study was to determine how phosphate (Pi) starvation signaling coordinates root hair growth under combined low-Pi and salt stress, focusing on the transcription factors PHR1 and PHL1.
Materials and Methods: Root hair phenotypes were evaluated in wild-type, phr1, phl1, and double-mutant plants under individual and combined stress treatments. Time-resolved RNA-seq profiles collected at 6, 12, and 24 h from wild-type, phr1, and phl1 seedlings were analyzed using differential expression and network inference. Candidate regulators were further examined through mutant phenotyping and promoter motif analysis.
Results: Loss of PHR1, unlike loss of PHL1, impaired the root hair elongation response under combined low-Pi and salinity, indicating a predominant role for PHR1. Network analysis highlighted HB5, HB40, and OBP4, together with auxin-related genes, as candidate downstream regulators. hb5 and hb40 mutants displayed enhanced sensitivity to salinity, whereas obp4 reproduced key features of the phr1 root hair phenotype under combined stress. OBP4 provides a potential connection to abscisic acid signaling and RSL2, a central regulator of root hair elongation. PHR1-binding motifs were also detected in the promoters of several candidate genes.
Discussion: These results support a model in which PHR1 acts as a regulatory hub linking phosphate status with salt-responsive transcriptional pathways to shape root hair growth. The proposed network identifies candidate nodes for future functional validation and provides a framework for understanding how plants maintain nutrient acquisition under challenging soil conditions.

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OS1.3 Salt-responsive alternative splicing modifies *HHO3*/*NIGT1.1* isoforms balance during root adaptation to salinity in *Arabidopsis thaliana*.
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Introduction: Soil salinity is a major environmental constraint limiting plant growth and agricultural productivity worldwide. Although transcriptional responses have been extensively investigated, the contribution of alternative splicing (AS) to root

adaptation and the functional consequences of salt-responsive splicing events remain largely unexplored. Here, we integrated transcriptomics, phenomics, molecular biology and microscopy to identify and characterize a candidate gene regulated by AS in *Arabidopsis* roots.
Materials and Methods: We performed RNA-seq of roots exposed to 150 mM NaCl for 2, 4 and 24 h to explore the temporal dynamics of AS. Integration with public transcriptomic and long-read Iso-Seq data led to the selection of the transcription factor *NIGT1.1*/*HHO3*. Splicing was validated by RT-PCR and RT-qPCR, while *hho3* knockdown mutants were characterized under salinity using conventional, multivariate and automated time-resolved root phenotyping. HHO3 isoform localization was assessed by confocal microscopy. To explore upstream and downstream regulation we built regulatory networks with RIP-seq, iCLIP and co-expression data.
Results: RNA-seq identified 405 differentially alternatively spliced genes presenting marked temporal dynamic. *HHO3* displayed a salt-responsive intron retention with the resulting *HHO3.2* transcript decreasing under salinity conditions without changes in overall *HHO3* transcript accumulation. This event was predicted to truncate HHO3, altering its Myb DNA-binding domain. *hho3-2* mutant showed a distinct root architecture under salinity, characterized by increased lateral root growth. Canonical HHO3.1 localized predominantly to the nucleus, while HHO3.2 accumulated mainly in the cytoplasm. Finally, network analyses and RT-qPCR validation identified candidate *HHO3* targets associated with root development and cytokinin signaling, and five splicing factors that potentially bind to *HHO3*.
Discussion: Together, our results position *HHO3* as a potential link between salt-responsive AS and root architectural remodeling, supporting a model in which changes in *HHO3* isoform balance modulates transcription factor activity during root adaptation to salinity.

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OS1.4 Exogenous Trehalose application enhances thermotolerance in tomato plants via downregulation of the Glutamyl-tRNA(Gln) amidotransferase gene.
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Introduction: Global warming and extreme temperature fluctuations threaten tomato (*Solanum lycopersicum*) productivity. Trehalose, a disaccharide, mitigates abiotic stress by stabilizing biomolecules and membranes, improving water-use efficiency, and acting as a signaling molecule. This study evaluated the protective effect of exogenous trehalose against heat stress (HS) in tomato cv. Micro-Tom, using transcriptomics to identify candidate genes for CRISPR/Cas9 editing to generate HS-tolerant lines.
Materials and Methods: Four experimental groups were established: plants were treated with either 10 mM trehalose or water and subjected to either normal conditions (NS) or a 7-day heat wave (25 °C at night, 42 °C at the peak for 4 h). Leaf sampling occurred every 48 h: before HS (T0), during the heat peak (T1, T2, T3), and one day after HS (T4). Physiological and transcriptomic analyses were performed to evaluate the protective effect of trehalose compared to the water control.
Results: Under HS, trehalose-treated plants exhibited improved agronomic traits, including increased fruit biomass, a lower proportion of open stomata, and a rapid induction of *SlHSFA2a*, compared to water-treated controls. Transcriptomic data showed differential gene expression between treatments, notably during T1 and T3. Specifically, the Glutamyl-tRNA(Gln) amidotransferase (Solyc12g070090.1) gene was downregulated in the trehalose-HS group and upregulated in the control-HS group.
Discussion: To elucidate its role as a putative negative regulator of thermotolerance, a targeted gene-editing strategy using the CRISPR/Cas9 system is underway. Mutating this gene is expected to confer enhanced HS resistance by preserving the accumulation of N-acylethanolamines (NAEs), lipids that stabilize membranes and act as molecular signals to activate Heat Shock Proteins (HSPs).

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OS1.5 SCL28 regulates epidermal ploidy to control nitrate-mediated shoot growth.
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Introduction: Nitrate, one of the main sources of nitrogen, functions not only as a nutrient but also as a signaling molecule that regulates shoot growth plasticity by modulating processes such as cell expansion. Nitrate availability determines shoot size through compensatory effects on endoreplication and cell division. However, how nitrate coordinates these processes with cell expansion to regulate shoot growth remains poorly understood.
Methodology: To dissect cell type–specific transcriptional programs underlying this response, we applied single-nucleus RNA sequencing (snRNA-seq) to *Arabidopsis thaliana* shoots grown under contrasting nitrate conditions. We further combined epidermal cell trajectory inference with molecular genetic approaches to investigate the contribution of endoreplication to nitrate-mediated shoot growth.
Results: Using the 10x Genomics platform, we obtained 27,672 high-quality single-nucleus transcriptomes covering more than 23,000 genes and identified 12 distinct cell types within cotyledon tissues. Trajectory inference of epidermal cell differentiation uncovered previously unrecognized intermediate states during pavement cell development. These intermediate states were associated with endoreplication and ploidy transitions linked to cell expansion. Our analysis revealed that nitrate responses are highly cell type specific, with 2,998 genes differentially expressed across the identified cell populations. By integrating chromatin accessibility data (ATAC-seq) with single-nucleus transcriptomics, we reconstructed cell type–specific gene regulatory networks. This approach identified SCARECROW-LIKE28 (SCL28) as a candidate regulator of epidermal cell differentiation and growth. Functional analyses demonstrated that SCL28 plays a key role in nitrate-mediated shoot growth, as loss-of-function mutants showed impaired nitrate-induced epidermal cell expansion and reduced cotyledon growth.
Discussion: Together, our results provide a framework linking nutrient signaling to cell type–specific gene regulatory networks and identify epidermal ploidy as a critical regulatory layer controlling plant organ growth.

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OS1.6 Nitric oxide sustains Lateral Root formation and water status under moderate water deficit in tomato (*Solanum lycopersicum*).
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Introduction: Drought is characterized by a reduction in water availability resulting from decreasing soil moisture, which severely limits crop growth and overall yield. An adaptive mechanism in plants facing this stress is the modulation of lateral root formation (LRf). Under moderate water deficit (mWD) conditions, LRf is stimulated in some crops, including tomato (*Solanum lycopersicum*). Within this signaling framework, nitric oxide (NO) represents a key regulatory candidate in this process: its endogenous levels increase during WD, and under well-watered conditions, it actively promotes root organogenesis. However, the role of NO in root plasticity under water stress remains unclear.
Materials and Methods: To evaluate the effect of NO on subsequent LR development, seeds from three distinct tomato varieties (*Solanum lycopersicum* cv. Moneymaker, var. Rosado and cv. M82) were subjected to seed priming with sodium nitroprusside (SNP, a known NO donor), 2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazoline-1-oxyl-3-oxide (cPTIO, a NO scavenger) or a combination of both treatments. Seeds were sown in a soil substrate at 100% saturating water (SW). Then, they were maintained under well-watered conditions (80-90% SW) or until reaching 55-65% SW, which moderate water deficit was defined. LR primordia and emerged LR events were quantified in one-month-old primary root seedlings.
Results: SNP application induces LR primordia only in cv. MoneyMaker and var. Rosado under optimal irrigation. This feature was reversed in the NO scavenger treatment, confirming that NO participates in LR formation. Under mWD, NO sustained LR primordia induction and mitigates the water potential decline caused by this condition.
Discussion: Together, these results support NO mediates LR development and plant water status under moderate water deficit in tomato plant. The variety-dependent response supports NO biosynthesis/signaling as a potential determinant of adaptive root plasticity in tomato under water stress.

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OS1.7 A bZIP Transcription Factor Orchestrates Genotype-Specific Regulatory Hubs involved in Nitrogen and Water Deficit Signals integration in *Solanum lycopersicum.*

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Introduction: Water (W) and Nitrogen (N) availability are primary factors influencing plant growth and productivity. To mitigate yield losses induced by W-deficit (WD), intensive agriculture relies on N-rich fertilizers, driving significant environmental pollution. Understanding how plants integrate WD and N signals are crucial for advancing sustainable practices. In *Arabidopsis thaliana*, the Transcription Factor (TF) NIN-LIKE PROTEIN 7 integrates NxWD responses, balancing the trade-off between growth and WD resilience. However, these mechanisms remain underexplored in relevant crop species. We propose characterize how N availability modulates WD responses in tomato (*Solanum lycopersicum*), a globally significant crop, to uncover species-specific strategies for maintaining growth and stress response.

Material and Methods: We evaluated the *in vitro* performance of 10 tomato cultivars and *Solanum pimpinellifolium* under low (1 mM) and high (10 mM) nitrate concentrations during mannitol-induced osmotic stress. Phenotypic profiling across developmental, detoxification, and metabolic traits revealed distinct, genotype-dependent response patterns. From these, four representative cultivars were selected for soil-based experiments to analyze phenotypic and transcriptional responses to genotype-specific NxWD crosstalk, aiming to identify key TFs co-regulating both signals.

Results: We identified significant genotype-dependent differences in phenotypic and transcriptional reprogramming under varying N in WD response. Co-expression analysis revealed both global and genotype-specific gene expression modules. Specifically, N availability altered stomatal, water transport, and nutrient metabolism pathways in a genotype-dependent manner to modulate WD responses. Using gene regulatory networks, we identified a candidate bZIP TF that control N-, and WD-responsive pathways. Expression profiling confirmed that N availability regulates both this TF and its target genes. Finally, DAP-seq validated direct binding of the bZIP to its targets, which include downstream TFs, establishing it as a central regulator of genotype-specific N×WD integration.

Discussion: These findings provide fundamental insights into the transcriptional architecture underlying N×WD plasticity and establish a strategic foundation for breeding more climate-resilient tomato cultivars.

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OS1.8 Beyond model plants: Genome-wide mapping and validation of drought regulatory networks in Tomato using the TARGET assay.

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Introduction: Understanding the interactions between transcription factors (TFs) and their target genes is essential for constructing gene regulatory networks (GRNs) that help us understand the regulatory circuit behind environmental adaptations. Traditionally, techniques used to evaluate these interactions are optimized for model organisms, require considerable time, or lack cellular context. Herein, we have established the TARGET (Transient Assay Reporting Genome-wide Effects of Transcription Factors) assay, which uses transient cell transfection to identify direct targets at genome scale of a TF within a short timeframe. In this study, we used such assay in *Solanum lycopersicum* (tomato) and evaluated three members of the bZIP transcription factor family, known as ABFs, which are known for their role in drought tolerance in *Arabidopsis thaliana* but remain poorly characterized at the genomic level in tomato.

Materials and Methods: Protoplasts from *Solanum lycopersicum* cv. Moneymaker were isolated and transfected with the pBeaconGFP_GR vector, which contains the TF fused to the glucocorticoid receptor and a GFP reporter. Empty vectors served as controls, and cells were treated with cycloheximide followed by dexamethasone. Positive events were cell-sorted for RNA extraction, RNA sequencing (RNA-seq), and bioinformatic analysis.

Results: We identified direct targets of SlABF5 (Solyc04g078840), SlABF7 (Solyc10g050210), and SlABF10 (Solyc11g044560). SlABF5 and SlABF10 targets were enriched in signaling and drought-response processes, whereas SlABF7 targets were associated with salicylic acid pathways. Collectively, their targets significantly overlapped with drought-responsive genes in tomato, accounting for one-third of the response. SlABF10 showed the broadest regulatory contribution,

targeting the highest number of genes and downstream TFs. SlABF5 downstream TFs included cuticular wax biosynthesis and stomatal number regulation. SlABF5 results were independently validated by DAP-seq, suggesting it may act as a master regulator.
Discussion: Our findings demonstrate the value of TARGET for characterizing poorly studied TFs and support its broader application to other regulators and crop species.

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ORAL SESSION 2

OS2.1 Short and long-term signaling triggered by *Helicobacter pylori* infection in gastric cells.
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Abstract: *Helicobacter pylori* infection has been associated with the etiology of intestinal-type gastric cancer via different virulence factors. Previously, we described that *H. pylori* infection promotes stabilization of HIF-1α (hypoxia-inducible factor 1α), a transcription factor associated with tumor progression and metastasis. Our recent studies show that *H. pylori*-dependent HIF-1α stabilization is followed by short-term and long-term signaling events in gastric cells. At early time-points, *H. pylori* promotes the formation of a β-catenin/HIF-1α protein complex associated with the induction of target genes involved in cellular adaptation and tumor invasion. In the long-term, *H. pylori* infection induces the expression of ALS2, a guanine exchange factor that activates the endosomal GTPase Rab5. In turn, Rab5 promotes endosomal sequestration of the so-called "β-catenin destruction complex", allowing for stabilization and nuclear translocation of β-catenin, thereby increasing the expression of TCF/Lef-target genes. The impact of these events on gastric cancer development and progression remains to be defined.

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OS2.2 A DHODH R135C Variant Promotes Mitochondrial Dysfunction in Cytokine-Stimulated Cardiomyocytes.
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Introduction: Chagas disease (CD), caused by Trypanosoma cruzi, affects nearly 6 million people worldwide, and approximately 30% of infected individuals develop chronic Chagas cardiomyopathy (CCC). CCC is characterized by persistent inflammation, myocardial fibrosis, and mitochondrial dysfunction. A predominantly Th1-mediated response, involving cytokines such as IFN-γ and TNF-α, may contribute to cardiac damage by impairing mitochondrial function. Genetic studies suggest that host polymorphisms, including variants in the DHODH gene, may influence susceptibility to CCC.
Materials and Methods: AC16 cardiomyocytes and THP-1 monocytic leukemia cells, either wild-type or carrying the heterozygous DHODH R135C variant, were stimulated with IFN-γ and TNF-α. Mitochondrial morphology and membrane potential were evaluated in AC16 cells, together with the expression of proteins involved in mitochondrial fusion and biogenesis. THP-1 cells were differentiated into macrophage-like cells using PMA, and polarization toward an M1-like phenotype was assessed by HLA-DR expression. Conditioned-medium experiments were performed to evaluate the effects of THP-1-derived cell secretomes on AC16 cardiomyocytes.

Results: AC16 cardiomyocytes carrying the heterozygous DHODH R135C variant showed increased susceptibility to cytokine-induced mitochondrial dysfunction, including enhanced mitochondrial fragmentation and reduced expression of proteins involved in mitochondrial fusion and biogenesis. IFN-γ and TNF-α induced an M1-like phenotype in THP-1-derived cells; however, no differences in the proportion of HLA-DR-positive cells were observed between wild-type and DHODH-mutant clones. The secretome of DHODH-mutant THP-1-derived cells caused greater mitochondrial membrane depolarization in AC16 cardiomyocytes than that of wild-type cells.
Discussion: These findings suggest that the DHODH R135C variant increases cardiomyocyte vulnerability to inflammatory stress and may alter the secretome of THP-1-derived macrophage-like cells. This altered cell-to-cell communication could contribute to mitochondrial dysfunction and cardiac injury in CCC. Further studies are needed to determine whether the mutation promotes a more inflammatory phenotype and to identify the soluble mediators involved.

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OS2.3 Molecular Profiling and Functional Drug Screening Reveal Therapeutic Opportunities in Gallbladder Cancer.
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Introduction: Gallbladder cancer (GBC) is a highly lethal malignancy with limited therapeutic options, highlighting the need for novel treatment strategies. Precision medicine may provide new opportunities by identifying molecular alterations and genotype-specific therapeutic vulnerabilities. The aim of this study was to identify potential therapeutic opportunities in GBC by integrating tumor molecular profiling with functional drug screening.
Material and Methods: Molecular profiling of 67 tumor samples was performed to identify somatic driver alterations, copy-number alterations, tumor mutational burden (TMB), and microsatellite status. Based on the recurrent alteration of *ARID1A*, a tumor suppressor of the SWI/SNF chromatin-remodeling complex, *ARID1A* knockout (KO) and wild-type (WT) GB-d1 GBC cells were used for functional drug screening. A library of 160 epigenetic compounds was screened, and 37 compounds showing differential responses were selected for further evaluation. Drug sensitivity was evaluated using MTS viability assays, and IC50 values were estimated for selected compounds.
Results: *ARID1A* alterations were detected in 16/67 (23.9%) tumors. Among evaluable samples, 18/61 (29.5%) showed high TMB, whereas all were microsatellite stable. Additional potentially relevant alterations included *ERBB2* amplification. Functional screening identified genotype-dependent drug responses. *ARID1A*-KO cells showed increased sensitivity to AZ5704 (IC50: 1.534 vs. 9.226 μM in WT), triptolide (0.023 vs. 0.098 μM), and GN44028 (0.944 vs. 2.898 μM). Conversely, ARID1A loss conferred resistance to BIX-01294 (0.829 vs. 0.017 μM) and I-BRD9 (2.106 vs. 0.329 μM).
Discussion: Molecular profiling revealed potentially targetable subgroups in GBC. Furthermore, functional screening demonstrated that *ARID1A* loss generates specific pharmacological vulnerabilities. Integrating genomic characterization with genotype-guided drug screening may provide a strategy to identify precision medicine opportunities for GBC.

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OS2.4 Mitochondrial DNA as a diagnostic and prognostic biomarker for thyroid cancer in a chilean patient cohort.
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Introduction: Thyroid cancer (TC) is the most prevalent endocrine neoplasia, and its increasing incidence is largely attributed to overdiagnosis and molecular heterogeneity, highlighting the need for biomarkers to improve diagnosis and risk stratification. Mitochondrial DNA (mtDNA) is susceptible to mutations, copy number (mtDNA-CN) alterations, and large-scale deletions, providing a potential readout of mitochondrial dysfunction, metabolic remodeling, and genomic instability. The aim of this study is to evaluate mtDNA mutational profiles, mtDNA-CN, and deletions in a Chilean TC cohort and their association with clinical-pathological characteristics for diagnostic and prognostic purposes.
Materials and Methods: Paired samples, tumor and adjacent tissues, and plasma were collected from 15 TC patients. Tissues were sequenced via Nanopore to identify somatic variants.mtDNA-CN was quantified by qPCR and dPCR across four genes (D-Loop, ND1, ND4, ND5). Five cancer-associated deletions (4,977-bp; 3,895-bp; 7,984-bp; 7,436-bp; 2,851-bp) were

detected by nested PCR; deletion heteroplasmy was quantified by qPCR. Data was associated with patient clinical-pathological characteristics.
Results: A bioinformatic pipeline was developed for data analysis (MytoTyro). 17 somatic mtDNA variants were identified that primarily affected Complex I (53%). Based on their functional effect, most mutations in this complex were nonsense and missense. Additionally, the highest mutational burden was found in patients with intermediate/high ATA risk. Tumor tissues and plasma samples exhibited an increased mtDNA-CN compared to adjacent tissue or controls. Among the analyzed regions, D-loop showed the greatest abundance, while ND4 levels were consistently the lowest, suggesting mtDNA fragmentation or deletions. Consistent with this, deletions of 4977-bp and 3895-bp were the most frequent, with heteroplasmy ranging from 17% to 67%, with higher levels in advanced-stage tumors.
Discussion: These findings contribute to a distinctive mitochondrial genomic signature associated with TC risk and disease progression, supporting a potential link between mitochondrial genomic instability and tumor aggressiveness.

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OS2.5 JC polyomavirus, bacterial cofactors, and bile acid interactions in colorectal cancer.
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Introduction: Colorectal cancer (CRC) is a leading cause of cancer-related mortality worldwide, with rising incidence in Chile, particularly among young adults. Beyond classical risk factors, emerging evidence implicates JC polyomavirus (JCPyV), bacterial genotoxins, and secondary bile acids such as deoxycholic acid (DCA) in promoting genomic instability and tumor progression. Our group has investigated these viral–microbial–metabolic interactions to better understand their contribution to CRC.
Matherials and Methods: Formalin-fixed paraffin-embedded colon lesions were analyzed by PCR for JCPyV large T antigen (AgT) and bile acid–producing bacteria (*C. scindens, P. hiranonis*). Colon cancer cell lines (SW480, HT29) were exposed to DCA, ursodeoxycholic acid (UDCA), and transfected with JCPyV AgT, alone or in combination with *Campylobacter jejuni* lysates expressing cytolethal distending toxin (CDT). DNA damage was assessed by γH2AX immunofluorescence, comet assay, and Western blot, while NRF2 activation was evaluated by luciferase reporter assays.
Results: AgT-JCPyV was detected in 21% of proliferative lesions, consistent with its association with CRC risk. Generic polyomavirus positivity reached 43%. In vitro, co-exposure of colon cells to JCPyV AgT and CDT markedly increased γH2AX expression and DNA damage compared with controls. DCA treatment induced oxidative stress and DNA damage, while UDCA significantly activated NRF2 and reduced γH2AX levels, indicating a protective effect against DCA- and JCPyV-induced damage.
Discussion: These findings support a model in which CRC progression involves a complex interplay between viral infection, bacterial genotoxins, and bile acid–mediated signaling. The co-presence of JCPyV and bacterial factors enhances DNA damage, while UDCA emerges as a chemopreventive modulator by attenuating oxidative stress and genomic instability. This integrative approach underscores the importance of considering viral–microbial–metabolic interactions in CRC pathogenesis and highlights potential avenues for prevention and intervention.uy

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OS2.6 An abortive EBV lytic program driven by benzo[a]pyrene in preneoplastic lung epithelium.
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Introduction: Epstein-Barr virus (EBV) is an oncogenic herpesvirus associated with epithelial malignancies. Its reactivation from latency is driven by the immediate-early genes BZLF1 and BRLF1, transcribed from the Zp and Rp promoters, respectively. Benzo[a]pyrene (BaP), a tobacco smoke carcinogen, activates the aryl hydrocarbon receptor (AhR) and may

cooperate with EBV in the respiratory cells. We therefore characterized the EBV lytic cycle in BaP-exposed lung epithelial cells.
Materials and Methods: BEAS-2B lung epithelial cells were chronically exposed to low doses of BaP and characterized by viability, clonogenic and anchorage-independent growth assays, RT-qPCR, RNA-seq and protein arrays. After infection with Akata-derived EBV, the lytic cycle was assessed by immunofluorescence, and viral genome by qPCR. Rp and Zp regulation was evaluated by dual-luciferase reporter assays.
Results: Chronic BaP exposure activated the DNA damage response and induced dose-dependent transcriptome remodeling consistent with an early preneoplastic state, without compromising viability or inducing full transformation. BaP-treated cells remained susceptible to EBV infection. BaP did not affect viral genome persistence but increased BRLF1, BHRF1 and EBER1 transcript levels, and selectively activated Rp in a dose-dependent manner, leaving Zp unresponsive.
Discussion: These findings indicate that BaP modulates EBV transcription in the lung epithelium through an Rp-restricted, consistent with an abortive rather than a complete lytic program. This selective activation could promote genomic instability during preneoplastic progression, providing a model of cooperation between environmental carcinogens and EBV in lung carcinogenesis.

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OS2.7 Epigenetic modulation of macrophage polarization in colorectal cancer.
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Introduction: Colorectal cancer (CRC) is a major cause of cancer-related morbidity and mortality worldwide. Tumor microenvironment contains abundant immune cells, including macrophages with high functional plasticity. Depending on environmental signals, macrophages can acquire pro-inflammatory M1 phenotypes with antitumor activity or immunosuppressive M2 phenotypes that support tumor progression. Signal transducer and activator of transcription 3 (STAT3), activated in CRC, contributes to M2 polarization. Histone deacetylase 6 (HDAC6) inhibition may modulate STAT3 signaling and represent a strategy to reprogram macrophage polarization. This study evaluated whether selective HDAC6 inhibition modulates macrophage polarization through STAT3 suppression and whether macrophage-conditioned medium affects gene expression in CRC cells.
Materials and Methods: THP-1 monocytes were differentiated into macrophages with phorbol 12-myristate 13-acetate (PMA) and polarized M1 or M2 phenotypes. Cells were treated with the selective HDAC6 inhibitor Nexturastat A (NextA). HDAC6 activity, STAT3 phosphorylation, and macrophage polarization markers were assessed by Western blot, RT-qPCR, flow cytometry, and immunofluorescence. HCT-116 cells were subsequently exposed to conditioned medium from polarized macrophages with or without NextA, and genes associated with tumor proliferation and migration were analyzed by RT-qPCR.
Results: NextA treatment increased α-tubulin acetylation and reduced STAT3 phosphorylation without altering total STAT3 levels, confirming HDAC6 inhibition and modulation of STAT3 signaling. NextA also showed a trend toward increased M1-associated markers and decreased M2-associated markers, suggesting partial macrophage reprogramming. Furthermore, conditioned medium from NextA-treated macrophages modified the expression of genes related to tumor progression in HCT-116 cells, indicating an indirect effect of macrophage modulation on CRC cell behavior.
Discussion: These findings suggest that HDAC6 inhibition attenuates STAT3 activation and may promote an antitumor macrophage phenotype. Although changes in polarization markers were modest, the effects on CRC cells support targeting the HDAC6/STAT3 axis as a potential strategy to modulate macrophage function within the CRC microenvironment. Further studies are required to define the underlying mechanisms and therapeutic potential.

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OS2.8 Functional loss of TET enzymes reveals their critical role in controlling the epigenetic landscape and heterochromatin function in mouse embryonic stem cells.
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Introduction: Epigenetic modifications, like DNA methylation (5mC), are essential for genome stability and regulation of both gene and transposable elements (TEs). 5mC is catalyzed by DNA methyltransferases (DNMTs) and reversed by Ten-Eleven Translocation (TET) dioxygenases. Dysfunction of TET enzymes leads to profound and time-dependent epigenetic and transcriptional changes. Our research aims to elucidate the molecular mechanism by which TET depletion affects TE and gene expression patterns.
Methodology: We used mouse embryonic stem cells (mESCs) carrying an inducible genetic system that yields a triple TET1/2/3 knockout (*Tet*-iTKO) to assess the role of TET-enzymes on transcription and chromatin features through RNA-seq/RT-qPCR and 6-base sequencing, respectively. Binding of chromatin-associated proteins, epigenetic regulators and histone marks were interrogated through ChIP-seq/ChIP-qPCR. These different approaches unveiled the TET dependent epigenetic landscape on mESCs.
Results: TET-loss-of-function led to marked transcriptional changes with predominant upregulation of genes and TEs. We found that activated gene clusters frequently contained TEs with elevated expressions, suggesting a regulatory crosstalk between them. Moreover, TE-families such as MERVL and L1 displayed a dependence on TET-proteins for proper transcriptional control. We determined the changes in 5mC and association with transcriptional changes. We found that many upregulated TEs in Tet-iTKO mESC were reactivated from heterochromatin, accompanied by changes in the distribution of epigenetic regulators at specific locus of genes and repetitive regions, indicating the dysfunction of heterochromatin when TET-functions are altered, as has been observed in different cancers where TET genes are mutated.
Discussion: Our findings highlight the intricate link between TET activity, TE regulation, chromatin organization and the role these enzymes play at maintaining cellular identity. This work provides new perspectives on the epigenetic control of genome integrity and gene expression, underscoring the potential role of TEs in the etiology of epigenetic disorders.

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ORAL SESSION 3

OS3.1 Functional characterization of human acylaminoacyl-peptidase (APEH) variants designed through integration of population genomics and protein language models.

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Introduction: Human acylaminoacyl-peptidase (E.C. 3.4.19.1; APEH) is a serine protease composed of an N-terminal βpropeller domain and a C-terminal catalytic domain, involved in proteostasis and oxidative stress responses, with emerging links to neurodegenerative disorders. While there are no genome-wide significant disease-associations for APEH in genome-wide association studies (GWAS), we hypothesize that functionally relevant variation exists but remains cryptic within population datasets and can be uncovered using AI-based computational approaches.
Materials and Methods: Single-residue APEH variants were curated from gnomAD (allele frequency $\geq 10^{-5}$), and protein language models (PLMs) were used to estimate mutational permissibility by evaluating all 19 possible amino acid substitutions at each residue. Twelve selected mutants, along with isolated β-propeller and catalytic domains, were expressed as His-tagged proteins in *E. coli*. Following solubility assessment, activity was measured in cell extracts
Results: The mutational landscape revealed clusters of non-permissive regions together with isolated low-permissibility positions across the protein sequence. E167A, G508R, and G598A showed reduced activity, while R538C was inactive. In contrast, T665A and R610W exhibited increased activity relative to wild type. All active variants remained sensitive to the covalent inhibitor dichlorvos, and the isolated catalytic domain lacked detectable activity.
Discussion: PLM-derived permissibility, combined with population variation, enabled prioritization of relevant mutations. Sensitivity to dichlorvos supports preservation of the catalytic serine mechanism, while loss of activity in specific variants and in the isolated catalytic domain indicates that residues outside the active site, including within the β-propeller domain, contribute to catalysis, although their precise extent remains to be defined. Ongoing work will purify selected variants and characterize them by size-exclusion chromatography, circular dichroism, denaturation, and kinetic analyses to assess effects on oligomerization, structure, stability, and catalytic efficiency.

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OS3.2 The C-terminal disordered motif (DM9) in CK1a modulates circadian period tuning in *Neurospora crassa.*

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Introduction: The *Neurospora crassa* circadian clock relies on a transcription-translation feedback loop (TTFL), where the protein FREQUENCY (FRQ) serves as a negative regulator and core scaffold. Clock precision depends on tightly orchestrated phosphorylation dictating FRQ dynamics. As the primary kinase targeting FRQ, Casein Kinase 1α (CK1α) progressively phosphorylates it, determining clock speed. Structurally, CK1α contains a conserved catalytic domain followed by an intrinsically disordered C-terminal tail. While an autoinhibitory tail role is well known in mammalian homologs (CK1δ), the comprehensive characterization of the *N. crassa* CK1a tail remains unexplored. This work aimed to systematically dissect the C-terminal tail of CK1a to evaluate how its distinct regions control circadian period and clock stability.

Materials and Methods: *In silico* structural modeling and C-terminal dissections guided the generation of a mutant library in *N. crassa*. This library comprised targeted internal deletions, phospho-mimetic, phospho-null, sequence-scrambled, positional-shift, and secondary-structure-disrupting variants. Real-time bioluminescence and conidiation assays determined circadian rhythmicity and period length.

Results: The C-terminal dissections revealed contrasting functional regions within the flexible tail: distal truncations consistently accelerated the clock, whereas deeper deletions caused severe clock deceleration. This period lengthening was traced to a discrete 9-amino-acid element, herein named Disordered Motif 9 (DM9). Deleting DM9 alone reproduced this extension, while truncations beyond the fungal C-terminal homology boundary were non-viable. Conversely, mutations that split or fully unfolded the predicted C-terminal a-helix maintained period, proving DM9 functions independently of a static fold. Ongoing characterization of the complete DM9 mutant library provides key insights into the functional rules governing this motif.

Discussion: Together, these results suggest that the CK1α C-terminal tail affects period modulation independently of secondary structure and cell survival, identifying DM9 as a flexible linear motif critical for clock speed control. Planned protein interaction, phosphoproteomic, and biophysical analyses will further elucidate the molecular mechanism calibrating the oscillator.

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OS3.3 Unveiling the origins of RfaH fold-switching by ancestral sequence reconstruction, structure prediction, functional and biophysical assays.

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Introduction: NusG factors are universal transcription regulators that modulate gene expression by binding to RNA polymerase. In *Escherichia coli*, the specialized paralog RfaH functions as a virulence factor activated via a reversible fold-switching mechanism in its C-terminal domain (CTD) from an autoinhibited α-helical hairpin (αCTD) to an active β-barrel (βCTD). While approximately 20% of specialized NusG proteins exhibit metamorphic behavior, its evolutionary origins remain elusive. The aim of this work was to trace the emergence of RfaH fold-switching using ancestral sequence reconstruction (ASR).

Materials and Methods: Homologs retrieved from UniProt were analyzed by phylogenetic reconstruction to infer ancestral nodes: 7 directly related to RfaH, 1 from the *Vibrio* clade, and 1 from the Alphaproteobacteria clade. Ancestral structures were predicted using AlphaFold2 (AF2). Ancestral variants were experimentally characterized using *in vitro* transcription assays, *in vivo* translation assays, and hydrogen-deuterium exchange mass spectrometry (HDX-MS).

Results: AF2 predictions revealed a structural transition from NusG-like βCTD states in early ancestors to RfaH-like αCTD states in more recent lineages. Functional assays demonstrated that these late ancestral variants exhibit RfaH-like activity *in vitro* and *in vivo*, along with HDXMS data that is compatible with their predicted autoinhibited state.

Discussion: Together, these results demonstrate that the fold-switching behavior of RfaH originated early in its evolutionary history, providing key insights into the emergence of structural plasticity into these metamorphic transcription virulence factors.

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OS3.4 Development of a CHO-S-Based Production System for Functional Recombinant Lactadherin as an Immunogen for the Generation of Anti-Lactadherin VHHs in Triple-Negative Breast Cancer.

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Introduction: Triple-negative breast cancer (TNBC) remains challenging due to its limited therapeutic options and high metastatic capacity. In this context, Lactadherin (MFGE8), a glycoprotein that promotes metastatic properties in tumor cells, has been proposed as a therapeutic target. Accordingly, the development of anti-Lactadherin VHHs represents a promising immunotherapeutic strategy. Their generation requires an immunogen that preserves protein conformation and exposes native epitopes linked to biological functions targeted for blockade. This study aimed to develop a mammalian production system for functional human recombinant Lactadherin and evaluate its quality as a potential immunogen.
Materials and Methods: A transient expression system combined CHO-S cells with a vector containing a RegCG/CMV chimeric promoter, secretion elements, and an affinity tag. Secreted Lactadherin was quantified to determine specific productivity and purified from supernatants by Ni-NTA chromatography. Purity and identity were assessed by SDS-PAGE and Western blot. Sample quality and molecular populations were analyzed by mass photometry, and conformational stability by Thermofluor. Biological activity was assessed by Transwell migration in MDA-MB-231 cells stimulated with recombinant Lactadherin.
Results: The developed system produced and recovered recombinant Lactadherin under conditions supporting native-like structure and function, with >90% purity and identity confirmed by Western blot. Quantification and specific productivity analysis showed marked Lactadherin production throughout the first five days of culture. Purification of supernatants yielded Lactadherin in the milligram range, sufficient for the planned immunization. Mass photometry revealed a low-abundance dimer population, consistent with previous reports. Thermofluor showed a thermal transition above 60 °C, indirectly supporting a structured state. Recombinant Lactadherin increased MDA-MB-231 migration relative to controls, demonstrating retained biological activity.
Discussion: The CHO-S system yielded sufficient recombinant Lactadherin while retaining relevant structural and functional properties. This platform constitutes a rational experimental design for producing a structurally and functionally relevant immunogen for alpaca immunization and subsequent development of anti-Lactadherin VHHs as potential therapeutic molecular tools against TNBC.

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OS3.5 Role of CCAR2/DBC-1 interaction with ECE1c in colorectal cancer cells.

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Introduction: The Endothelin-Converting Enzyme-1c (ECE1c) has a role in different types of cancer, including colorectal cancer (CRC). ECE1c's N-terminal domain is phosphorylated by protein kinase CK2 in Ser18 and Ser20, improving its stability, which promotes a malignant phenotype in CRC cells. Near of phospho-residues exists a Lys6 putatively poly-ubiquitinated, whose mutation to Arg promotes ECE1c's stability. Higher stability of ECE1c produces a malignant phenotype in different tumor cells, such as glioblastoma, lung and CRC cells. Nevertheless, the mechanism associated with higher stability and malignancy promotion remains unknown. A possible mechanism is that proteins can bind to phosphoresidues, avoiding Lys6 polyubiquitination and improving stability and CRC cell aggressiveness. We found that CCAR2/DBC-1 is a potential interacting protein that may regulate those processes in CRC cells.

Material and methods: DLD-1 stable CRC clones expressing different mutants of ECE1c (ie. phosphomimetic, phosphoresistant, superstable, and wild-type) were used for IP-MS/MS analysis, co-IP and pull-down to verify protein-protein interactions. To silence and increase DBC-1 levels, a siRNA and a plasmid were used, respectively, and ECE1c protein levels were evaluated by Western blot. Immunofluorescence was used to evaluate ECE1c subcellular localization.
Results: DBC-1 interacts with ECE1c stable mutants and change their protein levels. Furthermore, DBC-1 alters ECE1c's subcellular localization.
Discussion: DBC-1 regulates ECE1c stability and may be potentially regulated to decrease the aggressiveness of CRC cells.

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OS3.6 Molecular Basis of Dual-Site Engagement and Selectivity of CcoTx3-synth for hNa$_V$1.5.
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Introduction: Voltage-gated sodium channels (Na$_V$s) are critical membrane proteins in excitable cells, with Na$_V$1.5 playing a pivotal role in cardiac electrophysiology. Mutations of human Na$_V$1.5 (hNa$_V$1.5) are linked to severe cardiac channelopathies, including atrial fibrillation and Brugada syndrome, making it a prime therapeutic target. Natural peptide toxins from venomous animals, such as tarantulas, offer valuable molecular tools for exploring Na$_V$ function. Among these, CcoTx3, a toxin from the straight-horned baboon tarantula, selectively inhibits hNa$_V$1.5/β1 (IC50 = 447 nM), while other Na$_V$ subtypes are unaffected (hNa$_V$1.1/β1–1.4/β1) or only partially blocked at higher concentrations (hNa$_V$1.8/β1). Despite its pharmacological potential, the structural basis of CcoTx3 interaction with hNa$_V$1.5 remains unresolved, particularly for the resting-state voltage-sensing domains II (VSDII) and IV (VSDIV), for which no experimental structure exists.
Materials and Methods: This study combined molecular modeling and site-directed mutagenesis to elucidate the binding mechanism of the synthetic CcoTx3–hNa$_V$1.5. Models of CcoTx3 bound to VSDII and VSDIV were generated, and molecular interactions were analyzed. Key binding residues were validated through site-directed mutagenesis at neurotoxin sites 3 and 4, followed by two-electrode voltage clamp assays.
Results: S743, E746, E747, R800, and S802 were identified as critical hotspots for inhibition of channel activation in VSDII, while D1610 and K1614 were key for fast inactivation inhibition. Synthetic CcoTx3 toxin (CcoTx3-synth) also interacted with zwitterionic and negatively charged liposomes, supporting a reduction-of-dimensionality mechanism.
Discussion: These findings provide the first structural and functional insights into the selective multisite engagement of CcoTx3-synth with hNa$_V$1.5 and may guide the design of peptide therapeutics targeting cardiac channelopathies.

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OS3.7 Lapatinib inhibits SOCE response by modulating STIM1-SARAF interaction and Orai1 recruitment.
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Introduction: Store-operated calcium entry (SOCE), mediated by STIM1 and Orai1, plays a pivotal role in Ca^{2+} homeostasis and tumor progression. The negative regulator SARAF modulates STIM1 activation to limit excessive Ca^{2+} influx. Although SOCE dysregulation drives cancer cell invasion, targeted pharmacological modulators remain scarce. The aim of this work

was to identify novel small-molecule SOCE modulators and evaluate their mechanistic impact on STIM1-SARAF-Orai1 signaling and cancer cell invasion.
Materials and Methods: We performed a high-throughput virtual screening (HTVS) in Schrodinger Maestro to search for clinical-stage compounds in the ZINC20 database, using the STIM1-SARAF interaction interface as a reference. Next, we conducted an alanine scan using a script built in PyRosetta to identify the amino acids critical to the interaction STIM1-Lapatinib-SARAF. Additionally, Fura-2-AM Ca^{2+} imaging, BiFC, TIRF microscopy, and BRET assays were conducted in HEK293 cells to assess Ca^{2+} dynamics and molecular interactions. Finally, Transwell invasion assays were used in MDA-MB-231 cells.
Results: By HTVS, we identified lapatinib, a clinically approved HER2 inhibitor, as a STIM1-SARAF binder, as evidenced by its interactions with the S524 and D520 residues of STIM1. Conversely, functional assays revealed that lapatinib inhibits the SOCE response and reduces STIM1-Orai1 coupling in HEK293 cells. Interestingly, using live-imaging recordings, we observed that lapatinib promotes the STIM1-SARAF interaction and stabilizes non-conducting clusters in HEK293 cells. Finally, lapatinib inhibited SOCE response and reduced cell invasion in MDA-MB-231 cells.
Discussion: These findings demonstrate that lapatinib acts as a novel SOCE inhibitor by modulating the STIM1-SARAF complex, revealing a potential strategy with clinical availability for HER2-negative cancers.

Acknowledgment: FONDECYT 1240633, 1230446; FIA 2024; IMII ICN2021_045.

OS3.8 Antibacterial activity of plant meristematic cell extracts as a possible application in wound healing. Coral Febré Silva[1,2,3] (coralsilvafebre@gmail.com), Ignacia Fuentes[1], Felipe Aquea [3].

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Introduction: Cutaneous wounds represent a significant healthcare burden, particularly when healing is delayed and progresses to chronic conditions. The increase of bacterial antibiotic resistance has encouraged the search for alternative therapies for wound healing. Plant-derived bioactive compounds are promising candidates; however, conventional plant extracts face limitations related to biomass requirements and poor standardization. Rubisco Biotech's platform, based on plant meristematic cell culture extracts, enables the production of standardized, reproducible, and sustainable plant cell extracts, with previous reported antimicrobial, antioxidant, and moisturizing properties in cosmetic contexts. The objective of this ANID-funded Doctoral Thesis in the Productive Sector is to develop enhanced plant extracts with increased accumulation of bioactive molecules to improve bacterial load control and positively (or neutrally) affect skin cell activity for wound healing.
Materials and Methods: Antibacterial screening based on 24h growth curves was performed using extracts obtained from seven plant species, against wound-associated bacteria (*Staphylococcus aureus, Pseudomonas aeruginosa, Corynebacterium diphtheriae*, and *Staphylococcus epidermidis*), employing both reference (ATCC) and clinical strains. Therefore, cytotoxicity was evaluated in HaCaT keratinocytes and human dermal fibroblasts cell culture.
Results: Two extracts derived from Chilean native species inhibited the growth of pathogenic bacteria without affecting the commensal bacteria *S. epidermidis*. Growth curves of pathogenic bacteria showed a significant decrease compared with untreated controls. Furthermore, neither extract exhibited cytotoxic effects in skin cell lines (keratinocytes and fibroblasts).
Discussion: Together, these experiments suggest selective antibacterial activity of both extracts against pathogenic bacteria in wounds. These findings provide evidence of the potential pharmaceutical application of these extracts for the control of wound infections.

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ORAL SESSION 4

OS4.1 What makes a small RNA? Deciphering the machinery and classification of sRNA genes in fungi.
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Introduction: Small RNAs (sRNAs) are a discrete class of short ncRNAs found across all of biology, which modulate gene expression and epigenetic state. Eukaryotes share a conserved pathway: DICER proteins process dsRNA precursors into sRNAs, which convey function through an AGO complex. Technologically, sRNAs are identified by size-selected sequencing, allowing inference of sRNA-genes from expression profiles. However, this process is confounded by biases and by short

RNAs derived from degradation, presumably not sRNAs. In plants and animals a high signal-to-noise ratio makes these other sources manageable, but in fungi a much higher noise floor creates numerous challenges.
Materials and Methods: Here we combine multi-species analyses of sRNA machinery and transcriptomics to define sRNAs across fungi in the greater context of eukaryotes. We performed exhaustive annotation of sRNAs in fungal species following a common pipeline. Using empirical false discovery rate analyses, we defined thresholds requiring loci to replicate between studies, building a high-confidence set. To compare this with machinery, we built a fungi-wide catalog of DICER homologs, including definition of a fungi-specific PAZ domain.
Results: We find that noise is a major factor in fungal libraries, not just between species but between studies. Merging and filtering by reproducibility retains less than 10% of loci across projects, but the resulting set is more homogeneous and phylogenetically similar. sRNA profiles are less precisely processed than in other eukaryotes, with wide variation in sizing and source. Fungal DICERs point to several proteins per species participating in this role, but modeling suggests this does not explain the discrete sizes observed.
Discussion: This evidence supports the exceptional nature of fungal sRNA production and highlights the challenge of confidently identifying loci in this kingdom. The catalogs developed here describe what sRNAs look like in less-studied organisms, priming further insight into the functions of this pathway.

Acknowledgment: FONDECYT 11220727, Millennium Institute for Integrative Biology (iBio)

OS4.2 Comparative functional genomics across one billion years of evolution reveals the grammars of plant transcriptional effector domains.
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Introduction: Eukaryotic transcription factors regulate gene expression through activation and repression domains embedded within poorly conserved intrinsically disordered regions. Their rapid sequence evolution has made it difficult to identify the principles governing transcriptional regulation and to distinguish pan-eukaryotic conserved mechanisms from lineage-specific innovations.
Materials and Methods: We generated a genome-scale atlas of transcriptional effector domains across the entire *Arabidopsis thaliana* transcription factor repertoire using ENTRAP-seq, a high-throughput reporter assay for plants. We assayed the transcriptional regulatory activity of ~26,000 40-amino-acid fragments spanning 1,918 transcription factors and compared these measurements with a matching functional dataset obtained from the same protein fragments in *Saccharomyces cerevisiae*, representing two eukaryotic lineages that diverged more than one billion years ago. We integrated these cross-species measurements with machine learning to identify conserved and lineage-specific sequence grammars underlying transcriptional regulation.
Results: The atlas identified hundreds of known and previously undescribed activation and repression domains, including numerous bifunctional transcription factors. Comparative analysis revealed that plant activation domains encode both a deeply conserved activation grammar shared with yeast and additional plant-specific grammars. Machine learning identified the sequence features associated with each grammar, distinguishing conserved regulatory mechanisms from evolutionary innovations. We further found that repression domains, like activators, are also governed by distributed sequence grammars rather than discrete conserved linear motifs, unlike previously assumed.
Discussion: By functionally comparing the same genome-scale protein library in two eukaryotic systems separated by approximately one billion years of evolution, this work demonstrates that functional conservation can be used as an experimental framework to disentangle deeply conserved regulatory mechanisms from lineage-specific innovations. These findings provide a predictive foundation for understanding the evolution and engineering of plant transcription factors.

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OS4.3 Impact of genetic recombination on evolutive stress-tolerance in *Saccharomyces eubayanus.*
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Introduction: Throughout evolution, organisms have adopted two reproductive strategies: asexual and sexual. In asexual reproduction, the parent transmits a copy of its entire genome to its offspring. In contrast, sexual reproduction involves genetic recombination of two parental genomes; this recombination generates genetic diversity, resulting in offspring with greater potential to adapt to changing environments or to colonize new ecological niches. However, the true advantage of sexual reproduction and the reason it has persisted throughout evolution are not fully understood. Yeasts, such as *Saccharomyces*

species, are suitable models for studying the evolutive consequence of recombination, because they can reproduce asexually by budding and sexually through sporulation and mating.
Materials and Methods: An experimental evolution study was conducted on a diverse population of *Saccharomyces eubayanus* under ethanol stress conditions for 120 generations. Two conditions were considered: (1) strictly asexual reproduction and (2) asexual reproduction with periodic cycles of sexual reproduction (recombination). Finally, a kinetic characterization of the growth rate was performed, and based on these data, an isolate was selected for genome sequencing using Illumina and Nanopore.
Results: Growth kinetics analyses show that both reproductive mechanisms allow adaptation to ethanol within 120 generations. Individuals from evolution lines that show the greatest adaptation are obtained through sexual reproduction, where genetic recombination allows improvements in two distinct adaptation mechanisms: lag phase and growth rate. In the genetic analysis of the selected individual, no major chromosomal rearrangements were found, but mutations associated with ethanol tolerance and sexual reproductive efficiency were identified.
Discussion: These results highlight the potential benefits of sexual reproduction during adaptation, suggesting that genetic recombination may increase the evolutive response to environmental challenges.

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OS4.4 Endothelin-1 drives invadopodia formation and cell invasion through NOX-dependent ROS production in gallbladder cancer cells.
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Introduction: Gallbladder cancer (GBC) is a highly aggressive malignancy with a poor prognosis, in which tumor cell invasion is regulated by Endothelin-1 (ET1) through activation of its receptor (ET_AR). Reactive oxygen species (ROS), generated by mitochondria and the NOX protein family, act as second messengers that promote cell invasion. Src kinase has been implicated in NOX regulation, and although ET1 activates Src and promotes invadopodia formation in other cancer models, its role in NOX activation and cancer cell invasion remains poorly understood. Therefore, we aimed to determine the effect of ET1 on Src/NOX-mediated ROS production and its impact on invadopodia formation and cell invasion in GBC.
Materials and Methods: NOZ GBC cells were treated with ET1, Ambrisentan (ET_AR antagonist), DPI (pan-NOX inhibitor), and/or Saracatinib (Src inhibitor). ROS were measured with fluorescent probes by spinning disk confocal microscopy. Protein levels were measured by western blot. Cell invasion was determined by Transwell-Matrigel assay. Invadopodia formation was evaluated by confocal microscopy using fluorescent gelatin.
Results: ET1 increased NOX1 protein levels and promoted an increase in total ROS levels, effect that was prevented by ET_AR blockade or by inhibition of total NOX activity. In contrast, mitochondrial ROS levels were not affected by ET1 signaling. ET1 enhanced the invasive capacity of GBC cells by increasing invadopodia formation, an effect that was impaired by NOX inhibition. Mechanistically, ET1 increased NOX1 expression through Src activation, since inhibition of Src prevented NOX1 upregulation and reduced ET1-induced cell invasion.
Discussion: $ET1/ET_AR$ signaling promotes Src-dependent NOX1 activation and ROS production, which contributes to enhanced invadopodia formation and invasion of GBC cells. These findings reveal a novel mechanism by which ET1 regulates tumor cell invasiveness.

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OS4.5 Phosphorylation at Serine 474 by GSK3β directs ER exit and anterograde trafficking of the Kv3.1b potassium channel.
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Introduction: Voltage-gated potassium channel Kv3.1b (KCNC1) sustains high-frequency firing in GABAergic interneurons. A patient with severe developmental regression and epilepsy was identified harboring a heterozygous missense variant KCNC1: c.1421C>G, p.Ser474Cys) within a putative GSK3β consensus motif. Here, we sought to determine whether GSK3β-mediated phosphorylation of Ser474 acts as a regulatory switch for Kv3.1b early secretory trafficking and downstream cellular signaling.

Methods: Using the Retention Using Selective Hooks (RUSH) assay combined with live-cell imaging and immunofluorescence, we tracked $Kv3.1b^{WT}$, $Kv3.1b^{S474C}$, and phosphomimetic $Kv3.1b^{S474E}$ channels relative to ER (VAPA), exit site (Sec23a), and Golgi (ST-mCherry) markers. Phosphorylation was monitored using a validated phospho-specific anti-pS474 antibody with or without GSK3β and its inhibitor TDZD-8. Intracellular calcium dynamics were assessed in HEK293 cells using GCaMP-CAAX in response to Carbachol (CCh) stimulation.
Results: In RUSH assays, $Kv3.1b^{WT}$ displayed a transient, time-dependent peak in Ser474 phosphorylation during Golgi transit (30–90 min), which was absent in $Kv3.1b^{S474C}$ and $Kv3.1b^{S474E}$. While both $Kv3.1b^{WT}$ and $Kv3.1b^{S474E}$ exited the ER and accumulated in the Golgi (30–60 min), the $Kv3.1b^{S474C}$ variant showed persistent VAPA colocalization. Furthermore, coexpression with active GSK3β modulated the trafficking kinetics and pS474 signal of $Kv3.1b^{WT}$. Ca^{2+} imaging revealed that CCh- and Forskolin-induced Ca^{2+} signals were observed in $Kv3.1b^{WT}$-expressing cells, whereas $Kv3.1b^{S474C}$ showed a lower response and $Kv3.1b^{S474E}$ remained lowest, resembling the control condition.
Conclusions: GSK3β-mediated phosphorylation at Ser474 acts as a critical molecular checkpoint for Kv3.1b ER exit. Its disruption in the $Kv3.1b^{S474C}$ mutant leads to intracellular retention, providing a molecular mechanism for channel dysfunction in KCNC1-associated neurodevelopmental disorders.

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OS4.6 Effect of D-Allulose on Food Intake Regulation in Arcuate Nucleus Hypothalamic Circuits Involving NPY and POMC Neurons.
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Introduction: The hypothalamus regulates energy homeostasis through the arcuate nucleus (ARC), which contains orexigenic NPY/AgRP and anorexigenic POMC/CART neurons. Excess intake of simple sugars such as sucrose contributes to metabolic dysfunction and rare low-calorie sugars like D-allulose offers potential metabolic benefits. However, its effects in regulation of food intake in hypothalamic circuits remain unclear. We examined whether D-allulose exposure modulates ARC neuronal subpopulation and glial reactivity.
Materials and Methods: NPY-GFP mice and Wild Type mice were given 13% D-allulose, 10% sucrose or water for a 7 days adaptation period, during which daily body weight, solution intake, and food consumption were monitored. For acute experiments, mice received 200 µL of their assigned solution via pipette and were perfused 40 minutes post-exposure. Brain sections were processed for c-Fos immunofluorescence to quantify neuronal activation in NPY and POMC populations. We also assessed glial responses (GFAP and Iba1) after the treatment.
Results: Acute oral D-allulose dramatically increased c-Fos in ARC NPY neurons compared with water and sucrose, while POMC neurons showed no significant change. After 7 days of D-allulose ingestion, astrocytic and microglial activation was unchanged. Food intake and solution consumption markedly changed depending on the sugar consumption.
Discussion: These findings indicate that oral administration of D-allulose, despite its negligible caloric content, rapidly engages the orexigenic ARC whereas sucrose does not under the acute conditions tested. Together, data supports a model in which D-allulose fails to trigger hypothalamic satiety pathways, selectively activating NPY neurons without engaging POMC neurons, suggesting an influence on feeding behavior and energy balance.

OS4.7 The hepatokine LEAP-2 regulates lipid metabolism and mitochondrial dynamics in cardiomyocytes and modulates MASLD-associated cardiac remodeling and liver steatosis.
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Introduction: Metabolic dysfunction-associated steatotic liver disease (MASLD) alters hepatokine secretion, markedly elevating liver-expressed antimicrobial peptide 2 (LEAP-2). LEAP-2 acts as an endogenous antagonist and inverse agonist of the ghrelin receptor (GHSR). Given that ghrelin is diminished in MASLD and exerts robust cardioprotective effects, we investigated the impact of LEAP-2 on cardiomyocyte hypertrophy, metabolism, and mitochondrial dynamics, as well as its relevance in a mouse model of MASLD.
Materials and Methods: Neonatal rat ventricular cardiomyocytes (NRVCMs) were treated with LEAP-2 (1 µM), palmitate (220 µM), and ghrelin (1 µM) for 24 h to evaluate hypertrophy, lipid gene expression (RT-qPCR/Western blot), and

mitochondrial dynamics and function (3D-confocal microscopy/flow cytometry). Simultaneously, male C57BL/6J mice were injected with adeno-associated virus 8 (AAV8-shLEAP-2) to silence hepatic LEAP-2 and fed with a control or high-fat diet (HFD) for 18 weeks.
Results: *In vitro*, LEAP-2 increased NRVCM cell area without activating the canonical fetal hypertrophic gene program. However, it dysregulated lipid metabolism by upregulating *CD36* and downregulating oxidation/import markers (*CPT1B*, *CPT2*, *ACSL1*, *FASN*, *SREBP1*, and PPARα). LEAP-2 stimulated mitochondrial biogenesis (increasing PGC1α, TFAM, and organelle number) but significantly reduced mitochondrial membrane potential, without altering ATP levels. Furthermore, LEAP-2 completely blocked the anti-hypertrophic effect of ghrelin on cell size in palmitate-induced hypertrophy. *In vivo*, LEAP-2 knockdown prevented the HFD-induced increase in circulating LEAP-2, reduced total cholesterol, and attenuated hepatic damage and steatosis. Importantly, systemic LEAP-2 silencing significantly reduced HFD-induced cardiomyocyte cross-sectional hypertrophy without affecting body-weight gain; however, it further impaired glucose tolerance.
Discussion: These findings demonstrate that LEAP-2 has direct effects on cardiomyocytes and modulates their lipid metabolism, mitochondrial dynamics, and bioenergetics. Crucially, LEAP-2 prevents ghrelin-mediated cardioprotection under lipotoxic conditions rather than exacerbating palmitate-induced hypertrophy. Consequently, targeting the LEAP-2/ghrelin ratio represents a novel therapeutic axis to mitigate MASLD-associated cardiac remodeling and liver steatosis.

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OS4.8 Cholesterol regulates Endoplasmic Reticulum (ER) remodelling via selective autophagy.
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Introduction: The endoplasmic reticulum (ER) senses intracellular cholesterol levels and coordinates its synthesis, uptake, storage, and distribution to maintain lipid homeostasis. Selective autophagy of the ER (ER-phagy) maintains ER homeostasis through specialized receptors, including the reticulon-family protein FAM134B, which couples ER remodeling to lysosomal degradation. However, whether ER-phagy contributes to cholesterol sensing and homeostasis remains unclear. Here, we investigated the reciprocal relationship between cholesterol and FAM134B-dependent ER-phagy.
Materials and Methods: Cholesterol-induced ER remodeling and ER-phagy were investigated using quantitative proteomics, ER-phagy reporters, fluorescence microscopy, biochemical and biophysical assays, and computational analyses. FAM134B-deficient cells and lipidomic profiling were used to determine the contribution of ER-phagy to lipid homeostasis. Cholesterol-induced ER remodeling was further examined in primary hepatocytes and mouse liver.
Results: Increased intracellular cholesterol induced ER remodeling and activated ER-phagy, preferentially promoting degradation of ER membrane proteins. Quantitative proteomics identified ER structural proteins and cholesterol-biosynthetic enzymes, as substrates of cholesterol-mediated FAM134B-dependent ER degradation. Imaging revealed $FAM134B^{+}/LC3B^{+}$ structures containing a fluorescent cholesterol analogue, supporting the sequestration of cholesterol-enriched ER into autophagosomes. Mechanistically, FAM134B bound cholesterol in cells and in vitro, while cholesterol enhanced FAM134B ubiquitination and clustering, promoting ER-phagy activation. Conversely, loss of FAM134B-dependent ER-phagy caused broad remodeling of the hepatocyte lipidome, including increased cholesterol levels and altered cholesterol-biosynthetic enzymes. In primary hepatocytes and mouse liver, cholesterol also promoted ER-phagy and ER remodeling, whereas FAM134B deficiency resulted in altered ER organization and expansion.
Discussion: Our findings uncover a reciprocal regulatory axis in which increased ER cholesterol activates FAM134B-dependent ER-phagy, promoting degradation of cholesterol-biosynthetic machinery and cholesterol-enriched ER to maintain cholesterol homeostasis. Conversely, loss of this pathway disrupts cellular cholesterol metabolism. Thus, FAM134B functions as an ER cholesterol sensor linking ER-phagy to lipid homeostasis.

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POSTERS

P1. Targeting human uncoupling protein 2 with flavonoids: from structure-based virtual screening to mitochondrial functional analysis.

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Introduction: Uncoupling protein 2 (UCP2) is an inner mitochondrial membrane transporter that regulates proton re-entry into the mitochondrial matrix, partially dissipating the proton gradient generated during oxidative phosphorylation. Beyond its role in ATP production, UCP2 modulates energy metabolism, cell survival, and reactive oxygen species generation, making it a promising therapeutic target for metabolic disorders such as obesity. Flavonoids are plant-derived polyphenols widely recognized for their antioxidant, anti-inflammatory, and metabolic benefits. Increasing evidence indicates that dietary flavonoids can reduce body weight, adipose tissue mass, and plasma cholesterol by modulating energy homeostasis. Despite these beneficial effects, their potential to directly regulate UCP2 activity remains poorly understood.
The aim of this study was to evaluate the ability of selected flavonoids to enhance the activity of human UCP2, providing new insights into their mechanism of action and their potential application in the management of obesity and related metabolic diseases.
Materials and Methods: A validated hUCP2 model will facilitate docking and molecular dynamics simulations to identify flavonoid activators and elucidate their binding mechanisms. In parallel, mouse liver mitochondria were isolated, and oxygen consumption (QO_2) was measured using a Clark electrode to assess the effects of candidate flavonoids, both alone and in combination with palmitate, on UCP2 activity.
Results: Docking analysis identified 6 chalcones, 8 flavones, 1 flavanone, 1 catechin, and 1 isoflavonol exhibiting the most favorable binding affinities toward UCP2, with $\Delta G_{binding} < -11.0$ kcal/mol. In addition, both hesperetin and quercetin increased QO_2 compared with the palmitate control.
Discussion: Together, these findings suggest that flavonoids could play an important role in modulating UCP2 activity.

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P2. Evaluation of the biostimulant effect and modulation of plant immunity in *Solanum lycopersicum* induced by *Trichoderma atroviride* overexpressing strains of the transcription factors *taPRF1* and *taTAR*.

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Introduction: *Botrytis cinerea* causes significant losses in tomato (*Solanum lycopersicum*) crops. The environmental impacts associated with chemical fungicide use, together with the emergence of fungicide-resistant pathogen populations, highlight the need for sustainable disease-management alternatives. *Trichoderma* species are widely used as biocontrol agents, inhibiting phytopathogens, promoting plant growth, and enhancing plant immunity through defense priming and induction of systemic resistance (acquired-SAR or induced-ISR). However, the transcriptional regulators governing these traits remain poorly characterized. Here, we evaluated the effects of treating *S. lycopersicum* with *Trichoderma atroviride* strains overexpressing the transcription factors (TFs) *taPRF1* and *taTAR*, both associated with secondary metabolism and mycoparasitism against *B. cinerea*. Specifically, we assessed their contribution to plant growth promotion and the activation of ISR and SAR-associated defense responses against *B. cinerea*.
Materials and methods: *T. atroviride* overexpressing strains of *taPRF1* and *taTAR* TFs were inoculated into the Moneymaker, Micro-Tom, Perita, and Roma cultivars. Fresh and dry biomass of shoots and root systems were determined. Leaf area, root length, and root area were quantified. Leaves from inoculated cultivars were infected with *B. cinerea*. The lesion area was measured. In another assay, total RNA was extracted from the leaves of treated cultivars. The relative expression of ISR and SAR marker genes was measured by RT-qPCR.
Results: Plants inoculated with *T. atroviride* overexpressing strains are expected to show increased fresh and dry biomass, leaf area, root length, and root area. Inoculation with these strains is also expected to upregulate ISR and SAR marker genes and to reduce the lesion area in leaves challenged with *B. cinerea*.
Discussion: These results would suggest that the interaction between *S. lycopersicum* and *T. atroviride* strains overexpressing these TFs enhances plant growth and primes the immune system through the ISR and SAR pathways, contributing to increased resistance against *B. cinerea*.

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P3. Location of poly(dA:dT) tracts within the nucleosome core impedes the sliding activity of the RSC complex.

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Introduction: Nucleosomes conform the fundamental unit of chromatin. Their position can be modified by sliding mediated by complexes such as RSC, a chromatin remodeling complex present in *S. cerevisiae*, affecting transcription and other nuclear processes. Previous studies have shown that poly(dA:dT) tracts stimulate RSC activity. Interestingly, under a design that forces RSC to mobilize a tract into the nucleosome core, we have observed that sliding is impeded. However, the exact translational location where a tract exerts this impediment is unknown, as well as the effect of tract length and presence of other tracts nearby. In this work we addressed these issues, obtaining further insight into the effects of tracts on nucleosome remodeling activity.
Materials and Methods: DNA probes containing poly(dA:dT) tracts of different lengths and at different positions were generated by PCR from plasmids specifically generated for each design. The probes were then reconstituted into mononucleosomes and used to analyze the sliding activity of RSC. Exact changes in translational position of the nucleosome core were determined by ExoIII mapping.
Results: ExoIII mapping showed that the impediment of sliding appears when a poly(dA:dT) tract reaches SHL2 (20 bp from the nucleosome dyad). We determined that the minimal tract length exerting this effect is 7 bp, although lengths of 10 bp or longer give a stronger impediment. Additional analyses demonstrated that the sliding impediment exerted by a tract inside the core does not rely on the presence of an additional tract on linker DNA.
Discussion: We confirmed that poly(dA:dT) tracts have the property of impeding RSC's sliding activity when reaching an specific internal region of the nucleosome. These results suggest that some tracts could be strategically located at defined positions of gene regulatory regions to impede nucleosome repositioning at locations that might be incompatible with proper transcriptional regulation.

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P4. Antiproliferative effects of quercetin in gallbladder cancer cells and the potential role of Endothelin-1.

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Introduction: Gallbladder cancer (GBC) is the most common malignancy of the biliary tract and is usually diagnosed at advanced stages, when curative surgery is no longer feasible. Chile has the second highest incidence and mortality rates worldwide, with the Los Ríos Region being the most affected. Endothelin-1 (ET-1) signaling through the Endothelin A receptor (ET_AR) has been implicated in GBC progression. Quercetin, a dietary flavonoid with antiproliferative and pro-apoptotic properties, has also been reported to modulate the ET-1 pathway in non-tumoral models. The aim of this work was to evaluate the effects of quercetin on the viability of GBC cells while exploring the potential involvement of Endothelin-1/ET_AR expression.
Materials and Methods: Human GBC cell lines (NOZ and CAVE-1) were treated with quercetin, either alone or in combination with the selective ET_AR antagonist Ambrisentan. Cell viability was assessed using MTS and crystal violet assays. Protein expression was analyzed by Western blot.
Results: Quercetin significantly reduced cell viability in both NOZ and CAVE-1 cells. However, co-treatment with Ambrisentan did not enhance this effect. Furthermore, quercetin treatment did not modify ET_AR protein expression levels.
Conclusions: Quercetin exerts antiproliferative effects in GBC cells independently of ET_AR antagonism or changes in ET_AR expression. These findings suggest that quercetin may represent a promising candidate for combination therapies against gallbladder cancer, although additional studies are required to clarify the molecular mechanisms underlying its antitumor activity.

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P5. DNA Damage-Related Genes and Pathways Modulated by miR-1973 and miR-4485-3p in MDA-MB-231 Tumor Cells.

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Introduction. Breast cancer is the most diagnosed cancer in women worldwide. Our group described two types of transcripts derived from the mitochondrial 16S gene, known as sense (SncmtRNA) and antisense non-coding mitochondrial RNA (ASncmtRNA). Knockdown of the ASncmtRNA induces DNA damage and apoptosis in tumor cells, but not normal cells. ASncmtRNA knockdown also induces upregulation of microRNAs hsa-miR-1973 and hsa-miR-4485-3p, which may play a role in the events leading to tumor cell apoptosis by downregulating proteins involved in the DNA damage response (DDR).
Methods. We transfected MDA-MB-231 triple-negative breast cancer cells with miR-1973 and miR-4485-3p mimics, or a control mimic. RNA sequencing was outsourced and data was analyzed with DESeq2. The data were compared to DDR gene databases and pathway enrichment platforms like the Wood Laboratory at MD Anderson Cancer Center and Enrichr-KG. Select candidate downregulated genes were subsequently validated by RT-qPCR.
Results. The analysis rendered a list of genes significantly downregulated by miR-4485-3p and miR-1973 mimics, of 30 and 22 DDR-related genes, respectively. RT-qPCR validated downregulation of PARK7 and UNG by miR-4485-3p mimic, and of PHF20 and USP1 by miR-1973 mimic.
Discussion. Both miR-4485-3p and miR-1973 mimics downregulated several genes involved in the DDR. RT-qPCR validation showed that miR-4485-3p hinders oxidative stress sensing through downregulation of PARK7 (which can lead to oxidative DNA damage), and base excision repair by downregulation of UNG. On the other hand, miR-1973 is associated with epigenetic regulation and the DDR through PHF20 and USP1. Hence, both miRNAs may mediate DNA damage induced by ASncmtRNA knockdown, suggesting a miRNA-based cancer therapy.

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P6. Structural impact of phosphorylation of the neuronal variant of LSD1 on CoREST dissociation.
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Introduction: LSD1 is an epigenetic enzyme that acts as a transcriptional repressor by catalyzing the demethylation of H3K4me1/2. LSD1 has a neuro-specific isoform called neuroLSD1 (nLSD1), generated by alternative splicing of the microexon E8a, a short sequence of 12, which encodes for an Asp-Thr-Val-Lys tetrapeptide. Phosphorylation of the threonine within this microdomain promotes the dissociation of the CoREST/HDAC1/2 corepressors, thereby reducing nLSD1 repressive activity. However, the molecular mechanism underlying this dissociation remains unclear. In particular, it is unknown whether phosphorylation induces conformational changes in nLSD1 that weaken its interaction with CoREST or creates a new binding site for a competing factor. Here, we investigated the molecular and conformational dynamics of the nLSD1-CoREST complex.
Materials and Methods: Coarse-grained molecular dynamics simulations of CoREST bound to LSD1, nLSD1, or the phosphomimetic nLSD1 Thr369Asp mutant were performed for up to 5 μs. The dynamics and stability of each complex were analyzed to identify structural and molecular interactions affected by the phosphomimetic mutation.
Results: Our data show that CoREST progressively detached from both nLSD1 and the nLSD1 Thr369Asp mutant, with dissociation occurring more rapidly in the phosphomimetic complex. Notably, the nLSD1 Thr369Asp complex exhibited an earlier disruption of molecular interactions surrounding the phosphorylation site, including key salt bridges involved in stabilizing the protein-protein interface. These changes were accompanied by alterations in the local charge distribution of residues implicated in the interaction between nLSD1 and CoREST.
Discussion and Conclusions: Our results suggest that phosphorylation-dependent dissociation of CoREST from nLSD1 is not primarily driven by large-scale conformational rearrangements. Instead, phosphorylation appears to destabilize the nLSD1-CoREST interface through local changes in electrostatic interactions and disruption of critical salt bridges. These findings provide a mechanistic framework for understanding how a single post-translational modification can regulate the activity of the neuronal LSD1 corepressor complex.

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P7. NUAK1 inhibition enhances ceramidase inhibitor-induced cell death in colorectal cancer.
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Introduction: Colorectal cancer (CRC) treatment remains challenging due to therapeutic resistance and the limited availability of effective targeted therapies. NUAK1 has emerged as a promising therapeutic target in cancer, with increasing evidence supporting its role in tumor growth, survival, and metabolic adaptation. We previously identified a metabolic dependency arising from NUAK1 inhibition in CRC, characterized by lipid metabolic reprogramming and increased ceramide synthesis. Because intracellular ceramides can induce apoptosis, we tested whether ceramidase inhibition could further increase NUAK1-induced ceramide accumulation and promote CRC cell death.
Methods: SW480 and HCT116 p53-/- CRC cell lines were treated with HTH-01-015 (NUAK1 inhibitor) and Ceranib-2 (ceramidase inhibitor), and intracellular ceramide levels were assessed by confocal microscopy. CRC cell death was evaluated using IncuCyte following treatment with HTH-01-015 and Ceranib-2, while western blotting was performed to assess apoptosis-related proteins. CRC organoids were used to validate these findings in a clinically relevant CRC model.
Results: Combination of NUAK1 and ceramidase inhibition increased intracellular ceramide levels compared with either treatment alone. Consistently, real-time cell death analysis and western blotting demonstrated that co-treatment with HTH-01-015 and Ceranib-2 promotes apoptotic cell death in CRC cells. Similar results were observed in CRC organoids, where NUAK1 inhibition increased intracellular ceramide levels and triggered cell death.
Discussion: These findings support combined inhibition of ceramidase and NUAK1 as a potential strategy to treat CRC.

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P8. Functional properties of Chilean black rice: phenolic profile, cellular ROS modulation and mapping of digestive peptides.
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Introduction: Disrupted cellular redox homeostasis promotes excessive oxygen species (ROS) accumulation. Cyanidin-3-O-glucoside (C3G); the predominant anthocyanin in black rice, has demonstrated antioxidant and anticancer activity. Functionally, it may also depend on the phenolic matrix and digestive transformation of grain proteins. The aims of this study were to characterize first-flour phenolics, evaluate ROS modulation in Caco-2 cells and assess protein hydrolysis and intestinal peptide distribution in cooked black and white rice.
Materials and Methods: First-flour fraction from pigmented rice; black (‘Onix’, ‘Quila 292008’), brown (‘Quila 299802’), and white (‘Ambar’, ‘Zafiro’) rice were analyzed for total phenolics and by HPLC-QTOF-MS. Non-cytotoxic black rice extract (100 μg mL^{-1}) were evaluated after ethanol/t-BOOH challenge using DCFH-DA, with C3G as reference. Cooked ‘Onix’ and ‘Zafiro’ underwent INFOGEST digestion. Hydrolysis was assessed by OPA, intestinal peptides were analyzed by nano LC-MS/MS and mapped using Peptigram.
Results: ‘Onix’ showed the highest phenolic content (4.14 mg GAE g^{-1}), followed by ‘Quila 292008’ (2.85 mg GAE g^{-1}). Eighteen compounds were identified, C3G and peonidin-3-O-glucoside occurred only in black genotypes. ‘Onix’ and ‘Quila 292008’ reduced ROS associated fluorescence at 150 min by 57.14% and 51.58%, respectively, and cumulative ROS by 60.61% and 65.04%, comparably to C3G. Intestinal free amino groups were higher in ‘Onix’ than ‘Zafiro’ (850.41 ± 45.83 versus 709.94 ± 53.84 μmol·g $sample^{-1}$; $p = 0.0073$). Peptigram showed broadly conserved glutelin derived peptide distribution and protein region specific differences in RA05 peptide signal intensity.
Discussion: Black rice outer layer fractions attenuated ROS accumulation, consistent with a contribution to redox homeostasis under oxidative challenge. Independently, whole grain digestion revealed genotype dependent hydrolysis and regional peptide mapping differences that warrant further functional investigation.
Acknowledgment: The authors gratefully acknowledge the Rice Breeding Program of the Institute of Agricultural Research (INIA) and funded by ANID, FONDECYT 1260485, FONDECYT grant 11220151, FONDECYT 11251254 and ANID National Doctoral Scholarship No. 21210408.

P9. GOLPH3 Associates with ACSL3 and Contributes to Palmitate-Induced XBP1s Activation in Triple-Negative Breast Cancer Cells.
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Introduction: GOLPH3 is a cytosolic peripheral membrane protein recruited to specific domains of the Golgi apparatus (GA) through its interaction with phosphatidylinositol 4-phosphate (PI4P), where it regulates Golgi architecture, vesicular trafficking, and protein distribution. GOLPH3 overexpression pro motes protumorigenic phenotypes in several cancers, including breast cancer, where non-Golgi pools of the protein have also been described. In a preliminary interactome in MDA-MB-231 cells, we identified ACSL3, a key enzyme that activates palmitic acid (PA) for phospholipid synthesis or lipid droplet storage, as a GOLPH3 interactor. We therefore investigated whether GOLPH3 cooperates with ACSL3 to modulate palmitate-induced lipid bilayer stress.
Materials and methods: MDA-MB-231 lysates were analyzed by co-IP and immunoblotting to validate the GOLPH3–ACSL3 association. Basal ACSL3 abundance and PA-induced (100 μM) XBP1s activation were compared between wild-type (WT) and GOLPH3-knockout (KO) cells.
Results: Co-IP assays using lysates from MDA-MB-231 cells expressing GFP-GOLPH3, with GFP-negative lysates as controls, validated the association of GOLPH3 with ACSL3. GOLPH3-KO cells displayed higher basal ACSL3 abundance than WT cells. However, despite this increase, PA-induced XBP1s activation was attenuated in GOLPH3-KO cells.
Discussion: These findings indicate that GOLPH3 contributes to palmitate-induced XBP1s activation in MDA-MB-231 cells. The combination of increased ACSL3 abundance and reduced XBP1s activation in GOLPH3-KO cells suggests that this response is not determined solely by ACSL3 levels and may instead depend on GOLPH3-mediated regulation of ACSL3 localization or function. Further studies are required to define the mechanism connecting the GOLPH3-ACSL3 association to lipid bilayer stress signaling.

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P10. Topical trehalose, a GLUTs inhibitor, attenuates early neurovascular changes in acute and chronic retina damage.
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P11. Evaluation of lignocellulolytic capacity and transcriptomic response of evolved thermotolerant Neurospora crassa isolates.
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Introduction: *Neurospora crassa* is a filamentous fungus widely used in molecular genetics, circadian biology, and evolutionary research. Its lignocellulose-degrading capacity and heterokaryotic nature makes it a valuable experimental model. Therefore, *N. crassa* populations, including a transcriptionally rewired strain in which the circadian clock controls the heat-shock response, were evolved under high-temperature conditions in a glucose-based medium. Microconidial isolates were then evaluated to determine whether this evolutionary regime affected their capacity to degrade complex carbon sources and altered circadian clock function. In addition, we investigated the differentially expressed thermotolerance-related genes that could explain phenotypic differences between the evolved isolates and the unevolved parental strain, HRP.
Materials and Methods: The behavior of the clock was evaluated by measuring luminescence of a circadian reporter. The lignocellulolytic activity was evaluated by quantifying proteins in culture supernatants and measuring lignocellulolytic activity using DNS method; the protein profile was estimated via SDS-PAGE; and RNA was extracted from samples following a heat-shock induction and sequenced using Illumina technology.
Results: The evolved N. crassa isolates M1 and M3 retained the ability to grow on complex carbon sources without significant changes in circadian period or phase. Under heat-shock conditions, comparison of HRP and M1 identified at least 30 differentially expressed genes, which include genes associated with circadian regulation, thermal and light responses, transcriptional control, and metabolism.

Discussion: The evolved isolates retained the parental strain's capacity to grow on complex carbon sources without major circadian alterations, while exhibiting variable enzymatic activity and differences in the expression of several thermotolerance-related genes.

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P12 Effect of EZH2 activity inhibition on epithelial–mesenchymal transition-associated features in gallbladder cancer.
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Introduction: Gallbladder cancer (GBC) is a highly aggressive malignancy characterized by late diagnosis, limited therapeutic response, and poor survival. Among the mechanisms associated with its progression, epithelial–mesenchymal transition (EMT) promotes the acquisition of migratory and invasive properties through molecular and phenotypic changes, including the regulation of epithelial and mesenchymal markers. EZH2, the catalytic component of the PRC2 complex, epigenetically regulates gene expression through H3K27 trimethylation (H3K27me3) and has been associated with tumor progression. However, its involvement in the regulation of EMT-associated features remains poorly studied in GBC. Therefore, this study evaluated the effect of EZH2 inhibition on molecular and functional features associated with EMT in GBC cells.
Materials and Methods: EZH2 expression was analyzed using RNA-seq data from different stages of GBC progression. GB-d1 and G415 cells were treated with GSK126 (1, 5, and 10 μM). EMT markers (*CDH1*, *CDH2*, *VIM*, and *SNAI1*) by RT-qPCR and H3K27me3 were evaluated, Western blot, and immunofluorescence. Migration and invasion were assessed using Transwell assays with Matrigel.
Results: RNA-seq data analysis showed an increasing trend in EZH2 expression across GBC disease progression. GSK126 reduced the expression of *CDH1, CDH2, VIM,* and *SNAI1*. At the protein level, E-cadherin and N-cadherin were not detected in G415, whereas E-cadherin predominated in GB-d1. H3K27me3 decreased in GB-d1 but not considerably in G415. Migration and invasion decreased in both cell lines.
Discussion: The results show a differential response to EZH2 inhibition between both cell lines. The reduction in migratory and invasive features was not accompanied by the classical cadherin pattern associated with EMT, suggesting the involvement of other components of this process.

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P13. Inside the cellular niche: Assembly of Virus-Containing Compartments during HIV-1 infection in human microglia.
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P14. Design and Structural Evaluation of a Chimeric Neuraminidase Integrating Conserved Epitopes Across Influenza A Virus N1–N9 Subtypes
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P15. A *Botrytis cinerea* gene involved in salicylic acid degradation contributes to virulence.

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Introduction: Plant hormones coordinate defense responses against pathogens, with salicylic acid (SA) and jasmonic acid (JA) traditionally associated with resistance to biotrophic and necrotrophic pathogens, respectively. However, SA also participates in the interaction with the necrotrophic fungus *Botrytis cinerea*, where its contribution to resistance or susceptibility remains controversial. Intriguingly, we identified four genes in the *B. cinerea* genome predicted to encode salicylate hydroxylases (SH), enzymes capable of catabolizing SA into catechol. SA degradation could promote virulence by reducing SA availability and weakening SA-dependent plant defenses, while catechol production may alter ROS homeostasis during infection. We therefore investigated whether BcShy1 contributes to *B. cinerea* virulence through SA catabolism and its effects on plant defense and redox balance

Materials and Methods: We focused on *Bcshy1,* highly similar to a previously described bacterial SH. BcShy1 was heterologously expressed, purified, and subjected to biochemical and kinetic characterization. Its contribution to pathogen virulence was evaluated in *plants* using wild-type *B. cinerea*, and strains overexpressing *Bcshy* or *NahG*, a well characterized model SH.

Results: Bcshy1 displayed SH activity, supporting its ability to catalyze SA conversion to catechol. Characterization of the activity was performed through kinematic assays. Preliminary infection assays showed that *Bcshy1* overexpression significantly increased disease severity compared with the wild-type strain. In parallel, ROS-related responses are being evaluated to determine whether Bcshy1-dependent SA metabolism is associated with changes in the oxidative environment of infected tissue.

Discussion: These results suggest that SA catabolism may represent an unexplored component of the infection strategy of *B. cinerea*. We propose that Bcshy1 may contribute to virulence not only by altering SA availability, but also by generating catechol and modifying ROS homeostasis. Biochemical characterization of Bcshy1 will help define its certain properties and clarify why a necrotrophic pathogen retains the capacity to metabolize SA during plant infection.

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P16. Effect of Oleic Acid on Palmitic Acid-Induced Cardiac Hypertrophy in Neonatal Rat Cardiomyocytes: Role of Perilipins.

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Introduction: Obesity and cardiovascular diseases (CVDs) have high incidence, prevalence, and mortality rates in Chile and worldwide. Sustained obesity promotes CVD development and may induce cardiac hypertrophy (CH), characterized by cardiomyocyte growth and changes in gene expression that can progress to heart failure (HF). Palmitic acid (PA), a saturated fatty acid elevated in obesity, promotes CH, although the intracellular mechanisms underlying this response remain incompletely understood. Oleic acid (OA), a monounsaturated fatty acid, has shown protective effects against PA-induced lipotoxicity in several cellular models, including neonatal rat ventricular myocytes (NRVMs). However, if OA protects against PA-induced CH, and the molecular mechanisms underlying this effect remain unclear. In addition, both fatty acids alter lipid droplet (LD) morphology and organization, processes regulated in part by perilipins (PLINs). Therefore, we hypothesize that OA attenuates PA-induced CH in NRVMs through changes in PLINs expression.
Materials and Methods: PA-induced hypertrophy in NRVMs was assessed by RT-qPCR analysis of hypertrophic markers and by measuring cell area and perimeter by immunofluorescence. LD accumulation was evaluated by confocal microscopy using BODIPY™ 493/503. PLIN2, PLIN3, and PLIN5 gene and protein expression were assessed by RT-qPCR and Western blotting, respectively.
Results: OA attenuated PA-induced hypertrophic phenotype by reducing the expression of hypertrophic markers (*BNP* and *RCAN1.4*), as well as cell area and perimeter. Additionally, OA increased LD accumulation and upregulated PLIN5 gene and protein expression compared with PA treatment.
Discussion: These findings demonstrate the antihypertrophic effect of OA against PA-induced hypertrophy in NRVMs, supporting its potential beneficial role in the context of obesity and CVDs. In addition, this effect may be associated with the modulation of LD accumulation and PLIN5 expression. However, this relationship must be confirmed using gene-silencing approaches.

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P17. *In silico* identification of candidate transcriptional regulators of the alternative polyadenylation machinery in the *Drosophila* central nervous system

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Introduction: Alternative polyadenylation (APA) generates mRNA isoforms with distinct 3′ untranslated regions (3′UTRs) through the cleavage and polyadenylation (CPA) machinery. APA exhibits circadian oscillations, and disruption of CPA factors alters core clock properties. However, the transcription factors (TFs) controlling CPA gene expression in clock neurons remain unknown. We therefore implemented an *in silico* strategy to identify candidate regulators of CPA genes in the *Drosophila* nervous system and determine whether they exhibit circadian oscillations.
Materials and Methods: The TF2TG database, designed to link transcription factors to their target genes in *Drosophila* and that integrate modENCODE/modERN ChIP-seq data, *cis*-regulatory motif predictions, and tissue-specific expression data, was used to identify TFs potentially regulating 14 genes encoding components of the CPA machinery, considering regions within 5 kb upstream of their transcription start sites. Candidates were subsequently cross-referenced with available circadian transcriptomic datasets to determine whether their expression exhibited rhythmicity across the day.
Results: The analysis initially identified 29 candidate TFs and was narrowed to 14 TFs after filtering according to ChIP-seq binding location. Integration with circadian rhythmicity analyses prioritized five TFs. Among them, *Pdp1*, *vri* and *Mef2* are established components of the circadian system. *HmgZ* emerged as a novel candidate that also exhibited circadian cycling, strengthening its prioritization as a potential CPA regulator. *CG9932* showed strong binding evidence, although its circadian cycling remains unconfirmed.
Discussion: These results identify candidate TFs that may provide a transcriptional link between the circadian network and CPA machinery. The convergence of regulatory predictions, ChIP-seq evidence, and circadian expression provide a framework for experimental validation. Future ongoing experiments will test direct TF-dependent regulation of CPA gene promoters and determine how TF knockdown affects CPA gene expression, APA, and locomotor circadian behavior in flies.

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P18 Exogenous iron treatment of plant embryos as an approach to undercover its acquisition-accumulation processes.
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Introduction: The grain filling processes occur during the embryo maturation stage, this include micronutrients like iron. Considering this and since the mechanisms of these processes have not been totally undercover, we propose a novel *in vitro* experimental model of dissected Arabidopsis embryos treated with containing iron solutions to study the entry and storage of this metal.
Materials and Methods: In this research wild type and B3 maturation mutants (*lec2-1*, *abi3-6* and *fus3-3*) dissected Arabidopsis embryos, treated with exogenous iron at different conditions like time, temperature (4°C - 23°C), iron chelators and hormones (ABA, GA3) were used to visualize iron localization by Perls-DAB staining.
Results: Dissected embryos are capable of acquiring exogenous iron in a time and concentration dependent manner. Iron entry occurs via active transport in its Fe^{2+} form. The acquired and accumulated iron is primarily cytoplasmic in all cell embryos, although in mutants it may also be located in the nucleus. Treatment with the hormones in wild type embryos showed that ABA changes iron distribution and GA_3 might impair exogenous iron acquisition.
Discussion: Together, these results demonstrate that the experimental model works, and when is complemented with different methodologies like Perls-DAB, allow to study the processes like iron acquisition and accumulation. Important unknown details of these were undercovered and opened the way to unveil exact mechanisms with future proteomic research.

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P19 Optogenetics: light for regulating the expression of a fungal glucoamylase in *Saccharomyces cerevisiae*
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Introduction: One of the major obstacles of heterologous gene expression is the balance between biomass generation and protein expression yield. To overcome the above, several expression control strategies have been implemented in *S. cerevisiae*, including chemically inducible promoters; nevertheless, these inducible promoters require the addition of a chemical inducer in the media, increasing the complexity and cost of the process. Recently, optogenetics has opened the possibility to control recombinant protein expression with high temporal and spatial resolution using light, a low-cost and highly flexible inducer.
Materials and methods: To assess the advantages of optogenetic regulation, a proof-of-concept expression platform was developed using the FUN-LOV switch to control the heterologous production of a *Neurospora crassa* glucoamylase in *Saccharomyces cerevisiae*. Glucoamylases are enzymes responsible for starch decay, and the selected enzyme was GLA-1, which is an *N. crassa* extracellular glucoamylase poorly studied. Glucoamylase activity was characterized from supernatants by measuring the increase in reducing power in reactions containing starch as a substrate under different culture media and induction light regimes. The biochemical properties, degree of expression induction, and enzyme purity were evaluated using DNS assays and SDS-PAGE, respectively.
Results: The induction of glucoamylase was dependent on the duration of light pulses. The enzyme shows an optimal temperature near 57 °C and optimal pH near 5. The purest protein sample was obtained from the YNB auxotrophic medium in comparison with the YPD medium culture.
Discussion: The results demonstrate the versatility of the optogenetic system for protein expression and provide a new enzyme expression system with potential use in biotechnological processes.

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P20 Characterization of the condensate formation properties of the DSUP protein from *Ramazzottius varieornatus.*
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Introduction: The Damage Suppressor (Dsup) protein from *Ramazzottius varieornatus* is an intrinsically disordered protein (IDP). IDPs frequently exhibit a high propensity to form biomolecular condensates via liquid-liquid phase separation (LLPS), regulating diverse cellular processes. Bioinformatic sequence analysis of Dsup reveals multivalent sites and a polyampholytic nature, characterized by a balanced distribution of charged residues, suggesting a capacity to assemble into condensates through homotypic interactions. This study aims to investigate the physicochemical determinants of Dsup phase separation and its structural properties.

Materials and Methods: Recombinant Dsup *in vitro* condensates assembly was evaluated using polyethylene glycol (PEG) as a molecular crowding agent. The influence of varying ionic strengths and DNA binding on condensate stability was systematically analyzed. To complement this, coarse-grained molecular dynamics simulations using the CALVADOS3 forcefield were performed to determine structural properties, such as the radius of gyration (R_g), in both dilute and dense phases, alongside the identification of predominant inter- and intramolecular contacts. Finally, the internal dynamics of the condensates, including diffusion coefficients and viscosity, were assessed using fluorescence microscopy.
Results: Dsup forms biomolecular condensates under simulated crowding. Ionic strength and DNA binding modulate condensate stability, as corroborated by CALVADOS simulations showing distinct structural compactness and contact networks. Fluorescence microscopy confirms fluid-like internal dynamics via diffusion and viscosity measurements.
Discussion: This study provides biophysical insights into Dsup phase separation. By characterizing physicochemical determinants and dynamic properties, we elucidate how ionic interactions, molecular crowding, and DNA binding govern Dsup condensate stability, highlighting the intrinsic mechanisms driving macromolecular assembly.

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P21 Unveiling the HIV-1 full-RNA RBPome in human microglia
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Introduction: HIV-1 persistence in microglia constitutes a major barrier to viral eradication and a driver of HIV-associated neurocognitive disorders (HAND). While binding of host RNA binding proteins (RBPs) to the HIV-1 full-length RNA (FL-RNA) has been studied in CD4+ T cells, the specific RBPome within the Central Nervous System (CNS) reservoir remains completely unknown. Since HIV-1 FL-RNA functions as a genome, mRNA, and Pathogen-Associated Molecular Pattern (PAMP), mapping its interactions in microglia is critical to understanding how the virus replicates, persists and triggers neuroinflammation.
Materials and Methods: We characterized the HIV-1 FL-RNA RBPome using C20 cells, a cell line model of adult human microglia, infected with the HIV-1 molecular clone NL4.3. Ribonucleoprotein (RNP) complexes were purified via RNA affinity capture targeting the HIV-1 full-length RNA. Associated host proteins were identified using mass spectrometry. Data were processed to classify proteins into high-confidence interactors and candidate interactors based on the false discovery rate value.
Results: We identified 1,057 host proteins that interact with the HIV-1 FL-RNA in human microglia. Data filtering revealed193 high-confidence and 868 candidate interactors. Strikingly, 187 (18%) of the identified proteins are not classified as canonical RNA-binding proteins (RBPs). Functional ontology analysis revealed that these non-canonical RBPs include metabolic enzymes, mitochondrial components, and immune response molecules. This indicates that HIV-1 RNA directly recruits factors involved in cellular metabolism and innate sensing, potentially to remodel the host environment for viral advantage. Furthermore, silencing of Rab32, one of the identified high-confidence non-canonical RBPs resulted in less viral replication as measured by Western blot and RT-qPCR.
Discussion: This study provides the first comprehensive map of the HIV-1 RNA interactome in a non-T-cell reservoir. The discovery of metabolic and immune factors binding directly to viral RNA suggests that HIV-1 may manipulate microglial function through its viral RNA to drive persistence and inflammation.

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P22. Identification of key metabolites for ZIKV and DENV replication in mosquito cells using a metabolic model.
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Introduction: Arthropod-borne viruses are expanding due to globalization and climate change. This, coupled with the increase in imported dengue cases and the detection of the Aedes aegypti mosquito in mainland Chile, compels us to promote approaches that allow us to understand virus-mosquito interactions from a transdisciplinary perspective. We have previously reported a validated metabolic model of the mosquito that includes a representation of ZIKV synthesis. However, the lack of differential expression data impedes a more precise characterization of the metabolic phenomena underlying infection.
Materials and Methods: Aedes albopictus C6/36 cells were infected with a Brazilian isolate of ZIKV generated using a reverse-genetic system. Baseline cell growth curves and infection kinetics were performed for metabolic analysis and modeling.
Results: We observed reduced cell viability by 3 days post-infection and over a 28% reduction in the specific growth rate in cells infected with ZIKV or DENV. We did not observe a significant increase in intracellular vRNA for ZIKV or DENV, nor an increase in ZIKV viral titer during infection. From metabolic analysis, we identified glucose (Glc) and galactose (Gal) as the main carbon sources, and glutamine (Gln) as the main nitrogen source consumed by the C6/36 cells. The calculated ratio of their specific consumption rates, qGal/qGlc, revealed differences among infected cells by virus type, while the qGln/qGlc ratio differed between infected cells and the control. We further identified significant differences in the amino acid profile between control and infected cells, with a marked increase in glycine and histidine consumption. By comparing cumulative amino acid consumption profiles, amino acid concentrations, and cell growth, we identified amino acids that may play a more relevant role during infection with specific viruses.
Discussion: Growth parameters and metabolic requirements for C6/36 cells in culture were determined. Results show that, despite exhibiting similar growth in culture, mosquito cells infected with DENV and ZIKV undergo distinct metabolic changes, suggesting infection-induced gene expression profiles specific to metabolic pathways.

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P23. Antiviral activity of a methanolic *Ramalina* sp. extract against HIV-1 *in vitro*.
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Introduction: Human Immunodeficiency Virus type 1 (HIV-1) infection remains a major global health concern, and the emergence of drug-resistant variants highlights the need for new antiviral compounds. Lichens are a promising source of bioactive secondary metabolites with reported antimicrobial and antiviral properties. The aim of this study was to evaluate the antiviral activity of a methanolic extract of *Ramalina* sp. against HIV-1 *in vitro* and to investigate its potential effect on early viral replication events.
Materials and Methods: HEK293T cells were used to determine the cytotoxicity of the methanolic *Ramalina* sp. extract by an MTS assay. Non-cytotoxic concentrations were subsequently evaluated using a VSV-HIV-1-Luc pseudotyped virus, and infection was quantified through firefly luciferase activity. To investigate early replication events, viral DNA intermediates, including positive-strand strong-stop DNA (PSS), minus-strand strong-stop DNA (MSS), and integrated viral reporter DNA (Ffluc), were analyzed by qPCR.
Results: The *Ramalina* sp. methanolic extract maintained cell viability above 80% at concentrations up to 0.25 mg/mL. Treatment with the extract produced a concentration-dependent reduction in VSV-HIV-1-Luc infection. Preliminary qPCR analyses showed a reduction in viral DNA-associated signals; however, further biological replicates are required to determine the specific early replication step affected by the extract.
Discussion: These results suggest that the methanolic *Ramalina* sp. extract possesses antiviral activity against HIV-1 in vitro, and support further investigation of its bioactive compounds and mechanism of action.

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P24. Ursodeoxycholic acid activates NRF2 and attenuates oxidative stress induced by deoxycholic acid and JC polyomavirus T antigen in colon cells.
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Introduction: Colorectal cancer (CRC) is one of the leading causes of cancer-related morbidity and mortality worldwide, with an increasing incidence in Chile, particularly among young adults. Several studies have reported an association between environmental and biological factors and its development, including chronic exposure to secondary bile acids such as deoxycholic acid (DCA), which is linked to oxidative stress, genetic damage, and genomic instability, and the presence of JC polyomavirus (JCPyV), whose T antigen (Ag-T) has been linked to alterations in cell proliferation and survival pathways. Although these associations do not establish a direct causal relationship, they suggest relevant mechanisms in tumor progression. In this context, ursodeoxycholic acid (UDCA), recognized for its cytoprotective, antioxidant, and chemopreventive properties, emerges as a key modulator. This study evaluates the effect of UDCA on NRF2 pathway activation and its ability to mitigate oxidative stress and genetic damage induced by DCA and JCPyV Ag-T in colonic epithelial cell models, providing evidence of its potential as a protective agent against mechanisms implicated in colorectal carcinogenesis.
Materials and Methods: SW480 and HT29 cells, either transfected or untransfected with JCPyV Ag-T, were treated with DCA and UDCA individually or in combination, using pre- and post-treatment regimens. NRF2/ARE activation was assessed using luciferase assays, while DNA damage was determined by γH2AX immunofluorescence and comet assays.
Results: UDCA, administered in pre- and post-treatment regimens, significantly increased NRF2 transcriptional activity compared with DCA treatment. Furthermore, co-exposure to UDCA and DCA significantly reduced γH2AX levels compared with DCA alone, indicating reduced DNA damage in both regimens.
Discussion: UDCA reduces DCA-induced genetic damage and enhances the NRF2-mediated antioxidant response, supporting its potential as a chemopreventive agent against mechanisms involved in colorectal carcinogenesis.

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P25 Nanopore-based epitranscriptomic profiling of HIV-1: simultaneous detection of m6A and seven additional RNA modifications during infection in human microglia

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Introduction: HIV-1 RNA carries epitranscriptomic modifications that may influence viral gene expression, infectivity, and innate immune sensing. Although m6A is the best-characterized modification in HIV-1 RNA, additional modifications may contribute to viral RNA biology. Here, we characterized the epitranscriptomic landscape of HIV-1 RNA during infection in a model of human microglia, focusing on m6A and seven additional RNA modifications.
Materials and Methods: Direct RNA sequencing was performed on three biological replicates of HIV-1 NL4-3-infected C20 cells using Oxford Nanopore PromethION R10.4.1 RNA004 chemistry. Reads were analyzed against the HIV-1 NL4-3 reference sequence AF324493.2. Modified-base detection was performed with Dorado v2.0.0 using the rna004_130bps_sup@v5.2.0 model and Modkit v0.6.3 (--call-prob 0.6). For m6A, candidate sites were assessed using a ≥10% methylation threshold and candidate sites for the seven additional modifications were retained using a ≥40% confidence threshold across biological replicates and corrected position-by-position against unmodified in vitro transcribed (IVT) viral RNA.
Results: Among 249 m6A consensus motifs (DRACH), eight high confidence m6A candidate sites were identified in the 3′ LTR, together with one quasi-DRACH site. Fully methylated IVT RNA supported reliable estimation of m6A stoichiometry at positions 8947, 8975, and 8989. Additional modification candidates were detected after position-specific correction against unmodified IVT-based. Gm was the most frequently detected modification, whereas m5C signals overlapping the m6A-rich 3′ LTR were consistent with composite artifacts rather than bona fide m5C. An inosine candidate provided a preliminary signal compatible with A-to-I RNA editing.
Discussion: These findings support a multi-modification epitranscriptomic landscape in HIV-1 RNA. Further orthogonal validation is required to determine whether these modified sites have functional relevance during HIV-1 replication.

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P26.Transcriptomic Identification and In Silico Characterization of PTGR1 in a Carboplatin-Resistant Ovarian Cancer Model.

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Introduction: Ovarian cancer is associated with high mortality due to late diagnosis, recurrence, and resistance to platinum-based chemotherapy. Among the mechanisms involved, metabolic reprogramming, particularly lipid metabolism, promotes tumor adaptation to pharmacological stress. PTGR1 regulate bioactive lipophilic metabolites involved in proliferation, differentiation, apoptosis, and stress responses. However, their contribution to carboplatin resistance remains poorly understood. This project aims to evaluate the roles of PTGR1 as potential mediator of therapeutic resistance and as pharmacological target in ovarian cancer.
Materials and Methods: RNA-seq data from parental A2780 and carboplatin-resistant A2780 (CBDCA-R-A2780) cells were processed using Trimmomatic, SortMeRNA, STAR (hg38), and featureCounts. Differential expression was assessed with DESeq2, with $|\log2FC| \geq 1$ and $p < 0.05$, followed by VST-based correlation and Gene Ontology enrichment. In parallel, hierarchical structure-based virtual screening of curated approved or late-stage clinical compounds against PTGR1 employed AutoDock Vina, protocol validation, consensus rescoring, interaction analysis, and prioritization of the top five candidates for in vitro validation.
Results: In cell lines, PTGR1 showed significant overexpression in resistant cells (log2FC = 1,21), supporting its involvement in acquired resistance. Molecular screening of 2,552 FDA-approved drugs against PTGR1 identified the top 100 candidates with the highest predicted binding affinity, which were subsequently prioritized based on physicochemical properties, ADMET profiles, tissue exposure, PK/PD relationships, and compatibility with carboplatin. Alitretinoin, ursodeoxycholic acid, and oxymetholone emerged as the leading candidates, showing favorable binding energies (−9.42, −9.67, and −9.15 kcal/mol, respectively), adequate ligand efficiency, and favorable pharmacokinetic profiles.
Discussion: The convergence of several bile acids among the highest-ranked candidates suggests consistent structural recognition by PTGR1. Considering the involvement of this enzyme in lipid mediator metabolism and mechanisms associated with chemoresistance, these findings support the repurposing of the selected compounds as potential modulators of carboplatin sensitivity, although their activity requires further experimental validation.

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P27. Identification of Candidate Transporters Associated with Alkaloid Translocation in *Lupinus luteus*

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P28 Functional analysis of LIM and CH domains of LIMCH1.

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Introduction: Agmatine, derived from the decarboxylation of L-arginine, participates in physiological processes such as neuroprotection, renal homeostasis, and insulin secretion. In mammals, it is degraded to putrescine and urea by the agmatinase-like protein (ALP), which corresponds to the C-terminal region of LIMCH1. ALP/LIMCH1 contains a LIM domain at its carboxyl terminus associated with protein-protein interactions. The removal of this domain increases its catalytic activity and decreases its Km, suggesting a possible autoinhibitory role. In addition, only LIMCH1 possesses a CH domain at its amino terminus. This study evaluated the participation of the LIM domain in the formation of protein complexes and the possible association of the CH domain with F-actin.
Materials and methods: The pCMV-ALP and pCMV-ΔLIM-ALP constructs were generated, verified by restriction and sequencing, and expressed in HEK293T cells. Complex formation was assessed by DSS crosslinking, immunoprecipitation, and LC-MS/MS. Subcellular distribution was analyzed by immunohistochemistry. Recombinant LIMCH1 was expressed in E. coli BL21(DE3) and partially purified. Its association with F-actin was assessed by in vitro sedimentation assays.
Results: Both proteins (ALP/ΔLIM-ALP) were expressed in HEK293T cells. DSS crosslinking revealed species of approximately 180 and 245 kDa exclusively in ALP, suggesting that the LIM domain participates in the formation or stabilization of protein complexes. Initial LC-MS/MS analyses identified the regulator of signaling protein G18 (RGS18) and septin 9 (SEPT9) as potential interacting proteins, and we are continuing to analyze the results. Both variants showed predominantly cytoplasmic and peripheral distribution, with no evident differences associated with the deletion of the LIM domain. Regarding the complete and recombinant LIMCH1 protein, in vitro assays indicated an apparent association with F-actin.
Conclusions: The results suggest that the LIM domain contributes to the formation or stabilization of protein complexes and provide preliminary evidence of a possible association between LIMCH1 and F-actin.

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P29. Morphodynamics of the Interplay Between Endocytosis and Autophagy During Osmotic Stress in *Arabidopsis thaliana.*
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P30. Structural and functional consequences of the evolutionary divergence of the N-terminal intrinsically disordered region of GOLPH3 oncoprotein family.
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P31. Integrated Directed Evolution and Multipoint Covalent Immobilization of *Bacillus subtilis* Chitosanase for the Modulated Enzymatic Depolymerization of Chitosan.
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Introduction: The enzymatic production of chitooligosaccharides (COS) via the depolymerization of chitosan is a highly specific, environmentally benign alternative to chemical processing. However, wild-type chitosanases are often limited by low thermal stability and poor product control during extended hydrolysis. This study performed directed evolution and multipoint covalent immobilization to enhance the stability, reusability, and hydrolytic modulation of a recombinant *Bacillus subtilis* GH46 chitosanase.

Materials and Methods: The *B. subtilis* chitosanase gene underwent three rounds of directed evolution via error-prone PCR to select variants with improved thermal resistance. The enzyme was then covalently attached to glyoxyl-activated agarose beads using a multipoint immobilization strategy. We evaluated hydrolysis performance, thermal stability at 55°C and 60°C, and overall reusability. We characterized the resulting depolymerization products from the enzyme variants and the immobilized biocatalysts by dynamic light scattering (DLS) and MALDI-TOF mass spectrometry.
Results: Directed evolution generated variants (such as MT3) with modified active-site cleft dynamics, yielding up to a 322.4% increase in V_{max} and a half-life exceeding 120 minutes at 60°C. Immobilization of the chitosanase onto glyoxyl-agarose further enhanced operational stability at pH
4.5 and 55°C, enabling sustained biocatalysis across 10 reuse cycles. Additionally, both MT3 and the immobilized biocatalyst modulated the enzymatic depolymerization process, producing a narrower, stable particle size distribution and a persistent low-degree-of-polymerization (DP2-DP4) chitooligosaccharide profile.
Discussion: Both directed evolution and glyoxyl-agarose immobilization successfully address the stability limitations of chitosanases. This dual approach not only stabilizes the biocatalyst for industrial reuse but also tailors enzymatic chitosan depolymerization to yield consistent, specific chitooligosaccharide profiles.

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P32 Early SALL2 loss drives tumor microenvironment remodeling in colonic adenomas

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Introduction: Colorectal cancer (CRC) progression involves genetic alterations in epithelial cells and in the tumor microenvironment (TME). Interactions among tumor cells, immune cells, fibroblasts, and the extracellular matrix contribute to an environment that supports tumor progression. Identifying factors involved in TME regulation is essential to understand CRC progression. SALL2 is a transcription factor described as a tumor suppressor in CRC, although its role in the TME remains poorly characterized. Interestingly, as with the *APC* gene, genetic alterations and downregulation of *SALL2* are found in precancerous colorectal polyps, suggesting that *SALL2* loss is an early event during CRC progression.
Objective/Hypothesis: To characterize the association between *SALL2* loss and immune and stromal TME alterations during early CRC progression. We hypothesized that early *SALL2* loss promotes an immunosuppressive microenvironment accompanied by stromal activation.
Methods: Early-stage CRC models were generated using colonoscopy-guided microinjection and CRISPR/Cas9-mediated gene editing into the distal colon of mice. Lesions with *Apc* loss (A) were compared with those harboring both *Apc* and *Sall2* loss (AS). Histological and immunohistochemical analyses evaluated immune cell infiltration and stromal activation. Transcriptomic analyses were integrated to identify candidate genes associated with Sall2-mediated immune regulation.
Results: Loss of *Sall2* was associated with TME alterations in polyps, including lower CD8+ T-cell infiltration, increased M2 and CD63 infiltration, and enhanced stromal activation, indicated by increased α-SMA-positive area. Integration of RNA-seq, ChIP-seq, and TCGA CRC datasets identified candidate genes associated with the immune response, including CCL2, CCL5, NFKBIA, CD74, and IL10, which may contribute to the immune alterations following *SALL2/Sall2* loss.
Conclusion: *Sall2* loss is associated with immune and stromal TME alterations. Candidate genes related to the immune response suggest that SALL2/Sall2 regulate transcriptional programs involved in communication between tumor cells and their microenvironment. Overall, these findings position early SALL2 loss as a potential event associated with an immunosuppressive tumor microenvironment.

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P33. Association between Stage II–III Periodontitis and Human Herpesvirus Viral Load in Adults from Los Ríos Region, Chile

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Introduction: Periodontitis is a chronic inflammatory disease driven by microbial dysbiosis and an altered host immune response. Beyond bacterial pathogens, human herpesviruses such as Epstein–Barr virus (EBV) and herpes simplex virus type 1 (HSV-1) have been suggested as cofactors that may influence disease progression. Their detection in saliva and gingival crevicular fluid (GCF) has been linked to increased periodontal severity, highlighting the need for population-specific studies. This work aimed to evaluate herpesvirus presence and viral load in saliva and GCF according to periodontal condition, as an initial step toward understanding their association with Stage II–III periodontitis in adults from the Los Ríos Region, Chile.
Materials and Methods: A cross-sectional study was conducted in adults aged 18–65 years from the Los Ríos Region, Chile. Periodontal and radiographic examinations were performed, followed by saliva and GCF collection. DNA was extracted using the Wizard® SV Genomic DNA Purification System and assessed by β-globin PCR. Conventional PCR was performed for EBV-BNRF1, and HSV-1. Participants were classified according to periodontal condition. Quantitative PCR will subsequently be performed to determine viral load.
Results: Preliminary molecular analyses included 17 patients in saliva and 15 in GCF. In saliva, EBV-BNRF1 in 58.8%, and HSV-1 in 52.9%. In GCF, detection rates were 46.7%, and 93.3%, respectively. Stratification by periodontal condition showed HSV-1 detection in GCF in 80.0% of participants without periodontitis and 100% of those with periodontitis. EBV-BNRF1 detection in saliva was similar between groups (57.1% vs. 60.0%).
Discussion: Preliminary findings reveal a high frequency of HSV-1 detection in GCF, particularly among participants with periodontitis. EBV-BNRF1 showed similar detection frequencies between periodontal groups in saliva. These findings support further investigation of herpesvirus–periodontitis relationships through quantitative viral load assessment and inferential statistical analyses.

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P34. Molecular Networks Linked to Poor Prognosis Reveal Candidate Genes in Gastric Cancer

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Introduction: Gastric cancer (GC) progression is driven by coordinated changes in gene expression and protein-interaction networks. Genes associated with unfavorable prognosis may converge on molecular programs relevant to tumor aggressiveness. This study aimed to identify poor-prognosis molecular networks in GC and determine whether prioritized network genes also show transcriptomic dysregulation.
Materials and Methods: Prognostic genes were obtained from The Human Protein Atlas. The 171 unfavorable-prognosis genes were analyzed by functional enrichment and protein–protein interaction mapping using Metascape and Cytoscape/ClueGO. Recurrent candidates were contrasted with RNA-seq data from TCGA and GTEx. Differential expression was assessed with DESeq2 using $|\log_{10}$ fold change$| \geq 1$ and adjusted $p < 0.05$, and visualized by volcano plot.
Results: Poor-prognosis genes were enriched in processes, including platelet degranulation and post-translational protein phosphorylation. Network analysis identified recurrent candidates, among which F5, FN1 and THBS1 were supported by transcriptomic evidence. F5 showed the strongest upregulation (fold change 4.4), FN1 showed a moderate increase (fold change 1.2), and THBS1 was downregulated (fold change −1.2); these patterns were maintained across stages I–IV. These genes encode proteins involved in coagulation, cell–matrix interactions, angiogenic regulation and tumor progression.
Discussion: The convergence of functional-network and transcriptomic evidence identifies F5, FN1 and THBS1 as a molecular subset associated with unfavorable GC prognosis. Their sustained dysregulation across stages supports further experimental evaluation of their contribution to gastric tumor biology. These candidates may also provide a basis for biomarker-oriented studies aimed at improving molecular stratification and identifying molecular vulnerabilities relevant to gastric cancer progression.

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P35 miR-21-5p and miR-148a-3p in Plasma Extracellular Vesicle (EVs) Promote Metabolic Disease in Women with Obesity, in Contrast to Lactadherin in EVs.

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P36. flg22 and Xyn11e Differentially Modulate Early Systemic Defense Gene Expression in Tomato.

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Introduction: Local recognition of microbe-associated molecular patterns can activate systemic defense signaling, but the timing and dose dependence of early distal responses remain poorly understood. We evaluated whether local application of bacterial flg22 and fungal Xyn11e modulates defense-related gene expression in untreated distal leaves of tomato cv. M82.

Materials and Methods: Selected leaves were sprayed with Mock, BION (0.05 g/L), flg22 (0.5, 2, and 200 µM), or Xyn11e (10 and 100 µg/mL). Untreated distal leaves were collected at 1 and 2 h post-application. Expression of *PR1a, PR1b, PI1, PI2, LoxD, ERF1,* and *Pti5* was quantified by RT-qPCR using *LeRPL8* as the reference gene. Data were analyzed using the Kruskal–Wallis test followed by post hoc multiple comparisons ($p < 0.05$).

Results: Among the seven genes analyzed, *PR1a, PI1,* and *ERF1* showed significant systemic responses. At 1 h, *PR1a* and *PI1* increased following flg22 at 0.5 and 200 µM and Xyn11e at 10 and 100 µg/mL. *ERF1* decreased with BION but increased with Xyn11e at 100 µg/mL. At 2 h, *PR1a* increased only with Xyn11e at 100 µg/mL, whereas *PI1* increased with flg22 at 200 µM and both Xyn11e concentrations. *ERF1* decreased following flg22 at 2 µM and Xyn11e at 100 µg/mL.

Discussion: Local flg22 and Xyn11e treatments rapidly modulated defense-gene expression in untreated distal leaves. The distinct responses of *PR1a, PI1,* and *ERF1* reveal elicitor-, dose-, and time-dependent modulation of early systemic defense signaling in tomato.

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P37. Structural Insights into the ECE1c–CCAR2 Interaction Through Molecular Docking and Phosphosite Mutant Analysis.

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Introduction: The Endothelin-Converting Enzyme-1 isoform c (ECE1c) has been associated with cancer aggressiveness, linked to phosphorylation of residues S18 and S20 located in its N-terminal domain, which increases its protein stability, however, the underlying molecular mechanism remains uncharacterized. Experimental evidence (IP-MS/MS) demonstrated an interaction between the N-terminal region of ECE1c and the protein Cell Cycle and Apoptosis Regulator 2 (CCAR2), which was favored by the superstable mutant $ECE1c^{K6R}$. Nevertheless, the specific structural interface mediating this interaction remains unknown. CCAR2 is implicated in the regulation of proliferation and cell survival, and its structure comprises distinct domains together with intrinsically disordered regions. Thus, this work aims to identify plausible conformations that allow the modulation of a hypothetical Phospho-ECE1c-CCAR2 interaction, establishing a basis for future experimental validation of the residues involved.

Materials and Methods: Structural modeling of ECE1c and CCAR2 was performed using ColabFold v1.6.2, followed by docking with Rosetta 3.15, AlphaFold 3, Boltz-2 and Disobind, evaluating the effect of different N-terminal mutations of ECE1c (S18A, S18D, S20A, S20D) on interaction with distinct CCAR2 domains. Models were assessed using energy-based metrics (pLDDT, ipTM, interface ΔG), identifying potential regions and residues involved in the interaction.
Results: Favorable models of the ECE1c–CCAR2 complex were identified, along with potential interaction regions. In addition, the analysis assessed whether differential energetic trends and interface variations existed as a function of ECE1c mutations, particularly the phosphomimetic and phosphorresistant mutants.
Discussion: These analyses allowed the proposal of key interaction residues within the ECE1c–CCAR2 complex and the determination of the impact of ECE1c mutations on complex formation, opening the possibility for future *in vitro* validation.

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P38. Metformin as a potential drug for breast cancer: a possible role in lipid metabolism in the context of excess saturated fatty acids.

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P39. Transcriptomic Analysis of Neuroactive Signaling in Colorectal Cancer: GABRD Associated with Reduced Survival.

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Introduction: The gut–brain axis is a bidirectional system that integrates neural, endocrine, immune, and microbial signals, in which neuroactive molecules, including neurotransmitters, neurotrophic factors, and neuropeptides, participate. These signals may influence tumor-related processes. In colorectal cancer (CRC), neuroactive signaling has been implicated in tumor development and progression; however, its expression patterns and association with survival remain incompletely characterized. This study aimed to evaluate the expression and survival association of genes related to neuroactive signaling in CRC.
Materials and Methods: RNA-seq raw count data were obtained from The Cancer Genome Atlas (TCGA) (n = 719) and Genotype-Tissue Expression (GTEx) (n = 898). Differential gene expressions were assessed using DESeq2 (v1.36.0) in R (v4.2.1). Overall survival was estimated using Kaplan–Meier analysis. Univariable and multivariable Cox proportional hazards regression models were used to evaluate the prognostic significance of gene expression and clinical covariates.
Results: Of 108 genes evaluated, 82 were differentially expressed in colorectal tumors compared with normal tissue, including 14 upregulated and 68 downregulated genes. Univariable Cox regression identified genes significantly associated with increased or decreased risk. Integration of differential expression and survival analyses highlighted GABRD, encoding the δ subunit of the GABA type A receptor, which was upregulated in tumors ($\log_2$FC = 1.61) and associated with increased risk (HR = 1.56; 95% CI: 1.29–1.91; $p < 0.001$). Kaplan–Meier analysis consistently showed that high GABRD expression was significantly associated with reduced survival ($p < 0.0001$).
Discussion: Increased GABRD expression and reduced survival suggest that altered GABAergic signaling may be relevant to CRC progression. However, causality remains to be established, and functional studies are needed to determine its role in tumor aggressiveness and its potential as a prognostic biomarker or therapeutic target.

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P40. Microtubule Disruption and DYRK2-Dependent PSMC1 Phosphorylation Mediate SRF Accumulation in Poldip2-Deficient Vascular Smooth Muscle Cells.

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Introduction: Maintenance of the differentiated vascular smooth muscle cell (VSMC) phenotype protects against pathological vascular remodeling. We previously showed that deficiency of the mitochondrial protein Poldip2 disrupts the microtubule cytoskeleton and promotes VSMC differentiation. This response involves serum response factor (SRF) accumulation through inhibition of a nuclear proteasome, potentially mediated by reduced phosphorylation of the proteasomal ATPase PSMC1. However, the upstream kinase and the role of microtubule dynamics remain unknown. We investigated whether PSMC1 phosphorylation is mediated by DYRK2 and whether microtubules contribute to Poldip2-dependent VSMC differentiation.
Materials and Methods: Human aortic smooth muscle cells were transfected with Poldip2-targeting or control siRNA. Microtubule organization was evaluated by β-tubulin immunofluorescence. SRF accumulation following Poldip2 depletion was assessed by Western blotting in the presence or absence of the microtubule-stabilizing agent Taxol. PSMC1 phosphorylation was evaluated following siRNA-mediated DYRK2 depletion.
Results: Poldip2 depletion disrupted the microtubule network. Microtubule stabilization with Taxol prevented the increase in SRF abundance induced by Poldip2 deficiency. Furthermore, PSMC1 was phosphorylated under basal conditions, whereas DYRK2 depletion markedly reduced its phosphorylation.
Discussion: These findings identify microtubule destabilization as a component of Poldip2-dependent SRF accumulation and support DYRK2 as an upstream regulator of PSMC1 phosphorylation. Together, the results suggest a signaling axis connecting Poldip2, microtubule dynamics, DYRK2-dependent proteasome regulation, and SRF accumulation. Further studies are required to determine whether microtubule disruption directly regulates DYRK2 activity and PSMC1 phosphorylation following Poldip2 depletion.

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P41. Characterization of Protein Hydrolysates Biostimulants Made from Food Industry Wastes in Arabidopsis, Tomato and Lettuce.

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P42. *In vitro* evaluation of the effect of propolis extract on the mycelial growth of *Saprolegnia spp*.

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Introduction: Saprolegniasis is one of the major diseases affecting freshwater aquaculture in Chile. It is caused by oomycetes of the genus *Saprolegnia* and is associated with significant economic losses in salmonid production. Restrictions on the use of conventional chemical treatments have increased the search for safer and more sustainable alternatives for its control. The aim of this study was to evaluate the *in vitro* inhibitory effect of a propolis extract from the Biobío region on the mycelial growth of *Saprolegnia spp.*
Materials and Methods: Radial mycelial growth was evaluated in a *Saprolegnia* isolate cultured on potato dextrose agar (PDA) and exposed to propolis extract at concentrations of 0.8, 1.0, and 1.5 mg/mL for 48 h at 20 ± 1 °C. Formalin (0.02%) was included as a positive control, while DMSO was used as a solvent control and untreated PDA as a negative control. Differences among treatments were assessed by one-way analysis of variance (ANOVA), followed by Tukey's multiple comparisons test ($p < 0.05$).
Results: Propolis extract significantly inhibited mycelial growth compared with the controls ($F(5,12) = 42.8$; $p < 0.001$). The

inhibition rates were 100%, 91.1%, and 81.7% at 0.8, 1.0, and 1.5 mg/mL, respectively, with the highest inhibitory effect observed at 0.8 mg/mL.
Discussion: These findings may indicate that Biobío propolis extract inhibits the *in vitro* mycelial growth of *Saprolegnia* spp., supporting its potential as a natural alternative for the control of this oomycete in aquaculture. Further studies are needed to elucidate the mechanisms underlying their inhibitory activity and to assess effectiveness under more complex experimental conditions.

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P43. Role of the Mitochondrial Antiviral Signaling Protein (MAVS) in Palmitic Acid-Induced Cardiomyocyte Hypertrophy
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Introduction. Obesity is a major risk factor for cardiovascular disease and promotes cardiomyocyte hypertrophy (CH) through metabolic and inflammatory remodeling that ultimately compromises cardiac function. Palmitic Acid (PA), a saturated fatty acid elevated in obesity, has been shown to promote CH; however, the intracellular signaling mechanisms linking lipid overload to hypertrophic and inflammatory responses remain incompletely understood. Beyond its canonical antiviral function, the mitochondrial antiviral signaling protein (MAVS) has recently emerged as a regulator of cardiomyocyte homeostasis. Whether PA-induced metabolic stress modulates MAVS signaling and how MAVS-dependent inflammatory pathways contribute to CH are still unknown. We hypothesized that MAVS links PA-induced metabolic stress to pro-inflammatory signaling during CH.
Materials and Methods. To induce metabolic stress *in vivo*, male C57BL/6J mice were fed either a high-fat diet (HFD) or a control diet. *In vitro* cardiomyocyte hypertrophy was induced in neonatal rat ventricular myocytes (NRVM) treated with increasing doses of PA. Cardiac remodeling was assessed by determining the heart weight-to-tibial length ratio. In both models, MAVS expression, hypertrophic and inflammatory markers were analyzed by RT-qPCR or Western blotting. In NRVM, these analyses were complemented by immunofluorescence.
Results. HFD-fed mice were accompanied by increased expression of *Ifn-β* gene as an inflammatory marker, while cardiac MAVS protein levels were decreased. In NRVM, PA treatment induced a hypertrophic phenotype, as evidenced by increased cell size and upregulation of the hypertrophic markers BNP and RCAN1.4. This was accompanied by a robust inflammatory response, characterized by decreased MAVS protein levels and elevated expression of pro-inflammatory genes, including *Il-6*, *Il8, Ccl2,* Il-1β and *Ifn-β.*
Discussion: Our findings support a potential role for MAVS in obesity-associated cardiomyocyte hypertrophy by linking lipid overload to pro-inflammatory signaling. The consistent reduction in MAVS protein abundance in both *in vitro* and *in vivo* models, together with the absence of changes in MAVS mRNA, suggests that MAVS may be regulated at the protein level under both acute lipotoxic and chronic metabolic stress. Together, these findings highlight MAVS as a potential mediator of obesity-associated cardiac inflammation and provide a basis for future mechanistic studies of its role in lipotoxic cardiac hypertrophy.

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P44. AI-Assisted Stomatal Phenotyping of Water-Deficit Responses in Arabidopsis Using Low-Cost Optical Microscopy
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Introduction: Water deficit limits plant productivity and requires rapid phenotyping strategies to characterize plant responses. Stomatal traits are essential because aperture and functional state (opened or closed) rapidly reflect changes in plant water status. However, conventional stomatal phenotyping relies on labor-intensive microscopy and time-consuming manual measurements. Here, we integrated controlled water deficit experiments, low-cost optical microscopy and artificial intelligence (AI) to automate stomatal phenotyping.
Materials and Methods: *Arabidopsis thaliana* plants were subjected to progressive water deficit and sampled at days 0, 6 and 9. Epidermal impressions from the abaxial leaf surface were obtained and imaged by optical microscopy, generating high-resolution images under controlled experimental conditions. These images were integrated with additional *Arabidopsis* and *Cicer arietinum* public datasets to train YOLO-based models for stomatal detection, segmentation and functional classification as open or closed.
Results: The detection model achieved 96.8% precision, 95.6% recall and an mAP@0.50 of 0.985. The optimized segmentation model reached 90.6% recall and an mAP@0.50:0.95 of 0.806. In an independent *Arabidopsis* dataset, the automated pipeline identified open stomata with 95.37% precision and closed stomata with 83.28% precision. The system also extracted morphological and spatial traits in approximately 17 seconds per image, compared with 3-5 minutes for manual analysis.
Discussion: These results connect experimentally generated water-deficit phenotypes with automated image analysis, providing a fast and scalable approach for stomatal phenotyping. The pipeline reduces manual processing while preserving biologically relevant information, supporting the study and early detection of plant responses to water deficit.

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P45. Self-assembling viral nanoparticles for targeted therapy in colorectal cancer

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Introduction: Colorectal cancer (CRC) is one of the deadliest neoplasms in Chile and globally, and is primarily diagnosed at advanced stages, with approximately 50% of cases at stage IV. Metastatic CRC has a high mortality rate, highlighting the urgent need for targeted therapies capable of selectively eliminating tumor cells without affecting healthy tissue. The constitutive activation of oncogenic signaling pathways, characteristic of advanced CRC, is a key therapeutic target for the design of genetic vectors that specifically activate programmed cell death mechanisms in malignant cells. Furthermore, the selective elimination of these cells could help reverse the immunosuppressive tumor microenvironment. The objective of this study is to evaluate the effect of self-assembling viral nanoparticles carrying therapeutic constructs regulated by oncogenic pathways on the viability of colon cancer cells in the presence of activatable prodrugs.
Materials and Methods: Recombinant systems were used to obtain capsid proteins that self-assemble into viral nanoparticle-like structures. In parallel, genetic constructs were designed to include therapeutic sequences regulated by oncogenic signaling pathways to evaluate their specific activation in tumor cells. The nanoparticles were characterized using standard biophysical and molecular techniques to confirm their assembly and ability to incorporate genetic material.
Results: The formation of self-assembling viral nanoparticles was confirmed in the analyzed samples. Furthermore, an increase in the expression of therapeutic transcripts was observed in relation to oncogenic pathway activity, suggesting transcriptional control that depends on the tumor context.
Discussion: Taken together, the results demonstrate the functionality of the essential elements for the development of a self-assembling viral platform with anticancer potential.

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P46. Detection of the co-presence of secondary bile acid-producing bacteria and JC polyomavirus in proliferative colon lesions from Chilean patients.

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Introduction: Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer death worldwide, with rising incidence in Chile among young adults. Emerging factors include JC polyomavirus (JCPyV), whose large T antigen (AgT) is detected more frequently in tumor tissue, and deoxycholic acid (DCA), produced by bacteria such as *C. scindens* and *P. hiranonis*, which activates proliferative pathways (NF-κB, Wnt/β-catenin) and may promote genomic instability. This project evaluates the co-presence of both in proliferative colon lesions.
Matherials and Methods: Histological formalin-fixed paraffin-embedded (FFPE) colon samples from proliferative lesions were obtained from Hospital Regional of Temuco and Hospital Base of Valdivia. DNA was extracted using protocols optimized for FFPE. PCR was performed for AgT-JCPyV, generic polyomaviruses, and the *baiE* gene (a marker of DCA-producing bacteria), with products visualized by agarose gel electrophoresis. Given the limited bacterial detection expected in FFPE tissue, later stages will assess secondary bile acid levels and bacterial DNA in stool samples.
Results: A positivity rate of 21% for AgT-JCPyV and 43% for generic polyomaviruses was found per sample processed. PCR for DCA-producing bacteria has been completed in 15% of samples to date, showing 1% positivity for *P. hiranonis* and 0% for *C. scindens*.
Discussion: The AgT-JCPyV positivity is consistent with international evidence linking its expression to increased CRC risk. Bacterial PCR is still ongoing (15% of samples completed), and the low *P. hiranonis* and *C. scindens* positivity observed so far may reflect this limited sample size together with expected constraints on bacterial DNA detection in FFPE tissue. Fecal samples and HPLC-based DCA quantification will complement this analysis.

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P47. Divergent Remodeling of Mitochondria-ER Contact Sites Drives Senescent Phenotype in Proliferative versus Post-Mitotic Cells during Therapy-Induced Senescence

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Introduction. Therapy-induced senescence (TIS) is a frequent outcome of anticancer treatments such as doxorubicin. While senescence is classically defined by stable cell-cycle arrest and acquisition of a senescence-associated secretory phenotype (SASP); organelle dysfunction and remodeling are also key features, particularly since some cells can display senescent traits without conventional cell-cycle arrest. However, these alterations may be highly cell-type specific. Mitochondria–endoplasmic reticulum contact sites (MERCS) regulate cellular homeostasis and survival, yet whether the structural adaptations observed in proliferative cells are conserved in post-mitotic cardiomyocytes, where senescence is associated with pathological hypertrophy, remains unclear.

Materials and Methods. We compared Doxorubicin-induced senescence in human lung fibroblasts (IMR90) and primary neonatal rat ventricular myocytes (NRVMs). Senescence was validated by p16/p21 immunoblotting and SA-β-galactosidase activity. MERCS remodeling in fibroblasts was assessed by Proximity Ligation Assays (PLA) for IP3R1/VDAC1, transmission electron microscopy (TEM), and mitochondrial Ca^{2+} uptake (Rhod-2). In NRVMs, we assessed cardiomyocyte hypertrophic remodeling and analyzed MERCS-tethering proteins by Western blotting to determine whether structural remodeling is conserved in a post-mitotic context.
Results. In IMR90 fibroblasts, TIS induced a structural reinforcement of the ER-mitochondria interface, evidenced by enhanced IP3R1/VDAC1 interaction and confirmed by TEM, which revealed increased MERCS coverage and reduced inter-organelle distance. This tightening was associated with limited mitochondrial Ca^{2+} uptake. In contrast, TIS in NRVMs induced robust senescence markers and hypertrophy. Preliminary immunoblotting indicates distinct alterations in MERCS-tethering proteins, suggesting that organelle communication remodeling in post-mitotic cardiomyocytes diverges from the adaptive response observed in fibroblasts.
Discussion. These findings support the concept that ER-mitochondria remodeling during TIS is cell-type dependent. While proliferative cells undergo a structural reinforcement of MERCS as an adaptive response, post-mitotic cardiomyocytes develop a senescent-hypertrophic phenotype associated with a divergent regulation of contact site components. Understanding these responses may guide cardioprotective strategies to limit therapy-induced cardiomyocyte senescence and pathological remodeling.

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P48. Tumor microenvironment heterogeneity across mismatch repair deficiency patterns in colorectal cancer: beyond MLH1 loss.
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Introduction: Mismatch repair (MMR) deficiency in colorectal cancer (CRC) is defined by loss of one or more MMR proteins (MLH1, MSH2, MSH6, or PMS2) detectable by immunohistochemistry (IHC). MMR protein loss patterns carry diagnostic significance: MLH1/PMS2 co-loss suggests sporadic methylation or Lynch Syndrome due to MLH1 germline mutation, while MSH2/MSH6 or MSH6/PMS2 loss points toward Lynch Syndrome from other germline mutations. Characterizing MMR IHC loss patterns alongside clinical, pathological, and AI-derived tumor microenvironment (TME) data provides comprehensive Lynch-like risk stratification. This study describes and compares clinicopathological and AI-quantified TME profiles across distinct MMR IHC loss patterns in a regional CRC cohort.
Materials and Methods: Anonymized institutional data from HGGB included IHC for all four MMR proteins, MSI signs, sex, age, tumor side, TNM staging, histology, and tumor grade. MMR loss patterns were classified as: (1) MLH1/PMS2 co-loss; (2) MSH2/MSH6 co-loss; (3) isolated MSH6 loss; (4) isolated PMS2 loss; (5) MMR-proficient. TumorQuantAI analysis quantified TME components per case. Kruskal-Wallis, chi-square, and logistic regression modeled group differences and predictors of each loss pattern.
Results: MLH1/PMS2 co-loss was the most frequent MMR-deficient subtype. Each pattern showed distinct clinicopathological profiles: MLH1/PMS2 cases concentrated in right-sided, higher-grade tumors. AI-derived TME analysis revealed pattern-specific immune infiltration, with highest lymphocyte density in MLH1/PMS2 co-loss cases. Vascular density also differed across patterns, with MLH1/PMS2 tumors exhibiting reduced intratumoral blood vessel density versus MMR-proficient cases, suggesting distinct angiogenic remodeling.
Discussion: MMR IHC pattern analysis combined with AI-derived TME quantification generates a clinically actionable Lynch-like risk stratification model. Characterizing immune infiltration and vascular remodeling across loss patterns enriches molecular diagnosis and supports prioritization for germline sequencing and genetic counseling. This integrated approach informs immunotherapy eligibility, positioning AI-assisted TME profiling as an oncology tool in regional centers where hereditary CRC remains undercharacterized.

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P49. Caveolin-1-dependent PAI-1 inclusion in adipocyte-derived extracellular vesicles promotes pro-angiogenic responses in endothelial cells.
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Introduction: Adipocyte-derived extracellular vesicles (EVs), key mediators of intercellular communication, transfer bioactive molecules that modulate recipient cell function. Caveolin-1 (CAV1), a protein highly expressed in adipose tissue, has been implicated in regulating EV protein composition. Here, we investigated whether CAV1-dependent changes in the protein cargo of adipocyte-derived EVs contribute to their pro-angiogenic activity in endothelial cells.
Methods: Human SW872 cells were differentiated into adipocytes, and stable shCAV1 and shLUC populations were generated by lentiviral transduction. EVs were isolated from conditioned media of WT, shLUC, and shCAV1 adipocytes and characterized by nanoparticle tracking analysis and Western blotting. Their protein cargo was analyzed by shotgun mass spectrometry. EV-associated protein topology was examined using a proteinase K protection assay. To assess the functional role of specific proteins, EVs were preincubated with pharmacological inhibitors before evaluating their effects on EA.hy926 endothelial tube formation.
Results: Adipocyte-derived EV preparations were enriched in vesicles <200 nm and positive for canonical EV markers. Proteomic profiling revealed CAV1-dependent changes in EV protein composition, identifying PAI-1 among the proteins most significantly reduced in shCAV1 EVs. Western blotting confirmed lower PAI-1 levels in EVs from CAV1-deficient adipocytes. Proteinase K assays suggested that PAI-1 was present both on the EV surface and within the vesicular lumen. WT and shLUC EVs increased endothelial tube formation, whereas for shCAV1 EVs pro-angiogenic activity was reduced. Preincubation of WT EVs with tiplaxtinin, a PAI-1 inhibitor, markedly attenuated their ability to enhance endothelial network complexity.
Discussion: These findings suggest that adipocyte CAV1 expression enhances the pro-angiogenic activity of adipocyte-derived EVs by promoting PAI-1 inclusion. Thus, CAV1-dependent EV cargo regulation is identified here as a mechanism through which adipocytes control endothelial angiogenic responses.

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P50. Molecular Characterization and Stability Profiling of an Interfering Oligonucleotide for Cancer Therapy
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Introduction: Interfering oligonucleotides are promising molecular tools for specifically modulating gene expression and protein function associated with cancer development and progression. However, their therapeutic application depends on sequence specificity, concentration, molecular integrity, and stability under different experimental conditions. This study aimed to design and characterize an interfering oligonucleotide and evaluate its stability for potential application in cancer therapy.
Materials and Methods: Oligonucleotides were designed using bioinformatic tools, considering complementarity to the target sequence, length, and nucleotide composition. Sequence specificity was assessed using BLAST to confirm correspondence with the selected target and identify potential nonspecific matches. Stability was evaluated by monitoring changes in concentration and molecular mass profiles at different storage times and temperatures. Single-stranded DNA concentration was determined by fluorometric quantification using the Qubit™ ssDNA assay. Samples were also analyzed by *mass photometry* to estimate apparent molecular mass, characterize molecular populations, assess sample homogeneity, and detect potential aggregation or degradation.
Results: Oligonucleotide concentration was measured using Qubit™ ssDNA at 0, 15, 30, and 60 days of storage. These data are currently being analyzed to identify variations associated with storage time and temperature. *Mass photometry* characterized the molecular populations present, revealing species consistent with degradation and aggregation. It also enabled estimation of apparent molecular mass, comparison with the theoretical value, and assessment of sample homogeneity.
Discussion: These preliminary results provide an initial characterization of oligonucleotide behavior and stability over time under different storage conditions. Identifying conditions that preserve concentration, molecular integrity, and molecular population distribution is essential for establishing optimal storage and handling parameters. This characterization may support future preclinical evaluation and the development of more stable formulations for potential application in cancer therapy.

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P51. Modulation of CD8+ T-cell Functionality through the Oncogenic Interaction between MYC and NSD3S in Colorectal Cancer.

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Introduction: Colorectal cancer is a molecularly heterogeneous disease whose progression is influenced by the interaction between tumor cells and the immune microenvironment. Among tumor-infiltrating immune cells, CD8+ T cells play a key role, although their antitumor activity can be modulated by oncogenes. In this context, MYC plays an important role in tumor and immune regulation and can be stabilized by NSD3S, a protein also associated with oncogenic processes. Thus, the MYC–NSD3S interaction may regulate the expression of immunomodulatory molecules and influence T-cell responses.
Materials and Methods: HT29 NSD3SWT and HT29 NSD3SΔ15 colorectal cancer cell lines were used in a doxycycline-inducible model designed to investigate the interaction between MYC and NSD3S. The Δ15 variant contains a deletion within the NSD3S region involved in its interaction with MYC. The expression of immunomodulatory molecules in tumor cells, including PD-L1, was evaluated by flow cytometry and RT-qPCR.
Results: Higher PD-L1 expression was observed in HT29 NSD3SWT cells compared with HT29 NSD3SΔ15 cells, consistent with the results obtained by flow cytometry, which also showed increased PD-L1 expression in the NSD3SWT condition. The functional relevance of the MYC–NSD3S interaction was further assessed using co-cultures of HT29 WT or Δ15 cells with CD8+ T cells. The absence of the MYC–NSD3S interaction was associated with changes in the immunomodulatory capacity of tumor cells and in CD8+ T-cell responses.
Discussion: The results demonstrate higher PD-L1 expression in HT29 NSD3SWT cells compared with HT29 NSD3SΔ15 cells in colorectal cancer. These findings support the hypothesis that the oncogenic interaction between MYC and NSD3S may contribute to the establishment of a more immunosuppressive tumor phenotype, thereby potentially favoring tumor progression.

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P52. Characterization of innexin expression across aphid species, developmental stages, and insecticide resistance profiles: as potential molecular targets for novel aphid control strategies.

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P53 Functional Interaction between T Antigen of JC Polyomavirus and *Campylobacter jejuni* CDT+ to Promote Genetic Damage in Human Colon Cells.

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Introduction: Colorectal cancer (CRC) remains a major global and national health challenge. Despite extensive research, its underlying mechanisms remain poorly elucidated. Viral pathogens such as JC polyomavirus (JCV) have been detected in up to 93% of CRC samples. The viral protein Large T antigen (TAg) is implicated in tumorigenesis by promoting cell proliferation and inhibiting apoptosis through the sequestration of cellular proteins. However, viral infection alone is insufficient to induce neoplasia, suggesting the involvement of additional cofactors. Among bacterial pathogens, Campylobacter jejuni has gained attention for its genotoxin, cytolethal distending toxin (CDT), which directly induces DNA damage. Based on this evidence, we hypothesize that the combined presence of JCV and *C. jejuni* synergistically enhances DNA damage in colon epithelial cells.
Materials and Methods: Human colon cancer cells (SW480) and normal colon epithelial cells (CCD841 WT) were exposed to *C. jejuni* total protein lysate, transfected with CdtB (the catalytic subunit of CDT), and/or transfected with TAg or the complete JCV genome. Cellular viability was assessed by MTT assay, while DNA damage was evaluated through γ-H2AX Western blotting and comet assay.
Results: In SW480 cells, the minimum lethal dose of bacterial lysate was 1 μg/mL. Treatments combining bacterial lysate or CdtB with TAg or JCV transfection resulted in a marked increase in γ-H2AX expression and DNA damage compared with controls.
Discussion: Our findings indicate that DNA damage is significantly enhanced by the co-presence of JCV and *C. jejuni* in colon cell lines, supporting the hypothesis of a synergistic interaction between viral and bacterial pathogens in colorectal carcinogenesis.

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P54. Pharmacological Activation of ClpP by TIC10 Induces HSF1 and HSP27 and Protect Intestinal Barrier Integrity Under Inflammatory Conditions.
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Introduction: Disruption of the intestinal epithelial barrier is a hallmark of inflammatory gastrointestinal diseases. Heat-shock proteins contribute to epithelial proteostasis and barrier integrity. Caseinolytic mitochondrial matrix peptidase proteolytic subunit (ClpP) is a mitochondrial serine protease involved in protein quality control and mitochondrial stress signaling. TIC10 is a pharmacological activator of ClpP; however, whether it modulates the cytosolic HSF1/HSP27 stress-response pathway and protects intestinal barrier function remains unknown. We therefore evaluated the effects of TIC10 on HSF1/HSP27 signaling in intestinal epithelial cells and on intestinal permeability in a zebrafish model of diet-induced inflammation.
Materials and methods: Cytosolic (C), mitochondrial (M), and nuclear (N) cell fractions were prepared from intestinal epithelial cells treated with TIC10 (1 μM, 48 h) and analyzed by Western blot for heat shock factor 1 (HSF1) and p-HSF1 levels. HSP27 protein expression was evaluated in cell lysates following TIC10 treatment, as well as in cells transfected with siRNA against ClpP (siClpP) or CLPX (siCLPX). In vivo, 5 dpf zebrafish larvae were fed either a fishmeal (FM) control diet or a soybean meal (SBM) diet in the presence or absence of TIC10 (2 μM) until 9 dpf. Intestinal permeability was quantified by Texas Red dextran microgavage and fluorescence diffusion measurement using confocal microscopy.
Results: Western blot analysis of cell fractions showed that TIC10 treatment (1 μM) leads to the phosphorylation and translocation of HSF1 to the nuclear fraction (N). In whole-cell lysates, TIC10 increased HSP27 protein levels. Conversely, siRNA knockdown of ClpP or CLPX reduced HSP27 expression, indicating that HSP27 levels depend on ClpP and CLPX. In vivo, zebrafish larvae fed the SBM diet showed a significant increase in intestinal permeability compared to FM controls ($p<0.0001$). Co-administration of TIC10 significantly reduced SBM-induced dextran diffusion, restoring fluorescence intensity to levels comparable to the control group ($p<0.0001$, N=10-14).
Discussion: TIC10 activates HSF1-associated signaling, increases HSP27 abundance through a mechanism involving ClpP and CLPX, and attenuates diet-induced intestinal hyperpermeability. These results identify an association between mitochondrial ClpXP activity, the HSF1/HSP27 stress-response pathway, and preservation of intestinal barrier function. Further studies are required to establish whether HSF1/HSP27 signaling directly mediates the barrier-protective effect of TIC10.

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P55. Transcriptional Regulation of *FER2* During Embryogenesis and Its Response to Iron Availability in *Arabidopsis thaliana.*

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Introduction. Ferritin2 (FER2) is an iron-storage protein that contributes to iron homeostasis and protection against iron-induced oxidative stress in plants. In *Arabidopsis thaliana*, *FER2* expression is strongly associated with seed development during late embryogenesis. We investigated the transcriptional regulation of *FER2* by characterizing promoter activity during embryogenesis and evaluating its response to iron availability and its expression in mutants of key seed maturation transcription factors.
Materials and Methods. Transgenic *Arabidopsis thaliana* lines carrying p*FER2::GUS* reporter constructs were used to evaluate the spatial and temporal activity of the *FER2* promoter during different stages of embryogenesis and plant organs. To evaluate the response to iron availability, embryos were incubated under increasing iron concentrations and subsequently analyzed for GUS activity. In addition, p*FER2::GUS* lines were crossed with mutants affected in the transcription factors ABI3 and FUS3, which are key regulators of seed maturation.
Results. *FER2* promoter activity increased progressively during the later stages of embryo development. Increased iron availability enhanced GUS activity, indicating that *FER2* transcription responds positively to iron supply. In contrast, genetic backgrounds *abi3* and *fus3* showed reduced GUS activity, suggesting that these transcription factors contribute to the activation of *FER2* expression during embryo maturation.
Discussion. The results indicate that *FER2* transcription is dynamically regulated during embryogenesis and integrates developmental and possible iron-related signals. The reduced promoter activity observed in *abi3-6* and *fus3-3* backgrounds supports a regulatory relationship between these seed maturation factors and *FER2* expression. Whether ABI3 and FUS3 directly regulate the *FER2* promoter or act through downstream regulatory pathways remains to be determined.

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P56. Strain-Dependent Sensitization of Cisplatin-Resistant Gastric Cancer Cells by Lactic Acid Bacteria-Derived Cell-Free Supernatants.

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Introduction: Gastric cancer (GC) is the fifth most diagnosed cancer and fifth leading cause of cancer-related mortality worldwide, with most patients diagnosed at advanced stages, where chemoresistance limits cisplatin (CDDP) efficacy. Lactic acid bacteria (LAB) and their metabolites from cell-free supernatants (CFS) have demonstrated anticancer potential via apoptosis induction, proliferation inhibition, and enhancement of chemotherapeutic responses. The aim of this work was to determine if CFS derived from two different species of LAB can modulate the response of CDDP-resistant GC cells.
Materials and Methods: CFS from *Weissella viridescens* UCO-SMC3 and *Lacticaseibacillus paracasei* L100 were evaluated in AGS-RCDDP and SNU-638 cells. Cell viability was assessed by MTT after 72 h of treatment with CFS alone or combined with CDDP. CDDP sensitivity was evaluated by determining IC_{50} values and the resistance index (IR). The combined effects of CFS and CDDP were further assessed in 3D spheroids derived from AGS-RCDDP and SNU-638 cells using CellTiter 96 and in wound-healing assays at 24 and 48 h. To characterize the stability of bioactive components, CFS were subjected to trypsin, proteinase K, or heat treatment before cell exposure.
Results: Combined CDDP+CFS treatment reduced the CDDP IC50 and significantly decreased the resistance index (IR) in resistant GC cells, with the strongest effect observed for *W. viridescens* UCO-SMC3-derived CFS. In 3D spheroids, combined treatment significantly reduced viability compared with CDDP alone in both resistant models, with strain-dependent effects. In AGS-RCDDP cells, combined CDDP+CFS treatment significantly reduced wound closure at 48 h for both LAB strains. Enzymatic and thermal inactivation revealed strain- and cell-line-dependent stability of the bioactive components associated with CFS activity. The chemosensitizing effect of *W. viridescens* CFS in AGS-RCDDP cells was abolished by proteinase K but preserved after heat treatment, whereas *L. paracasei* displayed a distinct stability profile.
Discussion: Together, these findings demonstrate that LAB-derived CFS can sensitize CDDP-resistant GC cells to CDDP in a strain and cell-line dependent manner. The differential sensitivity to proteolytic and thermal treatments suggests the involvement of heat-stable, protease-sensitive proteinaceous or peptidic components, as well as highly stable compounds, in the modulation of CDDP response.

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P57. Comparative genome-wide binding of HB7 transcription factor reveals differential promoter preferences and regulatory architectures between cultivated tomato and drought-adapted *Solanum pennellii.*

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Introduction: Drought threatens tomato production, particularly in water-limited regions such as central Chile. Wild relatives *Solanum pennellii* and *Solanum chilense* are adapted to arid environments and provide models to investigate drought adaptation. We aimed to determine how differences in regulatory architecture contribute to divergent drought-responsive gene expression among cultivated and wild tomatoes.
Materials and Methods: Public leaf RNA-seq datasets from *S. lycopersicum*, *S. pennellii*, and *S. chilense* under control and drought conditions were analyzed. One-to-one orthologs identified with OrthoFinder v3 enabled interspecific comparison. Regulatory networks integrating GENIE3 co-expression inference and promoter cis-regulatory motifs, followed by Fisher's exact tests, prioritized transcription factors (TFs). HB7.2 was selected for DNA affinity purification sequencing (DAP-seq) in *S. lycopersicum* and *S. pennellii* for identification of TF binding events genome-wide. Reciprocal swap-DAP assays combined HB7.2 proteins and genomic DNA from both species to distinguish cis-regulatory sequence differences from TF-associated effects.
Results: Comparative transcriptomics revealed a conserved drought response involving abscisic acid and cellular stress, together with repression of photosynthesis, growth, and biosynthetic processes, alongside species-specific responses. HB7.2 showed strong drought induction and significant enrichment of regulatory interactions across all three species. Native DAP-seq identified 27,041 and 46,883 HB7.2-binding peaks in S. *lycopersicum* and *S. pennellii*, associated with 1,307 and 1,038 drought-responsive DEGs, respectively. Reciprocal assays yielded 65,875 peaks and 1,174 associated DEGs for SlHB7.2 on the *S. pennellii* genome, and 43,408 peaks and 2,204 DEGs for SpHB7.2 on the *S. lycopersicum* genome.
Discussion: These results reveal conserved and species-specific drought responses and identify HB7.2 as a candidate regulator. Comparative binding profiles provide an experimental framework to assess whether regulatory divergence between cultivated and wild tomato is primarily driven by cis-regulatory variation, HB7.2 differences, or their interaction.

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P58. Physiological, biochemical and agronomic responses to heat stress in *Lupinus luteus.*

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Introduction: *Lupinus luteus* is a high protein cool season legume whose productivity is increasingly threatened by heat waves associated with climate change. However, the physiological mechanisms underlying heat tolerance and their relationship with agronomic performance remain poorly understood. This study aimed to integrate physiological, biochemical and field responses to heat stress in two *L. luteus* accessions: the wild accession C98 and the elite cultivar Alu*Prot-CGNA* (C195).
Materials and Methods: Plants were exposed to three consecutive days of heat stress (40°C), followed by seven days of recovery. Chlorophyll fluorescence (Fv/Fm, Y(II), Y(NPQ), ETR and 1-qL), stomatal conductance, relative water content, malondialdehyde, antioxidant enzymes (SOD and POX) and soluble sugars were evaluated. The same accessions were subsequently assessed under field heat stress to determine grain yield and stress tolerance indices (STI, SSI, TOL, MP and GMP).
Results: Heat stress significantly reduced PSII photochemical efficiency in both accessions, with a greater decline in C195. Nevertheless, C195 exhibited superior recovery of Fv/Fm, Y(II) and plant water status, together with greater sucrose and fructose accumulation during recovery. Conversely, C98 maintained higher SOD and POX activities and Y(NPQ), indicating a predominantly antioxidant and photoprotective strategy. Principal component analysis confirmed these contrasting

physiological and biochemical strategies. Under field conditions, C195 maintained significantly higher MP, GMP and STI than C98, whereas SSI remained unchanged between accessions.
Discussion: The integration of physiological, biochemical and field responses indicates that rapid recovery of photosynthetic performance, maintenance of plant water status and enhanced carbohydrate accumulation were more closely associated with grain yield maintenance under heat stress than antioxidant activation alone. Although C98 exhibited a stronger antioxidant response, C195 translated its superior photosynthetic recovery into greater agronomic performance under field conditions.

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P59. Effect of 17β-estradiol on mitochondrial dynamics and OPA1 processing in a model of cardiac lipotoxicity
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Introduction: Cardiovascular diseases show differences between men and women. During the reproductive stage, women exhibit protection against cardiovascular damage, which decreases with reproductive aging and reduced estrogen signaling. In this context, overload with saturated fatty acids, such as palmitic acid, promotes mitochondrial dysfunction and fragmentation in cardiomyocytes. OPA1 maintains mitochondrial fusion, and its processing from long isoforms (L-OPA1) to short isoforms (S-OPA1) is associated with mitochondrial stress and fragmentation. In this study, we evaluated whether 17β-estradiol (E2), a biologically active estrogen, prevents lipid overload-induced mitochondrial fragmentation through preservation of L-OPA1 *in vitro* and improves metabolic alterations in an *in vivo* model of lipotoxicity.
Materials and Methods: In the *in vivo* model, 18-month-old female C57BL/6J mice were fed a normal or high-fat diet for 6 months and treated with E2 (15 μg/kg/day) or vehicle during the last month. Body weight, fasting blood glucose, and glucose tolerance were evaluated. In the *in vitro* model, neonatal rat ventricular cardiomyocytes were pretreated with E2 (100 nM) and subsequently exposed to -BSA palmitate (250 μM). Mitochondrial morphology was analyzed using MitoTracker Green and confocal microscopy, while OPA1 processing was evaluated by Western blotting.
Results: In the *in vivo* model, the high-fat diet increased body weight and impaired glucose homeostasis. E2 treatment improved fasting blood glucose and GTT responses compared with the HFD-vehicle group. *In vitro*, palmitate induced mitochondrial network fragmentation and reduced the L-OPA1/S-OPA1 ratio compared with BSA. The E2+PAL group showed greater preservation of mitochondrial organization, while the L-OPA1/S-OPA1 ratio was not significantly different from BSA, although additional experiments are required.
Discussion: These preliminary results suggest that E2 attenuates lipotoxicity-associated metabolic and mitochondrial alterations. In cardiomyocytes, E2 preserves mitochondrial organization and and showed a pattern consistent with preservation of the L-OPA1/S-OPA1 ratio, suggesting that modulation of OPA1 processing may contribute to its protective effects under lipid overload.

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P60. Overexpression of taTAR and taPRF-1 transcription factors enhances the biocontrol activity of *Trichoderma atroviride* against phytopathogenic fungi.
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Introduction: Phytopathogenic fungi cause substantial economic losses in agriculture worldwide. The environmental impact associated with chemical fungicides underscores the need for sustainable disease-control strategies, including biocontrol agents such as *Trichoderma atroviride*. Previous transcriptomic analysis of the *T. atroviride-B. cinerea* interaction identified transcription factors (TFs) potentially involved in mycoparasitism and biocontrol. However, the functional contributions of these TFs remains poorly understood. Here, we evaluated whether overexpression of two *T. atroviride* TFs, taTAR and taPRF-1, enhances inhibition of four phytopathogenic fungi.
Materials and Methods: *T. atroviride* strains overexpressing taTAR or taPRF-1 were generated, and overexpression was verified by RT-qPCR. Biocontrol activity was evaluated against four phytopathogens using dual-culture confrontation and inhibition assays. Photographs were taken at 3, 5 and 8 days post-inoculation, and the percentage of pathogen inhibition was calculated.

Results: Overexpression of taTAR and taPRF-1 was confirmed by RT-qPCR. Both overexpressing strains shows increased inhibitory activity against phytopathogenic fungi in dual-culture confrontation and inhibition assays compared with the wild-type strain. The magnitude of inhibition varied depending on the phytopathogen evaluated.
Discussion: Overexpression of taTAR and taPRF-1 enhances the biocontrol capacity of *T. atroviride* against phytopathogenic fungi. These findings identify both TFs as candidate regulators of antagonistic activity and support their further evaluation for the development of improved *Trichoderma*-based biocontrol strategies.

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P61. Context-Dependent Regulation of c-MYC by the SALL2 Tumor Suppressor in Colorectal Cancer.
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Introduction: Today, cancer remains a leading threat to global health. The *c-MYC* oncogene drives progression across multiple malignancies. Recent evidence suggests that the SALL2 transcription factor acts as a tumor suppressor and may modulate c-MYC activity; however, their functional relationship and underlying regulatory mechanisms remain incompletely understood.
Material and Methods: To evaluate the role of SALL2 in regulating c-MYC, we performed co-immunoprecipitation assays to assess their association, and luciferase reporter assays using wild-type and mutant promoters constructs to evaluate changes on c-MYC promoter activity, in the presence of SALL2 isoforms. Complementary bioinformatic analyses of publicly available TCGA transcriptomic datasets evaluated the *SALL2*-*MYC* association across tumor types. In colorectal cancer (CRC), tumors were stratified by SALL2 expression to investigate transcriptomic differences. Gene Set Enrichment Analysis (GSEA) using Hallmark sets was conducted with emphasis on the consensus molecular subtype4 (CMS4).
Results: Coimmunoprecipitation assays confirmed physical association between SALL2, and c-MYC. Luciferase reporter assays showed that SALL2 isoforms decreased c-MYC transcriptional activity. PanCancer TCGA analysis revealed a context-dependent relationship between SALL2 and MYC. In CRC, *SALL2* and *MYC* expression showed a modest but statistically significant inverse correlation (Rho = -0.15, $p < 0.05$). Notably, within the CMS4 subtype, SALL2-high tumors exhibited significantly lower c-*MYC* expression than SALL2-low tumors (FDR < 0.05). Consistently, GSEA showed a significant negative enrichment of the Hallmark MYC Targets gene set in SALL2-high CMS4 tumors.
Discussion: Together, our *in vitro* findings and transcriptomic analysis of CRC tumors suggest that SALL2 interacts with c-MYC, represses its activity, and is linked with reduced MYC-driven transcriptional programs in the CMS4 subtype. These independent lines of evidence suggest that SALL2 loss may promote a MYC-dependent tumor phenotype. These findings support evaluating whether SALL2 expression influences the efficacy of MYC-targeted therapies according to individual tumor genetic background.

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P62. Endothelin-1 regulates ET_AR stability and promotes invasion in gallbladder cancer cells.
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Introduction: Gallbladder cancer (GBC) is associated with high mortality due to late diagnosis and its high invasive potential. Endothelin-1 (ET1) is a peptide associated with tumor progression in GBC and signals through the Endothelin A receptor (ET_AR). Evidence from GBC and other cellular models supports the involvement of the ET1/ET_AR axis in tumor-associated signaling, including Src activation. However, while ET1 levels and activity have been investigated, much less is known about the regulation of ET_AR protein levels and localization. Since cell-surface receptor availability is a key determinant of cellular responsiveness, this study aimed to determine whether ET1 regulates ET_AR half-life and membrane stability and to investigate their contribution to Src activation in GBC cells.
Materials and Methods: GBC cells CAVE1 and NOZ were used as models of primary and metastatic GBC, respectively. ETAR membrane stability was evaluated by total internal reflection fluorescence (TIRF) microscopy, while receptor half-life was determined using cycloheximide treatment followed by western blot. Activation of AKT, ERK1/2, and Src, as well as nuclear β-catenin localization, was evaluated by western blot. Cell invasion was assessed using matrigel-coated Transwell assays.

Results: ET1 modulated ET_AR membrane stability in NOZ cells and altered ET_AR half-life in CAVE1 cells. In addition, ET1 induced activation of AKT, ERK1/2, and Src, with increased nuclear β-catenin levels. These responses were attenuated by the selective ET_AR antagonist Ambrisentan and the Src inhibitor Saracatinib. Functionally, ET1 increased the invasive capacity of NOZ cells, whereas Ambrisentan and/or Saracatinib, reduced this effect.
Discussion: These results suggest that ET1/ET_AR signaling modulates receptor stability and promotes Src activation, associated with AKT and ERK1/2 activation and increased nuclear β-catenin levels, thereby promoting an invasive phenotype in GBC cells.

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P63. Polystyrene nanoplastics pollution: search for genetic determinants of the response in *Arabidopsis thaliana*.
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Introduction: Nanoplastic pollution constitutes an emerging environmental problem due to its increasing accumulation in ecosystems and potential effects on organisms. In plants, exposure to nanoplastics can alter growth and development, generating, among other effects, a decrease in plant biomass. However, nanoplastics can be composed of different polymers, such as polystyrene (PS) and polyethylene terephthalate (PET), and the extent to which these materials differentially affect plant development remains poorly understood. In addition, the genetic components underlying the variation in plant responses to nanoplastic exposure are largely unknown. Therefore, this work aimed to compare the effects of PS and PET nanoplastics on *Arabidopsis thaliana* and to identify genetic determinants associated with the response to nanoplastic exposure through a genome-wide association study (GWAS) using natural *A. thaliana* accessions.
Methods: Natural *A. thaliana* accessions were phenotyped under PS NP exposure and used for GWAS analysis. Candidate genes were selected from associated genomic regions. As an initial functional approach, fresh biomass of mutant lines for the candidate gene *AT5G47990* was evaluated under different PS NP concentrations using Col-0 plants as reference. Gene expression and reactive oxygen species accumulation are also being analyzed under the same conditions, while additional accessions are being incorporated to increase GWAS statistical power.
Results: PS NPs significantly reduced plant biomass. GWAS analysis of the PS NP response identified *AT5G47990*, encoding a cytochrome P450 family protein, as a candidate associated with phenotypic variation. Its potential role in the response to PS NPs was evaluated using mutant lines, gene expression analysis, and ROS accumulation.
Discussion: These analyses will allow us to evaluate whether this candidate contributes to the phenotypic alterations induced by PS NPs. In parallel, expanding the GWAS panel will facilitate the identification of other candidate genes that may contribute to the variation in the response of *A. thaliana* to this pollutant.

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P64. Loss of SALL2 transcription factor in colorectal cancer cells promotes a protumoral stromal remodeling
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Introduction: The tumor microenvironment (TME) of colorectal cancer (CRC) plays a role in tumor progression and metastasis, with cancer-associated fibroblasts (CAFs) contributing to extracellular matrix (ECM) remodeling and acquiring protumoral properties in response to cancer cell signals. SALL2 is a transcription factor regulating genes involved in tumor suppression and CRC progression. However, whether SALL2-dependent signals from CRC cells influence the tumor stroma remains unclear. Aim: To determine whether SALL2-dependent paracrine signals from CRC cells reshape the tumor stroma using *in vivo* and *in vitro* models
Materials and Methods: Using colonoscopy-guided injection, AKP (*Apc*$^{-/-}$, *Kras*^{G12D}, *p53*$^{-/-}$) and AKPS (*Apc*$^{-/-}$, *Kras*^{G12D}, *p53*$^{-/-}$, *Sall2* $^{-/-}$) organoids were injected into the colonic mucosa of C57BL/6 mice. Tumor and stromal tissues were analyzed by immunohistochemistry, Masson's trichrome staining, and Gomori's reticulin staining. Human colonic fibroblasts (CCD18-Co) were treated with conditioned medium (CM) from SW480 CRC cells expressing endogenous (SALL2 WT), lacking SALL2 (SALL2KO), or expressing inducible SALL2 using the Tet-On system (SW480-iSALL2). Fibroblast responses were evaluated by western blot and Sirius Red assays.
Results: Severe desmoplasia was observed in both murine models. *Sall2* loss in advanced tumor tissue resulted in disorganization of reticulin fibers, increased collagen deposition in the ECM, and a larger CAF-positive area. *In vitro*,

treatment with CM from CRC cells increased collagen deposition in fibroblasts. Notably, fibroblasts exposed to CM from SALL2KO cells showed higher MMP-9 levels than those exposed to CM from SALL2 WT cells, whereas fibroblasts exposed to CM from SW480-iSALL2 cells showed increased pro-inflammatory markers.
Discussion: Our findings suggest that SALL2 loss in CRC cells alters paracrine signaling to the stromal compartment, promoting ECM remodeling and CAF-associated features. Moreover, modulation of SALL2 levels influences inflammatory responses in fibroblasts. Thus, SALL2 may contribute to the regulation of the acquisition of protumoral stromal properties in CRC.

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P65. Pharmacological ClpP Activation Differentially Modulates Mitochondrial Complex I Subunits in Vascular Smooth Muscle Cells.
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Introduction: Loss of the differentiated vascular smooth muscle cell (VSMC) phenotype contributes to vascular disease. The mitochondrial protease ClpP regulates mitochondrial proteostasis and function. We previously showed that pharmacological ClpP activation with TIC10 preserves the differentiated VSMC phenotype, partly by increasing the NAD+/NADH ratio. NDUFV1, a mitochondrial Complex I subunit, participates directly in NADH oxidation. We hypothesized that NDUFV1 would be relatively preserved following TIC10 treatment compared with NDUFS2, which belongs to a distinct Complex I functional module.
Materials and Methods: Human aortic smooth muscle cells were treated with TIC10 (1 μM) for 48 hours. NDUFV1 and NDUFS2 protein levels were assessed by Western blotting and normalized to ACTB or the mitochondrial protein HSP60. Control and TIC10-treated groups were compared using the Mann–Whitney U test.
Results: Median NDUFV1 levels decreased by 20.0% when normalized to ACTB ($n = 12$ per group; $p = 0.0449$) and by 31.9% when normalized to HSP60 ($p = 0.2189$). In contrast, NDUFS2 levels decreased by 46.3% when normalized to ACTB ($n = 16$ per group; $p < 0.0001$) and by 43.9% when normalized to HSP60 ($p < 0.0001$). Thus, TIC10 treatment produced an apparently smaller reduction in NDUFV1 than in NDUFS2 abundance.
Discussion: These findings suggest that pharmacological ClpP activation may differentially affect Complex I subunits, potentially reflecting differences in the susceptibility or turnover of specific functional modules. Relative preservation of NDUFV1 may help maintain NADH oxidation capacity and contribute to the increased NAD+/NADH ratio and preservation of the differentiated VSMC phenotype observed following TIC10 treatment. These results provide preliminary insight into Complex I remodeling induced by pharmacological ClpP activation in VSMCs.

P66. Assessment of ALD6 role in metabolic flux control using light in *Saccharomyces cerevisiae*.
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Introduction: Yeasts can use several simple carbon sources, including glucose, fructose, sucrose, and galactose, to obtain energy. Once assimilated, these sugars are metabolized through glycolysis, generating pyruvate, which can be directed toward either cellular respiration or fermentation. During fermentation, pyruvate is decarboxylated to acetaldehyde and subsequently reduced to ethanol. In this context, ALD6 (aldehyde dehydrogenase 6) contributes to carbon-flux partitioning by converting acetaldehyde into acetate, thereby diverting carbon away from ethanol production. In this study, we used an orthogonal light-induced optogenetic switch to control ALD6 expression and evaluate the consequences of redirecting metabolic flux in *Saccharomyces cerevisiae*.
Materials and Methods: An *S. cerevisiae* strain harboring the FUN-LOV optogenetic switch was engineered to control ALD6 expression. We then evaluated the behavior of the resulting strain under light-induced conditions across different carbon sources and cytotoxic stress conditions.
Results: The engineered strain showed improved growth upon ALD6 induction across several carbon sources. Under inducing conditions, growth increased by 46% in glucose, 40% in fructose, and 35% in the non-fermentable carbon source glycerol. In cytotoxic medium containing glucose and 9% ethanol, the engineered strain exhibited 30% greater growth under non-inducing conditions and 62% greater growth under light induction compared with the chassis strain (BY4741). During fermentation conditions, the engineered strain showed lower performance based on cumulative CO_2 loss (g/L). Nevertheless, under both induced and non-induced conditions, it produced more wet biomass than the chassis strain.
Discussion: These results show that the optogenetic control of ALD6 expression modifies the metabolic flux of *S. cerevisiae,* increasing the biomass yield.

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P67. SVCT2 knockdown impairs mitochondrial bioenergetics in breast cancer cells

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Introduction: The sodium-dependent vitamin C transporter 2 (SVCT2) is classically known for mediating ascorbic acid (AA) uptake into cells. SVCT2 is overexpressed in breast tumors and cancer cell lines, where it localizes mainly to mitochondria; whether its expression provides a selective or adaptive advantage to cancer cells remains unclear. Notably, mitochondrial SVCT2 has low AA-transport capacity, suggesting roles in cell survival beyond classical transport, potentially linked to oxidative-stress adaptation or mitochondrial metabolism. Our study aims to elucidate the functional role of mitochondrial SVCT2 (mitSVCT2) in breast cancer cells.
Materials and Methods: Stable SVCT2 knockdown MDA-MB-231 cell lines (shSVCT2 #1 and #2) were generated, and their mitochondrial function was characterized by assessing mitochondrial membrane potential (ΔΨm) with the JC-1 probe, ATP levels by HPLC with UV detection, and oxygen consumption rate (OCR) via high-resolution respirometry on an Oroboros O2k. Finally, we examined mitochondrial ultrastructure by transmission electron microscopy (TEM).
Results: Functional characterization revealed a significant decrease in oxygen consumption rate (OCR) and mitochondrial ATP production upon mitSVCT2 silencing, indicating impaired oxidative phosphorylation. JC-1 staining confirmed a significant reduction in ΔΨm, consistent with the disruption of the inner mitochondrial membrane observed by electron microscopy in knockdown cells.
Discussion: Collectively, these findings indicate that SVCT2 plays a central role in sustaining mitochondrial integrity and bioenergetic function in breast cancer cells, independent of its function as a vitamin C transporter.

P68. HDAC6-STAT3-PP2Ac interaction in colorectal cancer cell lines

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Introduction: Histone Deacetylase 6 (HDAC6) is a protein related to various cancer-promoting mechanisms through regulation of STAT3, a transcriptional factor that affects the expression of different oncogenes and tumor suppressors. In melanoma, HDAC6 interacts with and upregulates STAT3, increasing levels of p-STAT3 (Tyr705) and its translocation to the nucleus. HDAC6 also interacts with PP2Ab, a regulatory subunit of the phosphatase PP2A and a negative regulator of STAT3. Accordingly, in HT29 and HCT116 cells (colorectal cancer cell lines), we have observed that HDAC6 also interacts with STAT3. Nevertheless, the effects of HDAC6 in the STAT3 pathway in CRC is not well-known. The aim of this work was to further analyze the HDAC6-STAT3 axis to provide insight into HDAC6 signaling mechanisms and its potential as a therapeutic target in CRC.
Materials and Methods: Flag-HDAC6 WT, Flag-HDAC6 1-840, Flag-HDAC6 1-503 and HALO-Flag-HDAC6 were overexpressed in HCT116 and HT29 cell lines; additionally, cells were treated with IL6 and HDAC6 inhibitors. Whole cell lysate was then used for immunoprecipitation to analyze the HDAC6-STAT3 interaction under different treatments and western blot to confirm activation or inhibition of the STAT3 pathway.
Results: In colon cancer cell lines, HDAC6-Flag interacts with STAT3 and with PP2Ac, the catalytic subunit of PP2A. The interaction between STAT3 and HDAC6-flag decreased when truncated HDAC6 is immunoprecipitated, and HDAC6 inhibitor affects the STAT3 pathway activation mediated by IL6.
Discussion: Together, these experiments showed that HDAC6-STAT3-PP2Ac axis exist in CRC, which provide insight into HDAC6 signaling mechanisms and its potential as a therapeutic target in CRC.

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P69. Molecular mechanisms of FoxP1 dysfunction: Impact of pathogenic variants on biomolecular condensate dynamics.

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Introduction: Biomolecular condensates formed via liquid-liquid phase separation (LLPS) play crucial roles in transcriptional regulation. FoxP1, an essential transcription factor for neurodevelopment, contains, besides of its conserved DNA-binding domain (FKH), intrinsically disordered regions (IDRs) and a glutamine-rich (Q-rich) domain that have been hypothesized as driving phase separation. Pathogenic *de novo* mutations in FoxP's FKH cause FoxP1 Syndrome, leading to intellectual disability and neurodevelopmental deficits. However, the biophysical mechanisms linking these point mutations to altered LLPS dynamics remain poorly understood. The aim of this work was to evaluate the phase behavior of wild-type (WT) FoxP1 and pathogenic variants, characterizing their thermodynamic and structural properties.
Materials and Methods: *In vitro* phase separation of recombinant WT FoxP1 was evaluated by spectrophotometry measuring optical turbidity at 350 and 600 nm across varying protein and salt concentrations. *In silico*, coarse-grained implicit-solvent molecular dynamics simulations of WT FoxP1 and pathogenic variants (R465G, R514C, R525Q, W534R) were performed using the CALVADOS3 implemented in OpenMM. Systems were simulated at salt concentrations ranging from 10 to 500 mM NaCl to determine saturation concentrations (Csat), radius of gyration (Rg), and intra/intermolecular contact networks within the dense phase.
Results: Spectrophotometric assays demonstrated concentration-dependent turbidity for WT FoxP1, confirming its intrinsic capacity to undergo gel-like phase separation *in vitro*. CALVADOS3 simulations revealed that increasing the ionic strength significantly decreases LLPS propensity, shifting Csat. Pathogenic variants exhibited altered conformational compactness (Rg) and distinct intermolecular contact maps in the condensed phase compared to WT, altering condensate stability under physiological ionic strength (150 mM NaCl).
Discussion: These preliminary findings demonstrate that single-point pathogenic mutations alter the conformational landscape and inter-chain interactions of FoxP1 condensates. Altered LLPS dynamics may compromise transcriptional condensate assembly, providing a novel biophysical mechanism for FoxP1 dysfunction. Future experimental validation will link these *in silico* predictions to *in vitro* condensate formation and transcriptional activity.

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P70. Biochemical Characterization of an Anthocyanin-Degrading Enzyme from Rosehip (Rosa spp.)
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Introduction: Rosehip (*Rosa spp*.) is a valuable non-timber forest resource recognized for its high content of bioactive compounds, particularly anthocyanins, which contribute to fruit pigmentation and antioxidant capacity. Despite their nutritional importance, anthocyanins are susceptible to enzymatic degradation during ripening and postharvest storage. Glycoside hydrolases have been implicated in anthocyanin glycoside hydrolysis, leading to pigment loss. However, the enzymes responsible for anthocyanin degradation in rosehip have not yet been characterized.
Materials and Methods: The anthocyanin-degrading enzyme was partially purified by 65% ammonium sulfate precipitation, ultrafiltration using 100 and 10 kDa Amicon Ultra-15 filters, and size-exclusion chromatography on an ÄKTA Start system with a HiLoad™ Superdex™ 75 column. The enzyme-enriched fraction was characterized using pNPG and oNPG to determine optimal pH and temperature. Anthocyanin content was analyzed by HPLC UV-Vis (Hitachi Chromaster), and the fraction was further analyzed by LC-MS/MS using a timsTOF Pro 2 mass spectrometer.
Results: The partially purified protein fraction exhibited hydrolytic activity toward both oNPG and pNPG, with higher activity observed for oNPG, reaching a specific activity of 119,667 U/mg. Optimal activity occurred at pH 3 and 50 °C, approximately 13-fold higher than at pH 8 and 22-fold higher than at 80 °C. Mass spectrometry revealed glycoside hydrolases, including β-glucosidase, β-galactosidase and β-fructofuranosidase, supporting their possible contribution to anthocyanin degradation. HPLC-UV-Vis showed a 30.5% reduction in anthocyanin levels following incubation with the partially purified enzyme.
Discussion: These findings provide new insights into glycoside hydrolase activity in rosehip and its potential contribution to anthocyanin degradation, consistent with previous reports on β-glucosidases from Sicilian blood oranges (Barbagallo et al., 2007) and apricot (Hind & Shakir, 2023). This study advances the biochemical characterization of rosehip enzymes and highlights glycoside hydrolases as potential contributors to anthocyanin stability modulation.

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P71. SUMOylation, a Novel Post-Translational Regulatory Mechanism of Cx26.
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P72. Exploring Putative RNA Binding by GOLPH3 and the Role of Its N-Terminal Intrinsically Disordered Region.
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Introduction: Golgi phosphoprotein 3 (GOLPH3) is a Golgi-associated peripheral membrane oncoprotein involved in COPI-dependent vesicular trafficking. Its N-terminal region, comprising residues 1-51, is predicted to be intrinsically disordered, but its potential contribution to nucleic acid association has not been investigated. This exploratory study examined whether small RNA-sized nucleic acid species are recovered in GOLPH3 pulldowns and whether deletion of the N-terminal intrinsically disordered region affects their recovery.
Materials and methods: The amino acid sequence corresponding to the GOLPH3 N-terminal region was analyzed using HybridRNAbind to predict RNA-binding propensity. HeLa cells were transfected with constructs encoding GFP, GFP-GOLPH3 wild type (WT), or GFP-GOLPH3 Δ1-51. Following crosslinking with 1% formaldehyde and cell lysis, equal amounts of lysate were subjected to affinity pulldown using a GST-tagged anti-GFP nanobody immobilized on glutathione-Sepharose beads. Nucleic acids recovered from the bead-bound fractions were analyzed by capillary electrophoresis using a small-RNA assay.
Results: HybridRNAbind identified localized regions of predicted RNA-binding propensity within residues 1-51 of GOLPH3. Capillary electrophoresis detected low-molecular-weight nucleic acid species in the GFP, GFP-GOLPH3 WT, and GFP-GOLPH3 Δ1-51 pulldowns. The predominant species were approximately 20-27 nucleotides in length, accompanied by less abundant, longer fragments. Their recovery with both GFP-GOLPH3 WT and GFP-GOLPH3 Δ1-51 demonstrated that deletion of residues 1-51 did not abolish the detectable nucleic acid signal under the conditions examined.
Discussion: These preliminary results show that small nucleic acid species can be recovered from formaldehyde-crosslinked, GFP-based affinity pulldowns containing GOLPH3 constructs. However, because comparable species were also detected in the GFP control, the current findings do not establish a specific or direct association between GOLPH3 and RNA. The N-terminal intrinsically disordered region is not strictly required for detectable recovery, although a quantitative or regulatory contribution cannot yet be excluded. Nuclease-sensitivity assays, quantitative comparisons with appropriate controls, and sequencing of the recovered species will be required to determine their molecular identity and assess whether they associate specifically with GOLPH3.

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P73. Functional GST-Nanobody Fusions as a Versatile Platform for Production and Applications.
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Introduction: Single-domain antibodies, also known as VHHs or nanobodies, are compact and versatile affinity reagents. However, their routine implementation can be limited by production requirements and by the absence of a conserved Fc region that enables detection with conventional secondary antibodies. We developed a simplified bacterial expression strategy to produce functional GST-nanobody fusion proteins in which GST serves simultaneously as a purification handle, detection epitope, and affinity-capture module.
Materials and methods: The well-characterized anti-GFP nanobody Lag2 and anti-mCherry nanobody C11 were designed as N-terminal GST fusions. AlphaFold 3-based modeling was used to evaluate the predicted structural integrity of the fusion proteins. The constructs were expressed in the cytoplasm of *Escherichia coli* Origami 2 (DE3), whose *trxB* and *gor* mutations promote cytoplasmic disulfide bond formation. Following IPTG induction, soluble GST-nanobody fusions were purified by glutathione-affinity and size-exclusion chromatography. Antigen-binding affinities were determined by isothermal titration calorimetry. Reactivity was evaluated by native-state dot blot and denaturing Western blot. The fusion proteins were also tested for indirect immunofluorescence detection of GFP- or mCherry-tagged TGN38 in HeLa and H4 cells and for affinity capture from cell lysates.

Results: Structural models predicted preservation of both the GST fold and the characteristic VHH β-sandwich, including defined complementarity-determining region loops and an intradomain disulfide bond. Soluble GST-nb-GFP and GST-nb-mCherry were recovered at yields of approximately 8-12 mg/L. Isothermal titration calorimetry demonstrated nanomolar antigen binding, with estimated K_D values of approximately 123 nM for GFP and 199 nM for mCherry. Both fusion proteins recognized their respective antigens in native-state dot blots but showed no detectable reactivity in denaturing Western blots under the conditions examined, consistent with the recognition of conformational epitopes. Anti-GST antibodies enabled specific immunofluorescence detection of GFP-TGN38 and mCherry-TGN38 in HeLa and H4 cells. In addition, GST-nanobody pulldowns efficiently captured the corresponding fluorescent proteins from cell lysates.
Discussion: Direct cytoplasmic expression in *E. coli* Origami 2 (DE3) provides a simple route for producing soluble and functional GST-nanobody reagents. Retaining the GST moiety eliminates the need for tag removal while enabling glutathione-based purification, conventional antibody-mediated detection, and affinity capture. This low-cost and multifunctional platform complements formats such as VHH-Fc fusions and allows the nanobody architecture to be selected according to the intended application.

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P74. Molecular Characterization and Stability Profiling of a Lactadherin-Targeting DNA Oligonucleotide for Anticancer Applications

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Introduction: Lactadherin is a secreted glycoprotein involved in several biological processes, including apoptotic cell clearance, angiogenesis, cell migration and regulation of the tissue microenvironment. Its dysregulation has been associated with cancer progression, including increased tumor cell survival, invasion, and metastatic potential. Moreover, preclinical studies have shown that lactadherin blockade using antibodies can interfere with processes associated with tumor progression. However, limited evidence is available regarding the therapeutic effects of lactadherin-targeting interfering oligonucleotides in breast cancer. Given the immunomodulatory role attributed to lactadherin, its inhibition may also alter the composition of the tumor microenvironment. Emerging evidence suggests that neutrophils can promote tumor progression through extracellular matrix remodeling and by promoting angiogenesis and metastasis. Therefore, characterizing changes in this population following lactadherin blockade may provide insights into the mechanisms associated with its antitumor effects.
Materials and Methods: In a murine model of breast cancer, we evaluated the effects of lactadherin-targeting interfering oligonucleotide treatment on tumor growth and the tumor microenvironment. Inflammatory cell infiltration was assessed by immunohistochemistry in histological sections. Additionally, cellular proliferation and neutrophil infiltration within tumor tissue were evaluated by Histomorphology and immunofluorescence.
Results: Administration of Lactadherin-targeting DNA oligonucleotides resulted in reduced tumor growth, accompanied by increase of neutrophil infiltration within the tumor tissue compared with untreated controls.
Discussion: These results suggest that lactadherin blockade using interfering oligonucleotides has therapeutic potential in breast cancer and that its antitumor effect may be accompanied by changes in the tumor immune microenvironment, particularly in the neutrophil population.

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P75. Purification of the N-terminal domain of the endothelin-converting enzyme-1c: Methodological challenges and structural redesign with GST-tag.

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Introduction: The endothelin-converting enzyme-1c (ECE1c) promotes the malignant progression of glioblastoma, colorectal, and lung cancers, following its stabilization via phosphorylation of its short N-terminal domain (~7 kDa) at Ser18 and Ser20 by the protein kinase CK2. Thus, this domain is crucial for functional studies, however, purification of low-MW proteins represents a methodological challenge. Our objective was to establish optimal conditions for purifying the ECE1c's N-terminus (NT-ECE1c), laying the groundwork for future studies associated with novel therapeutic strategies.
Materials and Methods: Following transformation of *E. coli* BL21 DE3 with the NT-ECE1c-His6 vector and subsequent induction with IPTG, protein expression was evaluated using Tricine-SDS-PAGE electrophoresis on 16% gels supplemented with urea. *In silico* structural design of the NT-ECE1c-His6 fused to GST-tag was performed with Alphafold.

Results: The theoretical electrophoretic mobility was determined by extrapolating the retention factor (Rf) of NT-ECE1c, but no protein signal was detected under any induction condition. Thus, a new NT-ECE1c-His6-GST construct was designed, giving a clear and easily detectable Coomassie band (33.5 kDa) under standard electrophoresis conditions. In addition, protein induction was easily followed by Western blot against the His6-tag, demonstrating the correct distance of this tag from the globular GST.
Discussion: This work demonstrates the methodological challenge involved in purification of low-MW proteins, where the addition of GST proved to be crucial for their expression, visualization, and subsequent purification in order to study the implications of this domain in malignant progression of cancers.

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P76. N-Acetylcysteine Selectively Targets Senescent Fibroblasts and Reduces Fibrotic Features in Recessive Dystrophic Epidermolysis Bullosa. Evelyng Catalán (ecatalan@uc.cl)[1,2], Belén Dianta[1,2], Nicole Koplow[1], Paola Tiozzo-Lyon[1], Pilar Morandé[2], Francis Palisson[2], Boris Rebolledo[3], Alexander Nyström[4] & Ignacia Fuentes[1,2,3]. [1]Laboratorio de Genética y Biología Molecular, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile. [2]Fundación Debra Chile. [3]Centro de Genética y Genómica ICIM, Facultad de Medicina, Universidad del Desarrollo. [4]University of Freiburg, Germany.

Introduction: Recessive Dystrophic Epidermolysis Bullosa (RDEB) is a severe genetic skin disorder characterized by chronic nonhealing wounds and progressive fibrosis. Cellular senescence has emerged as an important contributor to chronic inflammation and fibrosis; however, its role in RDEB wound pathology remains poorly understood. The aim of this study was to characterize the senescence phenotype of fibroblasts derived from distinct RDEB cutaneous microenvironments and to evaluate the senescence-selective and antifibrotic effects of N-acetylcysteine (NAC) *in vitro*.
Materials and Methods: Primary fibroblasts from healthy skin, non-lesional RDEB skin, and chronic RDEB wounds (RDEB-CW) were analyzed. Senescence was assessed by transcriptomic profiling, SA-β-gal activity, nuclear morphology, and p21 expression. NAC dose–response assays were performed to assess senescence-selective cell loss, and 1 mM NAC was subsequently used as a subcytotoxic concentration to evaluate senescence and fibrotic phenotypes. Fibrotic activity was assessed by collagen gel contraction, α-SMA expression, and fibrosis-associated gene expression.
Results: RDEB-CW fibroblasts showed a transcriptional profile enriched in senescence- and fibrosis-associated pathways and increased SA-β-gal activity, nuclear enlargement, and p21 expression. NAC-induced cell loss correlated with baseline senescence levels, supporting a senescence-selective effect. At the selected subcytotoxic concentration of 1 mM, NAC reduced SA-β-gal positivity, nuclear enlargement, and p21 expression, while also decreasing collagen gel contraction, α-SMA expression, and *POSTN* and *TNC* expression. Proliferation of the remaining fibroblast population was preserved.
Discussion: These findings identify fibroblast senescence as a contributor to the profibrotic phenotype of chronic RDEB wounds and show that NAC preferentially targets senescence-enriched fibroblast populations while attenuating fibrotic features. NAC therefore represents a promising candidate for therapeutic repurposing in RDEB chronic wound management.

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P77. 17β-estradiol prevents palmitate-dependent rat cardiomyocyte hypertrophy by inducing the mitochondrial unfolded protein response (UPRmt).
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Introduction: Cardiovascular diseases are the leading cause of mortality worldwide, with increased incidence in postmenopausal women, supporting a cardioprotective role of estrogens. Cardiac hypertrophy (CH), a key event in disease progression, is characterized by cardiomyocyte growth, mitochondrial dysfunction, and altered proteostasis. Under lipotoxic conditions, palmitic acid (PA) induces CH and activates the mitochondrial unfolded protein response (UPRmt), although this response appears insufficient to prevent cellular damage. Given the cardioprotective effects of 17β-estradiol (E2) and its ability to modulate UPRmt, we investigated whether E2 attenuates PA-induced CH through UPRmt activation in cultured neonatal rat ventricular myocytes (NRVMs).

Materials and Methods: NRVMs were pretreated with E2 (10, 100, and 1000 nM) and subsequently exposed to PA (231 μM). Cardiomyocyte hypertrophy was assessed by microscopy through evaluation of cell area and perimeter, and by Western blotting and RT-qPCR analysis of hypertrophic markers. UPRmt activation was evaluated by RT-qPCR.
Results: Significant decreases in CH markers (ANP, BNP, RCAN1.4 and β-MHC) were observed, accompanied by a significant reduction in the area and perimeter of NRVMs pretreated with 10 and 100 nM E2 compared with PA-treated cells. Preliminary results show an increase in the expression of UPRmt markers (ATF5, CHOP, CEBPB, CLPP and mtHSP60).
Discussion: Taken together, these findings support an antihypertrophic effect of 17β-estradiol against PA-induced cardiomyocyte hypertrophy, could be associated with enhanced UPRmt activation. This response suggests that E2 may promote an adaptive mitochondrial proteostasis program that contributes to cardiomyocyte protection under lipotoxic stress. Further studies are required to establish the causal contribution of UPRmt activation to the protective effects of E2.

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P78. Molecular characterization of High Affinity Potassium Transporters (HKT) from *Pinus radiata.*
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Introduction: HKT (High-Affinity K^+ Transporter) proteins are membrane proteins involved in the homeostasis and transport of monovalent cations, primarily Na^+ and K^+. Although their function has been extensively studied in angiosperms, the characterization of HKT from gymnosperms still remains open. Herein, a molecular characterization of an HKT from Pinus radiata (PrHKT1) is reported.
Materials and Methods: One year old pine seedlings were subjected to inclination, and sampling was performed at 2.5, 10, and 24 hours after tilting. RNA was extracted and qRT-PCR was carried out in both transversal stems cut (basal, middle, and apical), and longitudinal cut considering upper and lower stem side. In parallel, a phylogenetic analysis was performed using MEGA 12, and alignment with CLUSTAL W. Subcellular localization of PrHKT1-GFP was evaluated via transient expression in onion cataphyll epidermal cells. In addition, X-ray spectrometer analysis was performed using M4 Tornado Plus software on tilted *P. radiata* samples from the field to analyze metal composition.
Results: Phylogenetic analysis placed PrHKT1 within the HKT clade, distinguishing it from members of the HKT2 subfamily. Subcellular localization revealed a predominantly peripheral distribution coinciding with the plasma membrane marker. Differential spatiotemporal regulation following tilting was detected. A significant increase in transcript accumulation was observed in the upper basal zone at 2.5 hours, whereas no changes were detected at 10 hours of tilting. Accumulation of transcripts increased significantly in the lower basal zone compared to the upper basal zone and the middle and apical regions at 24 hours**.** X-ray results showed a notable difference in metal content when comparing control samples (non-tilted) with inclined trunks.
Discussion: Overall, results indicate that PrHKT1 is a HKT transporter located in the plasma membrane. Its differential, time-dependent regulation in response to tilt suggests a potential role in modulating ion homeostasis during the gravitropic mechanical response in *P. radiata*.

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P79. Role of Aurora Kinase A (AURKA) in cell death of triple-negative breast tumor cells induced by ASncmtRNA knockdown.
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Introduction: Breast cancer is one of the leading causes of mortality in women worldwide, with more than 2 million cases registered in 2022. The triple-negative subtype is particularly difficult to treat due to the lack of molecular targets. Non-coding mitochondrial RNAs (ncmtRNAs), composed of sense (SncmtRNA) and antisense (ASncmtRNA) members, are differentially expressed in tumor and normal cells. Knockdown of ASncmtRNAs using the antisense oligonucleotide ASO-1537 causes massive apoptotic death of tumor cells but does not significantly affect normal cell viability. Recently, our group reported that ASncmtRNA knockdown reduces Aurora Kinase A (AURKA) levels in MDA-MB-231 triple-negative breast tumor cells while increasing them in normal human mammary epithelial cells (HMEC). This inverse behavior may explain treatment selectivity by protecting the genome of healthy cells while exacerbating genetic damage and tumor cell death. Here, we investigated whether AURKA downregulation mediates MDA-MB-231 cell death induced by ASncmtRNA silencing.
Materials and methods: The AURKA coding sequence was cloned into the pcDNA3.1(-) plasmid (pAURKA) and expressed in MDA-MB-231 cells. Protein levels were assessed by Western blot and viability assays determined whether increased

AURKA expression could reverse cell death induced by ASO-1537. Control ASO (ASO-C) and empty pcDNA3.1(-) were used as negative controls.
Results: AURKA overexpression partially reversed death of MDA-MB-231 cells transfected with ASO-1537, confirming that AURKA protects cells from death and that its reduction contributes to ASO-1537-induced cell death.
Conclusions: AURKA downregulation induced by ASncmtRNA silencing mediates, at least in part, treatment-induced cell death, while AURKA overexpression partially rescues cell viability. These findings contribute to understanding the mechanisms underlying ASO-1537 selectivity and support its potential for therapeutic development in breast cancer**.**

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P80. Beyond the disulfide bond: Characterization of non-covalent interactions in the oligomerization of the ECE1c catalytic domain.
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Introduction: Endothelin-converting enzyme-1c (ECE1c) is a key metalloprotease heavily implicated in cancer progression and metastasis. ECE1c is traditionally known to form homodimers through a single characterized extracellular disulfide bond. The complete biochemical nature of ECE1c's oligomerization, particularly regarding potential non-covalent interactions, remains poorly understood. We hypothesized that ECE1c dimerization is also driven by uncharacterized non-covalent interactions. Elucidating the oligomeric dynamics is crucial for understanding ECE1c structural regulation and identifying novel therapeutic vulnerabilities in cancer research.
Methodology: A commercially available recombinant human ECE1 catalytic domain was utilized. We investigated the dimerization of the ECE1 catalytic domain utilizing Mass Photometry (MP). This cutting-edge technique permits single-molecule mass analysis in native solutions, enabling the precise quantification of mono/oligomer relative abundances.
Results: Our MP data revealed that the peak observed at approximately 112 kDa corresponds to the glycosylated monomeric state of the ECE1 catalytic domain, an expected modification given its production in a mammalian expression system. Consequently, the signal detected at 224 kDa represents the dimeric form of the protein. Notably, low molecular weight signals observed at 52-56 kDa were identified as background noise generated by buffer components (PBS and DTT). Crucially, even in the presence of DTT to disrupt disulfide bonds, a substantial dimeric fraction (~224 kDa) persisted, indicating that ECE1c dimerization is strongly supported by non-covalent interactions. To definitively isolate this non-covalent interface, we evaluated ECE1 under conditions designed to systematically disrupt specific interactions (using DTT, Guanidinium chloride, and detergent digitonin) to drive the entire oligomeric population toward a fully monomeric state.
Discussion: Confirming this non-covalent dimerization mechanism provides critical biophysical insights into ECE1c, opening new structural avenues for targeted cancer therapies.

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P81. Not presented

P82. Cis-mediated upregulation of *RUNX2* gene transcription associated with tumor progression in glioblastoma cells
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Introduction: *RUNX2* is a master transcription factor classically associated with mesenchymal stem cell differentiation to osteoblasts. Interestingly, *RUNX2* expression has also been determined during tumor progression in several cancers, where its transcriptional activity can be upregulated by distal enhancers. Glioblastoma (GBM) is the most aggressive primary brain tumor, and although *RUNX2* was implicated in GBM progression, the mechanisms regulating its expression remain poorly understood. Here, we investigated epigenetic parameters associated with *RUNX2* upregulation in GBM cells and explored potential target genes.
Materials and Methods: Public RNA-Seq and Hi-C datasets from GBM cell lines were integrated with ChIP-Seq datasets of the chromatin marks *H3K27ac* and *H3K4me1* from U87-MG cells. These data were complemented with gene expression analysis in U87-MG cells following *RUNX2* knockdown. Chromatin interaction datasets and active regulatory regions were analyzed to identify candidate enhancers associated with *RUNX2* upregulation and potential *RUNX2* target genes.

Results: Integration of chromatin interaction and histone modification profiles revealed a chromatin loop between the *RUNX2* P2 promoter and a putative super-enhancer upstream of the *RUNX2* locus. Expression analysis identified *CD44* as a highly expressed gene across the analyzed GBM cell lines. This elevated expression and its promoter acetylation status were found to decrease following *RUNX2* knockdown. No prominent putative enhancer elements were identified within the 5–100 kb region surrounding the *CD44* TSS. Interestingly, a putative *RUNX2* binding site was identified at the *CD44* promoter, suggesting a regulatory relationship between *RUNX2* and *CD44*.
Discussion: Our integrated analysis identifies a potential distal enhancer-mediated mechanism upregulating *RUNX2* transcription in GBM and suggests *CD44* as a potential *RUNX2* target gene. Given the established role of *CD44* in GBM-associated processes, including invasion, migration, proliferation, and tumorigenesis, the *RUNX2–CD44* regulatory axis may represent a mechanism through which *RUNX2* contributes to the oncogenic phenotype of GBM.
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P83. Evaluation of the DNA Damage Response Induced by ASncmtRNA Knockdown in Breast Tumor Cells.
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Introduction: Breast cancer is the leading cause of cancer-related death among women in Chile and woldwide. It is classified into distinct subtypes that differ in their invasiveness, aggressiveness and response to treatment. Chemotherapy remains the first-line treatment; however, its lack of specificity results in damage to both healthy and cancer cells, negatively affecting patients' quality of life. Knockdown (KD) of the antisense non-coding mitochondrial RNA (ASncmtRNA) using the antisense oligonucleotide ASO-1537 selectively induces apoptotic death of tumor cells while sparing normal proliferative cells. This study aims to determine whether apoptotic death of tumor cells is mediated by DNA damage and if so, if the DNA damage response is induced by ASncmtRNA knockdown.
Materials and Methods: Triple-negative MDA-MB-231 and luminal A MCF7 breast cancer cells, in addition to normal epithelial breast cells (HMEC) were transfected with antisense oligonucleotides (ASO-Control or ASO-1537) for 24, 48 and 72 h, and DNA damage was evaluated using the comet assay. In addition, MDA-MB-231 cells were transfected in the same way for 4, 8, 12 and 24 h, after which DNA damage response (DDR) was assessed by Western blot analysis of γ-H2AX.
Results: Increased DNA damage was observed by comet assay in breast tumor cells transfected with ASO-1537, compared to ASO-control and non-treated cells, reaching a peak at 48 h post-transfection, while HMEC showed lesser signs of DNA damage. An increase in γ-H2AX and ubiquitinated γ-H2AX was evident as early as 4 h post-transfection with ASO-1537, and peak at 12-24 h, confirming activation of the DDR.
Discussion: Our results suggest that ASncmtRNA Knockdown induces DNA damage and activates the DNA damage response (DDR) in breast tumor cells, as indicated by an increase in come tail DNA and γ-H2AX levels.

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P84. RCOR3 sequesters LSD1 reducing its association with RCOR1 and H3K4me2 demethylation.
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P85. Role of alternative polyadenylation in the regulation of the circadian rhythm in *Drosophila* nervous system
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Introduction: Circadian rhythms coordinate daily cycles of physiology and behavior through molecular clocks operating within defined neuronal circuits. Although transcriptional and post-translational mechanisms of circadian regulation are well established, the contribution of post-transcriptional RNA processing remains poorly understood. Alternative polyadenylation (APA) is a conserved molecular process that generates mRNA isoforms with different 3′ untranslated region (3′UTR) lengths, thereby influencing mRNA stability, localization, and translation. APA is highly prevalent in the nervous system, suggesting a role in shaping neuronal function and behavior. Here, we tested the hypothesis that APA contributes to circadian rhythm regulation in *Drosophila melanogaster* by focusing on cleavage and polyadenylation (CPA) factors, key components of the mRNA 3′ end processing machinery that control APA site selection.
Materials and Methods: We performed an RNA interference (RNAi) knockdown screen targeting selected CPA factors in all circadian clock neurons (*timeless*-Gal4) and, separately, in a subset of pigment-dispersing factor (PDF)–expressing neurons (*pdf*-Gal4). PDF neurons play a central role as "pacemakers" for circadian network synchronization. Locomotor activity was measured under constant darkness to assess endogenous circadian rhythmicity and under light-dark cycles to evaluate the capacity of flies to anticipate morning and evening transitions.
Results: Knockdown of the CPA factor *CPSF6* reduced locomotor rhythmicity under constant darkness and impaired anticipation of light-dark transitions, supporting a functional requirement for CPA machinery in the neuronal control of circadian behavior.
Discussion: Our results provide functional evidence that proper mRNA 3′ end processing in clock neurons is necessary for circadian behavior. These findings identify *CPSF6* as a candidate regulator linking mRNA processing to the circadian system and support a broader role for APA regulation in biological timing. Further characterization of CPA-dependent transcript isoforms and the specific neuronal populations underlying these phenotypes will help define how post-transcriptional mechanisms contribute to circadian network function and behavioral rhythms in the *Drosophila* central nervous system.

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P86. NUAK1 controls lipid metabolic reprogramming in colorectal cancer through the mTORC1–SREBP1 axis.
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Introduction: Lipid metabolic reprogramming supports cancer growth and survival, with SREBP1 acting as a key driver of lipogenesis downstream of oncogenic pathways, including mTORC1. RNA-seq and pathway enrichment analyses revealed that NUAK1, an AMPK-related kinase (ARK), regulates transcriptional programs associated with lipid metabolism. Based on our previous finding that NUAK1 interacts with mTORC1 in colorectal cancer (CRC), we hypothesized that NUAK1 promotes lipid metabolic reprogramming through an mTORC1-SREBP1 signaling axis.
Methods: SW480 and HCT116 p53−/− CRC cells were treated with the selective NUAK1 inhibitor HTH-01-015 or vehicle for 24 h. Whole-cell lysates and cytoplasmic and nuclear fractions were analyzed by western blotting to assess SREBP1 expression and subcellular localization. SREBP1 and SREBP1 target gene expression were evaluated by RNA extraction followed by qPCR. Intracellular lipid accumulation was assessed 24 h after NUAK1 inhibition using BODIPY 488 and LipidSpot 610 fluorescent staining. Lipidomic analyses were performed in SW480 cells treated with HTH-01-015 alone or in combination with rapamycin.
Results: NUAK1 inhibition increased nuclear SREBP1 levels and upregulated the lipogenic genes FASN, LDLR, and ACC. These results correlated with a pronounced lipid droplet accumulation in CRC cells. Lipidomic analysis showed that NUAK1 inhibition promotes lipid reprogramming across multiple phospholipid classes and ceramides. However, this effect was not observed when rapamycin was combined with HTH-01-015, suggesting an mTORC1-dependent mechanism.
Discussion: Together, these findings suggest that NUAK1 is an important regulator of lipid metabolic reprogramming via the mTORC1-SREBP1 axis, highlighting this pathway as a potential therapeutic target in CRC.

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P87. Fructose as a Modulator of Endoplasmic Reticulum Homeostasis and Lipid Metabolism in Human Adenocarcinoma Models.

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P88. Integrated molecular surveillance of urban aquatic microbiomes using qPCR and Nanopore metagenomic sequencing.

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Introduction: Urban streams and wetlands can receive continuous inputs of fecal microorganisms, potentially affecting both sanitary conditions and resident microbial communities. Integrating targeted molecular markers with metagenomic sequencing may provide complementary information on contamination sources and bacterial community composition. This study aimed to characterize microbial contamination in urban aquatic ecosystems of the Province of Concepción using qPCR and Nanopore sequencing.
Materials and Methods: Surface-water samples were collected from 21 sites across seven municipalities between july 2025 and july 2026. Environmental DNA was concentrated by membrane filtration and analyzed by qPCR targeting bacterial 16S rRNA, the human-associated fecal marker CrAssphage, *Escherichia coli* (*uidA*), and virulence-associated genes. Selected samples were additionally analyzed by Oxford Nanopore metagenomic sequencing for taxonomic characterization and preliminary temporal comparisons.
Results: Among almost 200 qPCR records, bacterial 16S rRNA was detected in 98.6%, CrAssphage in 74.7%, and *uidA* in 50.7%, indicating widespread bacterial DNA and frequent human-associated fecal signals in water samples. In the sequenced samples, 16S rRNA and CrAssphage were detected in all samples, whereas *uidA* was detected in some of them. Metagenomic profiles showed temporal changes in dominant bacterial taxa, including persistent *Streptomyces* and *Photobacterium* populations, increases in *Microbulbifer* during January, and detection of *E. coli* in each selected samples.
Discussion: These preliminary results show that combining targeted qPCR with Nanopore metagenomic profiling provides complementary sanitary and ecological information and supports an integrated approach for microbiological surveillance of urban aquatic ecosystems.

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P89. Electrophysiological characterization of the HKT1 channel from *Pinus radiata* reveals a Na^+-selective transport mechanism.

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Introduction: HKT (High-affinity K+ Transporter) proteins are plant membrane transporters involved in Na+ and/or K+ homeostasis and salt tolerance. Based on a pore-loop residue, HKT transporters fall into two functional classes: Class I (serine, Na+ selective) and Class II (glycine, Na+/K+ permeable). Although extensively studied in angiosperms, their functional properties in gymnosperms remain poorly characterized. The aim of this study was to functionally characterize the HKT1 transporter from *P. radiata* (PrHKT1), an economically important forestry species, by determining its ion selectivity and current-voltage properties using heterologous expression.
Materials and Methods: *PrHKT1* cRNA was injected into *Xenopus laevis* oocytes, and whole-cell currents were recorded by two-electrode voltage clamp (TEVC) technique. External solutions in which Na+ was progressively substituted for K+ or the impermeant cation NMDG+. Currents were elicited by voltage steps between -160 and +50 mV. Reversal potentials (Vrev) were determined and analyzed as a function of external Na+ concentration.
Results: PrHKT1 expressing oocytes displayed large inward currents in 100 mM Na+ that increased with membrane hyperpolarization, whereas currents in 100 mM K+ were markedly smaller. Progressive replacement of $NMDG^+$ by Na^+ produced a concentration-dependent increase in inward current, while substitution with K+ had comparatively little effect.

Vrev shifted positively with increasing external Na+, following an approximately linear relationship on a logarithmic scale, consistent with Na+-dependent behavior of the reversal potential.
Discussion: These results indicate that PrHKT1 preferentially mediates Na+ transport, with limited K+ permeability consistent with a Class I HKT transporter**,** rather than the dual Na+/K+ permeability typical of Class II transporters in angiosperms. This provides functional evidence of HKT1 mediated Na+ transport conserved across vascular plants and insight into salt tolerance physiology in gymnosperms.

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P90. Environmental pollutants Al^{3+} and 3,4-dichloroaniline induce oxidative stress on human HepG2 hepatoma cells.
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Introduction: The toxicology evaluation of industrial pollutants is centered in their cytotoxicity in environment relevant species, with use of cell line-based bioassay emerging as a complementary approach in ISO 21115:2019. However, these pollutants can also be incorporated to the human body, where they may cause metabolic disruption, genotoxicity and neurotoxicity. This work studied earlier cellular effects of two industrial pollutants in the human HepG2 cell line.
Methods: The cytotoxic and oxidative effects of two contaminants (Al^{3+} and 3,4-dichloroaniline, 3,4-DCA) at four environment relevant doses was evaluate (50, 75, 100, and 150 μM) at 24 h of exposure. Cytotoxicity was evaluated using the trypan blue exclusion assay. Oxidative status was evaluated by measuring total antioxidant, using the 2,2-diphenyl-1-picrylhydrazyl assay (DPPH) at l_{517}, catalase (CAT) activity at l_{240}, lipid peroxidation through thiobarbituric acid-reactive substances (TBARS) at l_{532}, and protein carbonylation, recording the formation of adduct with 2,4-dinitrophenylhydrazine at l_{517}.
Results: The measurements showed a dose-dependent effect for both contaminants. Al^{3+} maintained cell viability above 80%, for 3,4-DCA, it was reduced to approximately 40% at higher doses. Interestingly, both contaminants induce a significant decrease in antioxidants capacity, ranging from 5 to 15 folds less in DPPH assays ($p<0,001$), and until 75% reduction in CAT activity ($p<0,01$). Regarding oxidative damage, the exposure to highest Al^{3+} concentration decreased TBARS level to 30%protein ($p<0.05$), meanwhile 3,4-DCA no induced alterations in lipid peroxidation. In contrast, no significant changes in carbonylation levels were observed following and Al^{3+}.
Discussion: Al^{3+} and 3,4-DCA induce oxidative stress in HepG2 cell line at doses where no evidenced cytotoxicity. These findings suggest that oxidative stress-related responses may occur before overt loss of cell viability. The observed effects in this human hepatic cell model highlight the potential biological relevance of exposure to these industrial contaminants in human.

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P91. Multilayer regulatory reprogramming: *Enterococcus faecalis* as a systems model for study metal homeostasis.
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Introduction: Transition metals are indispensable cofactors, but deviations from their intracellular set points disrupt redox balance, basal metabolism and stress adaptation. In this context, *Enterococcus faecalis* offers a particularly informative and experimentally tractable platform for studying metal-induced adaptation. Its well-characterized homeostatic systems, available regulatory networks and capacity for genetic and multi-omic interrogation make it possible to examine how copper, iron and zinc reshape cellular physiology across transcriptional, epigenetic, post-transcriptional and metabolic regulatory layers. Here, we present *E. faecalis* as an integrated systems biology model for dissecting cellular and regulatory responses to transition metals.

Materials and Methods: Public transcriptomic datasets from *E. faecalis* OG1RF exposed to metal perturbations (Cu, Fe and Zn) were integrated with a global transcriptional regulatory network. The strategy included targeted deletion mutants, intracellular metal quantification, metabolomics, genome-scale metabolic modelling, promoter methylome profiling and ncRNA identification and validation. Network reconstruction and functional analyses were performed using standard mapping, differential-expression, motif-discovery and Cytoscape-based workflows.

Results: The global network comprised 471 operons (879 genes) connected by 629 predicted regulatory interactions. Non-toxic iron excess altered 475 genes (~15% of the genome), whereas low and high copper concentrations activated distinct regulatory modules controlled by LysR, ArgR and CRP-FNR, together with the metal-responsive regulators CopY, Fur and Zur, revealing dose-dependent network reconfiguration and Cu-Zn cross-talk. Removal of the copper or homeostatic regulatory module induced compensatory transcriptional rewiring without compromising growth under the tested conditions. During iron exposure, glutathione deficiency reprogrammed 483 genes, reduced intracellular iron approximately threefold and redirected metabolism toward energy production and arginine utilization. Copper exposure also modified 20% of 918 promoter methylation patterns and altered 97 ncRNAs; deletion of ncRNA_1490 disrupted coordinated cop operon induction and increased intracellular copper accumulation.

Discussion: These results position *E. faecalis* as a controllable and information-rich systems model in which compact metal-specific homeostatic circuits are connected to broad transcriptional, epigenetic, post-transcriptional and metabolic plasticity. This framework enables mechanistic analysis of metal sensing, toxicity and adaptation from the cellular to the systems scale.

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P92. Lactadherin-Enriched MDA-MB-231-Derived Extracellular Vesicles Trigger Astrocyte Reactivity and Migration.

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Breast cancer (BC) is a systemic inflammatory disease frequently associated with cancer-related cognitive impairment (CRCI), a syndrome largely linked to neuroinflammation. BC tumor-derived extracellular vesicles (EVs) can interact with glial cells and promote neuroinflammatory responses. However, how peripheral tumors trigger astrocyte—a type of glial cell —reactivity within the central nervous system remains unclear. We previously showed that αvβ3-integrin regulates astrocyte reactivity and migration through the phosphorylation of FAK and Src kinases, while lactadherin activates αvβ3-integrin-dependent migration in tumor cells. We therefore hypothesized that lactadherin-enriched EVs derived from triple negative cancer MDA-MB-231 cells (MDA231-EVs) induce astrocyte reactivity and migration through lactadherin–β3-integrin signaling. To this end, astrocyte reactivity was induced in DITNC1 astrocytes using TNFα, followed by stimulation with MDA231-EVs. Migration and cytoskeleton remodeling were evaluated using transwell assays and immunofluorescence, while activation of β3-integrin signaling pathway was assessed by western blotting. Reactive astrocytes exposed to MDA231-EVs showed increased β3-integrin levels and enhanced phosphorylation of FAK at Y^{397} and Src at Y^{416}, concomitant with increased cell migration. Importantly, antibody-mediated blockade of EV-associated lactadherin attenuated the promigratory effect induced by MDA231-EVs, supporting a functional role for lactadherin in this response. Confocal microscopy further revealed cytoskeletal remodeling and migratory morphological features in MDA231-EV-stimulated reactive astrocytes. These findings suggest that BC-derived EVs activate β3-integrin/FAK/Src signaling axis in reactive astrocytes, promoting cytoskeletal remodeling and migration. Our results propose a novel lactadherin-dependent, EV-mediated mechanism that could contribute to BC-associated neuroinflammation and CRCI. Keywords**:** Breast cancer, Neuroinflammation, Cytoskeletal Remodeling, Astrocytes, Lactadherin, β3-integrin.

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P93. Bioprinted hydroxyapatite–alginate–gelatin microenvironments modulate dental pulp stem cell viability and morphology

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Introduction: Bioprinted scaffolds can function as artificial extracellular matrices, providing structural and biochemical cues that regulate cell–matrix interactions and cellular behavior. Alginate–gelatin (Alg–Gel) hydrogels are widely used in extrusion-based bioprinting due to their cytocompatibility and favorable processing properties, while gelatin provides cell-interactive motifs that support cell attachment and spreading. Incorporation of hydroxyapatite (HAp), a major inorganic component of bone tissue, may further modulate the cellular microenvironment toward bone tissue engineering applications. Human dental pulp stem cells (hDPSCs) are a relevant mesenchymal stem cell model to investigate how changes in 3D matrix composition influence cellular responses.
The aim of this work was to evaluate the effect of HAp incorporation into bioprinted Alg–Gel hydrogels on hDPSC post-printing survival and cellular morphology.
Materials and Methods: Bioinks with different Alg–Gel and HAp compositions were characterized for their physicochemical properties and printing performance. The resulting 3D hydrogel microarchitecture and swelling behavior were assessed by micro-computed tomography and swelling kinetics, respectively. hDPSCs were cultured in the bioprinted hydrogels, and cellular viability was evaluated over 21 days using Live/Dead fluorescence staining. Cell morphology and spreading were quantitatively assessed by fluorescence-based morphometric analysis.
Results: All formulations maintained high post-printing cell survival (>70%), with viability exceeding 90% after seven days and remaining high throughout the 21-day culture period. Notably, HAp-containing hydrogels supported higher cell viability. Also, a modest increase in cell spreading and decreased circularity were observed in a subset of cells.
Discussion: Together, these experiments demonstrate that HAp incorporation influenced early cellular responses within the 3D hydrogel microenvironment, supporting cell viability and subtle changes in cell morphology.

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P94. Functional regions of *MALAT1* in MCF7 Breast Cancer Cells.
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Introduction: Long non-coding RNAs (lncRNAs) are key regulators of gene expression and play essential roles in multiple biological processes associated with cancer initiation and progression. Among them, *MALAT1* (*Metastasis Associated Lung Adenocarcinoma Transcript 1*) has been widely implicated in tumor cell proliferation, migration, invasion, and survival. However, it remains unclear whether these functions depend on specific functional regions within the *MALAT1* transcript and how these regions contribute to the regulation of transcriptional programs associated with breast cancer.
Materials and Methods: CRISPR-Cas9 genome editing was used to generate targeted deletions across distinct regions of *MALAT1* in MCF-7 cells, a representative model of luminal A breast cancer, the most prevalent molecular subtype of breast cancer. Successful generation of edited clones was validated by PCR analysis using genomic DNA and cDNA. The biological impact of each deletion was assessed through real-time luminescence-based cell proliferation assays.
Results: We identified distinct functional regions of *MALAT1* that exert differential effects on breast cancer cell proliferation. Deletion of specific transcript regions resulted in unique transcriptional changes, indicating that *MALAT1* contains functionally specialized domains. Integration of phenotypic and transcriptomic data enabled the association of individual *MALAT1* regions with molecular programs involved in tumor cell proliferation.
Discussion: Our findings provide new insights into the functional organization of *MALAT1* and demonstrate that distinct transcript regions differentially contribute to gene expression regulation in breast cancer. Furthermore, the CRISPR-generated deletion model provides a valuable platform for investigating lncRNA-mediated molecular mechanisms and identifying functionally relevant regions with potential therapeutic implications.

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P95. An All-in-One ePEmax vector for Streamlined Prime Editing and RFLP-Based Screening of Editing Outcomes.
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Introduction: Prime editing (PE) is a CRISPR-derived genome-editing technology enabling template-directed genetic modifications without double-strand DNA breaks or exogenous donor DNA. However, PE requires coordinated delivery of a prime editor, an engineered prime-editing guide RNA (epegRNA), and a nicking single-guide RNA (sgRNA) encoded on separate plasmids. This architecture complicates transfection and may reduce co-delivery efficiency. We constructed a

selectable all-in-one ePEmax vector and evaluated its activity at an endogenous locus using an edit generating a *de novo* restriction site. We also assessed RFLP for cost-effective detection.
Materials and Methods: An all-in-one plasmid encoding PEmax, an epegRNA, a sgRNA, and a puromycin-resistance cassette was assembled. The epegRNA was designed to edit the human *HEK3* locus and create a *de novo* restriction site. HEK293T and HCT116 cells were transfected and subjected to puromycin selection. Pooled populations were analyzed by PCR amplification and restriction digestion of *HEK3*.
Results: The all-in-one vector produced the RFLP pattern at *HEK3* in puromycin-enriched HEK293T and HCT116 cells. The restriction fragments were consistent with the intended edit, demonstrating that the integrated system retains prime-editing activity across two human cell lines when its components are delivered from a single plasmid.
Discussion: These findings establish proof of concept for a single-vector ePEmax workflow combining coordinated delivery, cell enrichment, and sequencing-independent detection of editing outcomes. The platform is being applied to introduce patient-derived mutations into human cell lines to generate disease models and to small non-coding RNA loci for functional interrogation.

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P96. STIM1 increases nuclear calcium levels and promotes the expulsion of cytoplasmic chromatin fragments.
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Introduction: Cytoplasmic chromatin fragments (CCFs) are extranuclear portions of chromatin released from the nucleus and are found in the cytoplasm. These structures typically comprise DNA wrapped around histones and are often marked by DNA damage response proteins. The formation of CCFs is often triggered by persistent DNA damage, oxidative stress, or oncogene activation. Once in the cytoplasm, CCFs play a significant role in activating the cGAS-STING pathway, a crucial component of the innate immune system that detects cytosolic double-stranded DNA (dsDNA), which culminates in the production of IFN-1 and pro-inflammatory cytokines. In this context, recent findings demonstrate that STIM1 is a novel interactor of STING and acts as a repressor of STING, and that STIM1 activation activates the cGAS-STING pathway and produces pro-inflammatory cytokines. Additionally, recent data demonstrate that STIM1 localizes to the nucleus and binds to the chromatin. This suggests that STIM1 could regulate nuclear chromatin movements and is more than just an ER-associated, ion-channel-regulatory protein. However, the role of STIM1 in nuclear Ca^{2+} homeostasis and CCF expulsion is unknown.
Materials and Methods: We used live imaging of nuclear and extranuclear Ca^{2+} in HEK293 and HEK293$^{STIM1-/-}$ cells to evaluate compartmentalized signaling. Additionally, we evaluated activation of the cGAS-STING pathway and STIM1 recruitment to the nucleus by immunoblotting and subcellular fractionation, respectively. Finally, we assessed the presence of CCF by immunofluorescence in HEK293 and HEK293$^{STIM1-/-}$ cells in response to increases in nuclear Ca^{2+}.
Results: We observed that STIM1 increases the nuclear and reticular Ca^{2+} levels. Conversely, we found that the nuclear Ca^{2+} rise promotes CCF expulsion and, consequently, activation of the cGAS-STING pathway.
Discussion: These findings propose a novel Ca^{2+}-mediated signaling mechanism that promotes CCF expulsion and cGAS-STING activation.

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P97. Comparative network analysis reveals divergent organization of CAZyme-associated modules in *Rhizoctonia solani* AG1 and AG3.
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Introduction: *Rhizoctonia solani* comprises genetically diverse anastomosis groups (AGs) that differ in host range and pathogenic behavior. Gene-family evolution and changes in regulatory organization may contribute to this functional diversification. Here, we compared AG1 and AG3 to investigate differences in the organization of transcription factors (TFs) and carbohydrate-active enzymes (CAZymes), key components potentially involved in host colonization.
The aim of this work was to identify evolutionary and network-level differences associated with pathogenicity-related functions in *R. solani* AG1 and AG3.

Materials and Methods: Available AG1 and AG3 genomes were re-annotated using a standardized pipeline to obtain high-completeness, comparable proteomes. These proteomes were used for transcription factor and CAZyme annotation, comparative gene-family analysis, phylogenetic reconstruction, and inference of gene duplication patterns. Protein association networks were generated for each AG, filtered using an edge-weight threshold of ≥0.05, and analyzed for topology and community structure using GLay. Communities were characterized according to their TF and CAZyme composition.
Results: Gene-family reconstruction revealed extensive duplication across *R. solani*, with prominent duplication signals within the AG3 lineage. Network analysis identified strongly CAZyme-enriched communities in both groups. The main AG1 community contained 253 proteins, including 72 CAZymes and 12 TFs, whereas the corresponding AG3 community contained 220 proteins, 71 CAZymes and 6 TFs. Despite their remarkably similar CAZyme content, these communities differed substantially in TF composition. CAZyme-rich regions also included fungal Zn2Cys6 TFs carrying a xylanolytic transcriptional activator domain.
Discussion: These results suggest that AG1 and AG3 conserve CAZyme-rich functional modules while differing in their regulatory composition. Together with lineage-specific gene duplication patterns, this supports divergence in the organization of plant cell-wall degradation-associated functions that may contribute to pathogenic specialization among *R. solani* AGs.

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P98. How do they bind? Cdi0128 responsible for the adhesion in *Clostridium difficile.*
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Introduction: *Clostridium difficile* is a pathogen capable of colonizing tissues, causing infections normally refractory to antibiotic use. Its colonization depends on pilus-like structures capable of withstanding high mechanical forces; nevertheless, the mechanisms involved are not fully understood. The structural protein is Cdi0128, a homolog of the Spy0128 protein, which is well known in the field of adhesion for providing a mechanism of adhesion and energy dissipation based on isopeptide bonds, formed by the side chains of Asn and Lys residues. In this study, we inspected the formation of this bond in the Cdi0128 protein, pili protein from *C. diffficile*, seeking to understand its evolutionary origin and its contribution to protein stability.
Materials and Methods: We prepared a phylogenetic tree using PhyML and reconstructed ancestral sequences from there. The protein was expressed, purified, and prepared for single-molecule mechanical assay, while we conducted a structural characterization by X-ray crystallography.
Results: Phylogenetic analysis shows that Cdi0128 is grouped within the Streptococcus clade and is close to the last common ancestor with Clostridia sequences. Despite the conservation of the Asn and Lys residues, the isopeptide bond was not formed in all of the molecules analyzed. In the mechanical assay, we observed unfolding events –48 nm or 32+22 nm –, explaining the unfolding of a single domain that lacks the formation of the isopeptide. Similar results were observed in the crystal structure, where the isopeptide bond was observed in two of the four domains present in the crystal structure.
Discussion: Despite Cdi0128 presenting all the residues for the isopeptide bond, in vitro assays suggest that only a fraction of the protein can successfully form the bond. Together, our results suggest that although the isopeptide bond is introduced early in pili evolution, its functionality–limiting extension– became later operative, probably due to the introduction of other residues.

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P99. Functional Coupling of the Piezo1–TRPM4 Complex Drives Focal Adhesion Dynamics.
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Introduction: Cell migration is critical across numerous physiological and pathological contexts. This process depends on coordinated cytoskeletal remodeling, focal adhesion (FA) dynamics, and local fluctuations in intracellular Ca^{2+}. TRPM4—a Ca^{2+}-activated, monovalent cation-selective channel localized to FAs-facilitates FA disassembly, an event driven by local, oscillatory transients. Here, we demonstrate that Piezo1 and TRPM4 interact and colocalize at FA. Moreover, Piezo1-TRPM4 functional complex regulates FA turnover by modulating these localized signals. Specifically, TRPM4 amplifies FA Ca^{2+} signaling elicited by Yoda1, an agonist of the mechanosensitive channel Piezo1, which also localizes to FAs. These signaling dynamics directly correlate with FA assembly and disassembly rates. Together, our findings uncover a mechanism through

which FA-associated local Ca^{2+} signals are generated and shaped, establish that focal adhesions are electrically active microdomains, and identify the molecular complex that orchestrates these dynamics.
Materials and Methods: Co-immunoprecipitation (Co-IP) and proximity ligation assays (PLA) were used to detect the physical interaction between Piezo1 and TRPM4. To measure local signals in HEK293 and mouse embryonic fibroblast (MEF) cells via total internal reflection fluorescence (TIRF) microscopy, we developed several biosensors: TRPM4-GCaMP8f for local Ca^{2+} signals, mCherry-Paxillin-jGCaMP8f for FA-associated Ca^{2+} signals and Voltron-Paxillin for membrane potential. Additionally, we engineered a Ca^{2+}-dependent, FA-targeted proximity labeling tool (Paxillin-CalID) to biotinylate and identify FA-associated Ca^{2+}-responsive proteomes.
Results: TRPM4-Piezo1 interaction was detected by PLA and Co-IP assays. Piezo1 activation also induced TRPM4-associated Ca^{2+} signals. TRPM4 silencing or KO decreased the frequency of FA-associated Ca^{2+} oscillations induced by the Piezo1 activator Yoda1. Moreover, our data suggest that Yoda1-induced changes in local membrane potential at FAs are TRPM4-dependent.
Discussion: These data suggest that Piezo1 and TRPM4 form a functional complex at FAs that modulates local Ca^{2+} signaling and membrane potential following Piezo1 activation.

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P100. SALL2 loss promotes glycolytic reprogramming and metabolic vulnerability in colorectal cancer.
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Introduction: Metabolic reprogramming is a hallmark of cancer that enables tumour cells to sustain proliferation and adapt to nutrient availability. Among the major metabolic pathways, glycolysis plays a central role by providing ATP and metabolic intermediates that support multiple biosynthetic pathways. Consequently, increased glycolytic activity can contribute to the metabolic demands of proliferating cancer cells and may create exploitable metabolic dependencies. SALL2 is a zinc-finger transcription factor described as a tumour suppressor in CRC, with established roles in cell proliferation and migration. Recent evidence relating SALL2 to lipid metabolism and oxidative stress regulation suggests that its functions may also extend to cellular metabolism.
Aim: To investigate whether SALL2 regulates metabolic programs in CRC cells and the consecutive generation of exploitable metabolic dependencies followed by its loss.
Materials and Methods: Integrated genomic and transcriptomic analyses combining *in-house* SALL2 loss-of-function RNA-seq and ChIP-seq datasets with publicly available CRC TCGA datasets were analyzed to evaluate SALL2-candidate genes. The effects of SALL2 gain and loss of function on the mRNA and protein levels of selected metabolic-related proteins was assessed in SW480 CRC cells using qPCR and Western blotting. SALL2 influence on mitochondrial phenotype was assessed by western blotting and fluorescence microscopy. Cell viability on SALL2 KO cells was evaluated by violet crystal upon glycolysis inhibition and glutamine starvation.
Results: Integrated genomic and transcriptomic analyses identified metabolic regulation as a prominent process associated with SALL2 loss. Consistently, SALL2 loss induced coordinated changes in glycolysis-associated proteins and altered mitochondrial stability. These metabolic alterations were accompanied by changes in cell viability under glycolytic inhibition and glutamine deprivation, supporting a role for SALL2 in metabolic adaptation.
Conclusion: Together, our findings identify SALL2 as a regulator of CRC metabolism and suggest that its loss generates metabolic dependencies that could represent therapeutically exploitable vulnerabilities.

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P101. SlEIL3-1 is a conserved regulator of sulfate-deficiency responses in tomato.
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Introduction: Understanding how conserved nutrient-response regulators are integrated into crop-specific transcriptional networks remains a major challenge. Here, we used organ-specific gene regulatory networks to identify transcription factors associated with sulfate-deficiency responses in tomato (*Solanum lycopersicum* L.). *Sl*EIL3-1, a member of the conserved EIL3/SLIM1 lineage, emerged as the strongest candidate regulator in both roots and leaves and displayed regulatory features distinct from those of its paralog, *Sl*EIL3-2. The aim of this work is to elucidate the conserved role of *Sl*EIL3-1 in response to and characterize its function in tomato

Materials and Methods: Heterologous expression of S*l*EIL3-1 in *Arabidopsis thaliana* was used to evaluate the conserved role of S*l*EIL3-1 in response to sulfate deficiency. DNA Affinity Purification and sequencing (DAP-seq) analyses, Transient Assay Reporting Genome-wide Effects of Transcription factors (TARGET), and organ-specific gene regulatory networks (GNRs) were used to characterize the regulatory function of S*l*EIL3-1 in tomato.
Results: Heterologous expression of *Sl*EIL3-1 in *Arabidopsis* partially complemented *slim1* phenotypes and, under sulfate-sufficient conditions, preactivated a subset of the endogenous sulfate-starvation transcriptional program, particularly genes involved in sulfur-deficiency signaling and remobilization. DAP-seq analyses in tomato revealed a conserved EIL-like DNA-binding motif and significant enrichment of sulfur-related genes among *Sl*EIL3-1-bound loci, including sulfate transport and assimilation components and starvation-response genes. Integration of DAP-seq with TARGET and organ-specific GRNs defined a shared regulatory core, together with root- and leaf-specific branches.
Discussion: These findings connect conserved DNA recognition with species- and tissue-specific network organization. Collectively, our results identify *Sl*EIL3-1 as the principal tomato functional counterpart of Arabidopsis SLIM1 and support conservation of EIL3/SLIM1 function in the sulfate-deficiency response, particularly in the regulation of sulfur-starvation signaling and remobilization.

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P102. Comparative transcriptomics during fruit development in *Prunus avium* L. grown under open-field and high tunnel conditions.
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Introduction: The cultivation of sweet cherry (*Prunus avium* L.; cv. 'Santina') under high tunnel is a strategy to protect crops from adverse environmental conditions while modifying the fruit microclimate. Previous observations suggest that high tunnel cultivation may alter fruit development dynamics. However, the molecular mechanisms underlying these responses remain poorly understood. The aim of this study was to characterize the transcriptomic dynamics of sweet cherry fruit development under high tunnel and open field conditions, and to identify the temporal dynamics of differentially expressed genes (DEGs) in cherry fruits developing under high tunnels compared to open field conditions across four developmental stages.
Materials and Methods: Sweet cherry fruits were collected at four developmental stages under open and high tunnel conditions. Total RNA was extracted and transcriptomic profiling was performed by RNA sequencing (RNA-seq). Global transcriptional variation was evaluated using Principal Component Analysis (PCA), while differential expression and clustering analyses were performed to identify genes and temporal expression patterns associated with cultivation conditions and fruit development.
Results: Principal Component Analysis revealed a transcriptomic structure associated with developmental stage and cultivation conditions, with the first two principal components explain 73% of the variance. Clustering analysis of 3,000 genes identified 10 distinct temporal expression profiles, revealing condition-dependent patterns of transcript accumulation throughout fruit development. Differences between high tunnel and open field conditions became evident during later stages of fruit development, with the strongest transcriptomic divergence observed at T3.
Discussion: These results indicate that high tunnel cultivation modifies the temporal transcriptional dynamics of sweet cherry fruit development. The divergence observed at T3 suggests that the high tunnel environment affects transcriptional regulation during late fruit development and ripening. Functional characterization of these gene clusters will help identify the biological processes and regulatory pathways associated with the developmental response of sweet cherry fruit to high tunnel cultivation.

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P103. Cultivar-Specific Responses to flg22 and Xyn11e in Bacterial and Fungal Pathosystems of Prunus.
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Introduction: Pattern-triggered immunity can vary among plant genotypes, potentially determining the effectiveness of immune elicitors. The bacterial peptide flg22 and fungal xylanase Xyn11e activate distinct defense responses, but their

protective effects across *Prunus* genotypes remain poorly understood. We compared elicitor-induced resistance to *Pseudomonas syringae* pv. *syringae* and *Botrytis cinerea* among sweet cherry and peach cultivars.
Materials and Methods: Leaves from three *Prunus avium* cultivars (Lapins, Bing, and Santina) and four *Prunus persica* cultivars (Andes Nec 1, Dulcis, Maria Dolce, and Venus) were petiole-dipped in Mock, flg22, or Xyn11e for 24 h. Susceptibility assays were subsequently performed with *P. syringae* pv. *syringae* (Pss) and *B. cinerea* (Bc) on detached leaves. Lesion area was measured after pathogen incubation and used to determine susceptibility. Treatments were compared within cultivars and cultivars within treatments using the Kruskal–Wallis test followed by Dunn's test.
Results: In *Prunus avium*, Bing was significantly more susceptible to Pss than Lapins, but was the significantly most resistant cultivar to Bc, followed by Lapins. Lapins significantly increased its resistance to Pss in the presence of Flg22, whereas its resistance to Bc increased significantly in the presence of Xyn11e, reaching resistance levels comparable to those of Bing. In *Prunus persica*, Andes Nec 1 was the significantly most resistant cultivar to Pss, maintaining a significant difference from Venus and Dulcis and reaching resistance levels comparable to Maria Dolce in the presence of Flg22. In contrast, no significant differences in susceptibility among cultivars were observed against Bc.
Discussion: The different cultivars of the Prunus species studied exhibit differential responses to pathogens, even in the presence of resistance inducers.

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P104. Glycosylated Delphinidins, Natural Antioxidants, Functionally Modulate the COX-2/PGE2 Axis and Downregulate MDR1 in Glioblastoma Cells

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Introduction: Multidrug resistance (MDR), mediated primarily by the MDR1/P-glycoprotein (P-gp) transporter, is one of the main barriers to the therapeutic efficacy of glioblastoma (GB). Various signaling pathways associated with inflammation and cellular stress, such as NF-κB and COX-2, have been implicated in tumor survival and chemoresistance. In this context, the anthocyanins delphinidin-3-glucoside (DEL-3) and delphinidin-3,5-diglucoside (DEL-3,5)—natural compounds with recognized bioactive properties—stand out for their ability to modulate mechanisms linked to inflammation and cancer progression, positioning them as potential adjuvant agents in GB therapy.
Materials and Methods: U87-MG and GBM38 cells treated with delphinidin-3-glucoside (DEL-3) and delphinidin-3,5-diglucoside (DEL-3,5) were used. COX-2 activity was determined by quantifying PGE_2 via ELISA. MDR1 expression was assessed by RT-qPCR and Western blot, while the activity of its promoter was analyzed using a luciferase reporter assay. Finally, cell viability was measured using the MTT assay following treatment with chemotherapeutic agents, either alone or in combination with DEL-3.
Results: DEL-3 reduced PGE_2 production, indicating a decrease in COX-2 activity. Both DEL-3 and DEL-3,5 decreased MDR1 expression at the transcriptional level; however, only DEL-3 produced a sustained reduction in protein levels and promoter activity. In contrast, DEL-3,5 did not significantly alter this activity. Furthermore, combination therapy with DEL-3 and vincristine, doxorubicin, etoposide, or paclitaxel increased cytotoxicity in U87-MG cells, demonstrating greater sensitivity to chemotherapy.
Discussion: DEL-3 consistently regulates MDR1 at the transcriptional and protein levels, whereas DEL-3,5 showed limited effects. These differences suggest that glycosylation influences the modulation of pathways associated with inflammation and resistance. Taken together, these findings position DEL-3 as a potential adjuvant for reducing chemoresistance in glioblastoma.

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P105. Study of Plasma-Derived Small Extracellular Vesicles from Chilean Women.

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P106. Endothelin-1 increases ET_AR protein levels and promotes Src-dependent migration/invasion in gallbladder cancer cells. Ojeda Valentina[1] (valentina.ojeda05@alumnos.uach.cl), Vidal-Vidal Jetzabel[1], Ruiz-Uribe Matías[1]. Niechi Ignacio[1]. Instituto de Bioquímica y Microbiología,[1]Facultad de Ciencias, Universidad Austral de Chile, Valdivia, Chile.

Introduction: Gallbladder cancer (GBC) is an aggressive malignancy with a poor prognosis due to its late diagnosis and high metastatic potential. Chile has one of the highest incidence rates of GBC worldwide, particularly in the Los Ríos Region, highlighting the need to identify new therapeutic targets. Multiple studies have shown that the Endothelin-1 (ET-1) signaling pathway and its type A receptor (ET_AR) actively participate in tumor progression and are associated with reduced patient survival. ET-1/ET_AR signaling activates intracellular pathways involving Src, a central signaling node that promotes cell survival, proliferation, and invasion. However, the functional role of ET_AR/Src signaling in regulating GBC cell aggressiveness remains poorly understood. This study aimed to evaluate the effect of ET-1 on ET_AR protein levels and on the Src-dependent migratory and invasive capacity of GBC cells.
Materials and Methods: The GBC cell line NOZ was treated with ET-1 and/or the selective ET_AR antagonist Ambrisentan or the Src inhibitor Saracatinib. ET_AR protein levels were evaluated by Western blot, whereas cell migration and invasion were assessed using Transwell and Matrigel-coated Transwell assays, respectively. Cell viability was evaluated by crystal violet assays at different time points.
Results: ET-1 increased ET_AR protein levels and the migratory and invasive capacity of GBC cells. These effects were impaired by ET_AR blockade with Ambrisentan or Src inhibition with Saracatinib.
Discussion: These findings indicate that ET-1/ET_AR signaling regulates both ET_AR protein levels and the migratory and invasive capacity of GBC cells, and that these effects are dependent, at least in part, on Src activation.

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P107. The FAM162A-FUNDC1 mitophagy axis is uncoupled from autophagosome degradation in thyroid cancer as a potential mechanism of malignancy.
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Introduction: Thyroid cancer is the most prevalent endocrine malignancy, highlighting the need to understand mechanisms that support tumor adaptation. We previously showed that FAM162A promotes mitophagy; however, the underlying pathway remains unclear. Because FAM162A interacts with OPA1, which is functionally linked to FUNDC1, we hypothesized that FAM162A is coupled to mitochondrial fitness and FUNDC1-associated mitophagy.
Materials and Methods: FAM162A, FUNDC1, LC3, OPA1, and mitochondrial mass marker expression were assessed by Western blot in thyroid tumors and paired adjacent tissues. Loss- and gain-of-function experiments were performed in TPC-1 cells to evaluate mitophagic flux and bioenergetics. FAM162A mRNA expression was correlated with a mitophagy-related gene panel in 498 patients from the TCGA-THCA PanCancer Atlas dataset. RNA-seq from one Chilean patient was additionally analyzed.
Results: FAM162A, FUNDC1, and OPA1 protein levels were significantly increased in tumor tissue compared with paired adjacent tissue, whereas the LC3-II/LC3-I ratio was reduced. FAM162A overexpression in TPC-1 cells reproduced the reduction in autophagic flux while maintaining OPA1 and FUNDC1 abundance. In contrast, FAM162A silencing increased autophagic flux and reduced mitochondrial biomass and bioenergetic capacity. TCGA-THCA analysis showed that FAM162A

expression positively correlated with Complex I genes, FUNDC1, and CHMP2A, a gene involved in autophagosome closure, and negatively correlated with PGAM5, a regulator of FUNDC1, and NBR1, a selective autophagy receptor. A similar expression pattern was observed in RNA-seq data from one Chilean patient.
Discussion: Our findings suggest that FAM162A promotes mitochondrial fitness while limiting efficient autophagic clearance in thyroid cancer. Increased FAM162A, OPA1, FUNDC1, and Complex I expression supports preservation of mitochondrial structure and respiratory capacity, whereas reduced autophagic flux indicates impaired mitochondrial turnover. The inverse associations with PGAM5 and NBR1, together with increased CHMP2A, suggest dysregulation between mitophagy signaling, autophagosome maturation, and selective cargo degradation. Overall, FAM162A may favor mitochondrial maintenance and metabolic adaptation in thyroid cancer cells during tumorigenesis.

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P108. Bacteria from Chilean tomato fields differentially elicit oxidative bursts, modulate flg22 responses, and affect Pseudomonas syringae growth.
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Introduction: Soil bacteria can activate pattern-triggered immunity and modify responses to subsequent microbial signals. Flagellin-derived flg22 is perceived by FLS2, triggering ROS production. We evaluated 24 isolates from Chilean tomato fields, including flagellated and non-flagellated strains, for direct ROS elicitation, modulation of flg22-triggered responses, and effects on *Pseudomonas syringae* pv. tomato (Pst) growth.
Materials and Methods: ROS directly elicited by each strain was measured by luminol-based chemiluminescence. Tomato plants (cv. M82) were root-inoculated with each strain or with *Agrobacterium* sp. and water controls. At 14 dpi, cumulative ROS was quantified in leaf discs challenged with flg22. At 16 dpi, plants were foliar-inoculated with Pst, and pathogen populations were quantified seven days later.
Results: Strains differed in direct oxidative-burst elicitation. Root inoculation also altered cumulative flg22-triggered ROS (ΣRLU; Kruskal–Wallis, $p < 0.05$) and Pst populations ($p < 0.0001$). Flagellated AS116 induced the highest cumulative response (107,200 ΣRLU), whereas flagellated AS66 and AS104 reached 78,300 and 70,600 ΣRLU, respectively. Non-flagellated AS78 reached 76,300 ΣRLU, close to the water control (74,250 ΣRLU), revealing functional variation both between and among flagellation phenotypes. AS116- and AS78-treated plants displayed Pst populations of 7.46 and 6.72 $\log_{10}$ CFU/g, respectively. AS46 and AS88 showed comparatively low Pst populations, with the lowest reaching 6.02 $\log_{10}$ CFU/g versus 7.98 in the water control.
Discussion: The response of non-flagellated AS78, together with variation among flagellated isolates, suggests that flagellar status contributes to, but does not fully determine, subsequent flg22-triggered responses. *fliC* sequence analysis will test whether flg22 polymorphisms are associated with direct ROS elicitation and immune potentiation.

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P.109 TAGL1 and TAGL2: candidate triacylglycerol lipases as putative regulators of cold-responsive root hair elongation in Arabidopsis thaliana.
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Introduction: Root hair elongation is a plastic developmental response that modulates nutrient and water acquisition under changing environmental conditions. Although moderate low temperature (10 °C) enhances root hair elongation in *Arabidopsis thaliana*, the genetic variation underlying this response remains incompletely understood. A genome-wide association study (GWAS) in 160 *Arabidopsis* accessions identified *TAGL1* (*AT5G42930*), predicted to encode a triacylglycerol lipase, as a candidate gene associated with natural variation in this trait. *TAGL1* produces two transcript variants through alternative splicing, and *TAGL2 (AT1G56630*), a close homolog, was selected as a complementary candidate. This work characterizes both lipases structurally and evaluates their functional relevance in this response.

Materials and Methods: Structures of both TAGL1 isoforms (TAGL1-L, TAGL1-S) and TAGL2 were predicted with AlphaFold2, and catalytic residues assigned by structural alignment with the characterized lipase AtOBL1. Molecular docking with glycerol was used to evaluate active-site binding geometry. SALK T-DNA insertion mutants of *tagl1* and *tagl2* were phenotyped at 22 °C and 10 °C. Lipid droplets were stained with BODIPY 493/503 and imaged by confocal microscopy.
Results: TAGL1-L contains a complete catalytic triad (S290/D354/H447) and a productive binding geometry with glycerol. TAGL1-S carries a cysteine at the position corresponding to the catalytic histidine (C396), and no productive binding was predicted. TAGL2 retains an equivalent triad (S301/D365/H458) with productive predicted binding. *tagl1* and *tagl2* mutants showed altered lipid droplet accumulation and morphology in roots compared with wild type.
Discussion: The structural features of TAGL1-L and TAGL2 are consistent with functional serine lipases, whereas TAGL1-S is unlikely to act as a classical lipase. The altered lipid droplet phenotypes indicate that both proteins influence lipid droplet homeostasis in roots, linking lipid metabolism to root hair growth at low temperature. Expression profiling, enzymatic assays and lipid composition analyses are ongoing to establish the mechanistic basis of these functions.

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P110. Post-translational regulation of SALL2 transcription factor by Wnt/ β-catenin pathway modulators GSK3β and TNKS.
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Introduction: SALL2 is a member of the Spalt-like family of zinc-finger transcription factors involved in developmental processes such as cell proliferation, differentiation, and migration, which are frequently dysregulated in cancer. Although evidence supports a role for SALL2 in both neural development and tumorigenesis, the mechanisms that regulate SALL2 remain poorly understood. Previous studies from our laboratory revealed an inverse correlation between SALL2 levels and nuclear β-catenin, a marker of Wnt/β-catenin pathway activation. Interestingly, treatment with either the Wnt activator CHIR99021, a GSK3β inhibitor, or the Wnt inhibitor XAV939, a tankyrase (TNKS) inhibitor, increased SALL2 protein levels despite their opposing effects on the Wnt/β-catenin signaling. Aim**:** To investigate whether GSK3β and TNKS contribute directly to the post-translational regulation of SALL2.
Materials and Methods: *In silico* analysis of the SALL2 protein sequence was performed to identify putative GSK3β phosphorylation and TNKS-dependent PARylation sites. Subcellular fractionation, immunoprecipitation, and immunocytochemistry were performed in HEK293T and Caco-2 cells to assess protein localization and potential associations. The effects of pharmacological inhibition of GSK3β and TNKS on SALL2 protein levels were evaluated using CHIR99021 and XAV939, respectively, for 2, 4, and 24 h. SALL2 protein stability was assessed in HEK293T cells following expression of GSK3β or TNKS and cycloheximide-mediated inhibition of protein synthesis.
Results: Putative phosphorylation and PARylation sites were identified near the PEST region of the SALL2 protein. SALL2, GSK3β, and TNKS showed nuclear co-localization and were detected in coimmunoprecipitation assays, although direct physical interactions remain to be established. Pharmacological inhibition and protein stability assays were consistent with a negative regulatory effect of both GSK3β and TNKS on SALL2 protein levels.
Conclusion: These findings support a previously unrecognized mechanism of post-translational regulation of SALL2 involving GSK3β and TNKS, suggesting that these proteins contribute to the control of SALL2 protein stability.

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P111. Untapping prophages' role in antibiotic resistance across the Pseudomonadota human pathogens.
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Introduction: Antibiotic resistance is one of the most pressing global health issues, and it is increasing and spreading at an alarming rate. Common infections are becoming hard to treat, and traditional antibiotics are no longer effective against several deadly drug-resistant bacteria. The World Health Organization (WHO) list of critical pathogens includes mostly Gram-negative bacteria, mainly from the Pseudomonadota phylum (formerly Proteobacteria). Horizontal spread of antibiotic resistance genes (ARGs) mainly occurs via mobile genetic elements (MGE), such as plasmids, transposons, and integrons. Bacteriophages (phages), viruses that infect bacteria, are also capable of mobilising genes across populations. However, the role of phages integrated into their host genomes (prophages) on antibiotic resistance is less clear. Here, we identified and characterised the prophages present in 27 strains from alpha, beta, and gammaproteobacteria (Pseudomonadota phylum) along with their ARGs.
Materials and Methods: Three different tools were used to predict prophage clusters and the Resistance Gene Identifier (The Comprehensive Antibiotic Resistance Database, CARD) to examine the resistomes.

Results: Each strain contained between one and sixteen putative prophages, mostly from the Siphoviridae and Myoviridae families, and eighteen in total were not classified. Specific transposon elements are also located within some prophage clusters. Interestingly, six phage-plasmids were predicted for highly perilous pathogens. All the ARGs were found within chromosomes, except for two strains that also have plasmid-harboured genes. A high diversity of ARGs was detected across species, mainly linked to efflux and antibiotic target alteration, with a small set of bacteria sharing clinically relevant genes.
Discussion: Together, these data provide significant insights into prophages' potential roles in transmission and dissemination of ARGs in harmful human pathogens.

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P112. Photoreceptors regulate alternative splicing at the root of *Arabidopsis thaliana* when shoot is exposed to white light and shade

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Introduction: Light is a key environmental signal for plants, which have evolved photoreceptors such as phytochromes (PHYs) to detect red (RL) and far-red light (FRL). These light qualities differ between white light (WL, high RL/FRL) and shade (S, low RL/FRL). PHYs regulate plant morphology, including root architecture. Also, in whole plant, PHYs can regulate the alternate splicing (AS). However, the role of AS in the root's developmental response to WL or S when only the shoot is illuminated has not yet been studied. Therefore, the objective of this study was to determine the role of PHYA and PHYB in AS in Arabidopsis roots when the shoot is illuminated with WL or S.
Materials and Methods: Ler and *phyaphyb* genotype of 7 days old were treatment with WL or S in the shoot for one or three days, using D-root system. Then, we recollected roots samples that were sequenced for Illumina platform. We analyzed the Differential Expression Gene (DEG) using DESeq2 and Differential Splicing Genes (DSG) using rMATS.
Results: We analyzed the data between Ler and *phyaphyb* genotypes in the different conditions of treatment, identifying 3705 DSGs and 3935 DEGs. Enriched Gene Ontology (GO) in biological processes in DSGs include response to light stimulus, Defense response to other organisms, response to salt stress, while the GO in DEGs include response to far red light, response to jasmonic Acid. Validation of differentially spliced genes could be incorporated.
Discussion: These results show that stem illumination with WL or S regulates both alternative splicing and expression of genes in root mediated by PHYA and PHYB.

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P113. Role of Deoxycholic Acid in NF-κB regulated JC Polyomavirus Antigen T transcription on human colon cells.

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Introduction: An occidental diet is commonly related to a higher risk of colon cancer development. This diet is composed mainly by red meat and fat. Increased physiological levels of cholesterol induce greater production of bile acids (BA), detergent molecules that emulsify lipids in the intestines. DCA, a secondary BA, has been connected in many studies to colon cancer, modulating still unknown molecular pathways. Another agent that has also been connected to colon cancer in some studies is JC Polyomavirus (JCPyV). The Antigen T (AgT) protein of the virus interacts with pRb and p53, promoting dysregulated cell cycle progression. As they are both frequently found in the colon, the idea of a connection between them comes up. A common element is the NF-κB pathway, which is activated by DCA and is necessary for JCPyV viral transcription. In this study, we evaluate the effect of DCA on NF-κB activity and the subsequent AgT transcription.
Materials and Methods: The MTT and Viability assays were used to determine the DCA concentrations to be used in the following experiments. Reporter plasmids were used to measure changes in NF-κB and JCPyV promoter activity induced by different DCA treatments at different times.
Results: The doses commonly used in other studies were, in fact, similar to the interesting ones detected in this study (0.1mM-0.5mM) and thus chosen here. A significant increase in NF-κB activity was detected upon use of a high DCA dose. In a similar way, an increase was detected on the JCPyV promoter activity after DCA treatment.

Discussion: Together, these experiments suggest that DCA upregulates NF-κB activity and consequently JCPyV promoter activity. It is to be confirmed whether the upregulation is also detected in JCPyV protein transcription, such as AgT.

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P114. Physiological and biochemical responses to water deficit in *Lupinus luteus* L.

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Introduction: Water deficit is a major abiotic stress affecting grain legumes, particularly during reproductive development. *Lupinus luteus* is a high-protein grain legume cultivated in Mediterranean-type environments, but the physiological and biochemical mechanisms underlying its response to water limitation remain poorly understood. This study characterized responses among *L. luteus* accessions subjected to water deficit.
Materials and Methods: Accessions C98, C112, C195, C230, and C231 were grown under greenhouse conditions. Water deficit was imposed at flowering by maintaining plants at 40% pot capacity, while controls remained at 80%. Xylem water potential, relative water content, gas exchange, effective quantum yield of photosystem II (ΦPSII), photosynthetic pigments, and soluble carbohydrates were evaluated.
Results: Water deficit decreased xylem water potential to −0.99-−1.12 MPa and reduced relative water content, indicating moderate and broadly comparable stress among accessions. Multivariate analysis identified five distinct physiological profiles. C112 retained the greatest relative proportion of net CO_2 assimilation, stomatal conductance, transpiration, and intercellular CO_2 concentration. Conversely, C231 exhibited the strongest restriction of gas exchange, increased intrinsic water-use efficiency, and greater relative maintenance of ΦPSII. C195 showed an intermediate and distinct gas-exchange response under water deficit. C98 increased total chlorophyll content by approximately 54% and significantly accumulated neoxanthin, lutein, violaxanthin, and antheraxanthin. Fructose accumulation was greatest in C230 and C231, increasing approximately 4.5- and 4.9-fold, respectively. Raffinose and stachyose were detected only under water deficit.
Discussion: The accessions exhibited contrasting coordination between stomatal regulation, photochemical performance, pigment composition, and carbohydrate metabolism. C112 prioritized carbon assimilation, whereas C231 displayed a more conservative strategy that restricted gas exchange while proportionally maintaining ΦPSII. Pigment accumulation in C98 and carbohydrate accumulation in C230 and C231 indicate distinct photoprotective and metabolic adjustments. These findings indicate that water-deficit responses in *L. luteus* involve multiple interacting response strategies and putative tolerance-related mechanisms rather than a single tolerance trait.

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P115. *SlATG5a* from tomato promotes autophagic activity and water deficit tolerance in *Arabidopsis thaliana.*

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Introduction: Autophagy is a conserved cellular recycling mechanism vital for abiotic stress tolerance in plants. One of its main complexes is ATG12-ATG5-ATG16, which functions by conjugating the ATG8 protein with PE (phosphatidylethanolamine) and directing the expansion and maturation of the autophagosome membrane in a pathway known as canonical autophagy. Despite its relevance, its role or that of its members is poorly understood. In tomato (*Solanum lycopersicum*), there are two homologous genes encoding *ATG5*: *ATG5a* (Sl02g038380) and *ATG5b* (Sl06g43140); however, only *ATG5a* is functional, and its role under abiotic stress conditions, particularly drought, is unknown.
The aim of this work was to determine whether tomato *ATG5a* is capable of positively modulating the response to drought stress through the activation of autophagy.
Materials and Methods: Reporter plants containing *SlATG5a-mCherry* and *ATG8-GFP* were used to evaluate co-localization and autophagic activity. *Arabidopsis atg5-1* mutant seedlings complemented with *SlATG5a* were subjected to drought stress and their phenotypic response was evaluated.
Results: Under stress conditions, *SlATG5a-mCherry* showed partial co-localization with *ATG8-GFP*, and an increase in ATG8-positive puncta compared to non-stressed plants. After 7 days of stress, seedlings complemented with constitutively expressed *SlATG5a* showed superior root growth compared to wild-type plants.

Discussion: Together, the results showed that *SlATG5a* has a positive role in autophagy activation during the response to drought stress and is a potential candidate for tomato breeding.

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P116. A non-canonical mechanism of gain-of-aggressiveness in colorrectal cancer cells based in the phosphorylation of the N-terminal domain of endothelin-converting enzyme-1c. Paula Romero Vicencio[1] (paula.romero.1@ug.uchile.cl), Karla Villalobos-Nova[1], María de los Ángeles Toro[1], Leyha Morales V[1], Javiera Carvacho[1], Isabel Castro[2], Carlos Santiviago[3], Julio C. Tapia[1].[1]Laboratorio de Transformación Celular, [2]Laboratorio de Biología Celular; Núcleo Interdisciplinario de Biología y Genética (NiBG), Instituto de Ciencias Biomédicas (ICBM), Facultad de Medicina, Universidad de Chile. [3]Laboratorio de Microbiología, Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile.

Introduction: Endothelin-converting enzyme-1c (ECE1c) plays a key role in the gain-of-aggressiveness of several cancers, such as glioblastoma, lung, and colorectal cancer (CRC). We have demonstrated that phosphorylation at Ser18 and Ser20 of the ECE1c's N-terminus by protein kinase CK2 promotes its stability and favors the acquisition of a malignant phenotype in CRC cells. These findings raise the question of whether this phenomenon occurs through the canonical endothelin-1 (ET-1) pathway or through a non-canonical mechanism independent of ECE1c catalytic activity. The aim of this study was to evaluate the effect of ECE1c's N-terminal phosphorylation on the aggressiveness of CRC cells, independently of its catalytic domain.
Materials and Methods: DLD-1 CRC cells were transfected with plasmids encoding recombinant fusion proteins consisting of the ECE1c's N-terminus fused to GFP (NT^{X}-GFP). Three variants were evaluated: a phosphomimetic mutant at Ser18 and Ser20 (NT^{DD}-GFP), a phosphoresistant mutant (NT^{AA}-GFP), and the wild-type sequence (NT^{WT}-GFP). To evaluate CRC aggressiveness, proliferation (MTS), migration (transwell), and chemoresistance (5-FU) assays were performed.
Results: DLD-1 cells expressing the phosphomimetic NT^{DD}-GFP fusion protein showed increased proliferative, migratory, and chemoresistance capacities, meaning a more aggressive phenotype compared with cells expressing the phosphoresistant NT^{AA}-GFP protein.
Discussion: As the catalytic domain is absent in our recombinant fusion proteins, our results indicate that only the phosphorylation of the cytoplasmic ECE1c's N-terminal domain promotes an aggressive phenotype in CRC cells. This is evidence of a parallel non-canonical mechanism through which ECE1c contributes to CRC malignant progression.

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P117. Evaluation of the differential expression of long non-coding RNAs associated with apoptosis and autophagy in an *in vitro* model of cisplatin-induced nephrotoxicity.
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Introduction: Cancer is the second leading cause of death worldwide, and cisplatin remains widely used to treat solid tumors. However, its clinical use is limited by drug resistance and adverse effects, particularly nephrotoxicity, its most frequent and severe complication, which affects approximately 20% of treated patients. Because cisplatin-induced nephrotoxicity is multifactorial and involves genetic and epigenetic mechanisms, the role of long non-coding RNAs (lncRNAs) remains insufficiently understood. This exploratory study evaluated the differential expression of eight lncRNAs (UCA1, XLOC_032768, HOTAIR, ROR, PRNCR1, OIP5-AS1, GAS5, and PVT1) in an *in vitro* model of cisplatin-induced nephrotoxicity.
Materials and Methods: Human renal cell lines HEK-293 and HK-2 were exposed to increasing cisplatin concentrations for 24 hours. Cell viability was assessed using the MTS assay to determine CI_{25}, CI_{50}, and CI_{75} values. Apoptosis- and autophagy-related proteins were analyzed by Western blot, and lncRNA expression was measured by RT-qPCR.
Results: Cisplatin reduced cell viability, with CI_{25}, CI_{50}, and CI_{75} values of 8.8, 15.43, and 27 μM in HEK-293 cells, and 8.1, 13.57, and 22.8 μM in HK-2 cells, respectively. Western blot analysis showed increased cleaved caspase-9, decreased caspase-3, and an increased LC3-II/LC3-I ratio, with no changes in caspase-7 or Beclin-1. UCA1, XLOC_032768, HOTAIR, ROR, and PRNCR1 were downregulated, OIP5-AS1 was overexpressed, and GAS5 and PVT1 remained unchanged.
Discussion: These findings suggest that dysregulated lncRNAs are associated with apoptosis and autophagy in cisplatin-treated human renal cells, supporting an epigenetic contribution to cisplatin-induced nephrotoxicity.

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P118. Non-coding variants associated with gene-pesticide exposure interaction in a Drosophila model of Parkinson's disease may affect the affinity of the Dorsal/NF-kB transcription factor to its binding sites.

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Introduction: Idiopathic Parkinson's disease (iPD) accounts for 90% of all cases. Genetic risk factors explain 22% of the risk and environmental factors accounts for approximately 10%. Therefore, gene-environment interaction (GEI), or genetic susceptibility to environmental factors may largely explain this missing risk. Through Genome-Wide Association Studies, we found genetic variants associated with susceptibility to developing motor and sleep phenotypes in response to rotenone exposure, a Drosophila established PD model. Two of them localize upstream of *dMLF* and in the third intron of CG17271/*dMCFD2*. These variants map to Dorsal transcription factor binding sites, an homolog of Rel-A/NF-kB known to regulate neuroinflammation, a risk factor of PD. Our goal is to determine whether these genetic variants affect the expression of *dMLF* and CG17271/*dMCFD2*, and whether they affect the binding of Dorsal to its binding sites on these genes.
Materials and Methods: We performed gene expression analysis using RT-qPCR on fly heads from F1 crosses of DGRP lines exposed and non-exposed to rotenone that contained variants of interest in homozygosity. We modeled potential TFBS found by MEME-FIMO, and the Rel-homology domain of Dorsal using AlphaFold 3 server. Models were validated by all-atom molecular dynamics simulations utilizing GROMACS and CHARMM36 forcefield, finally the difference in affinity of the complexes was approximated with gmx_MMPBSA.
Results: Genetic variants in Dorsal TFBS in *dMLF* regulate expression independently of rotenone exposure, while in *CG17271/dMCDF2* affects expression in response to rotenone. The major allele of the *dMLF* variant and the minor allele of *CG17271/dMCFD2* showed better confidence in the AlphaFold 3 model but only the last showed a significantly better affinity in MMPBSA analysis.
Discussion: Our results suggest that genetic variants affecting affinity of Dorsal to its TFBS in *dMLF* and *CG17271/dMCDF2* may underlie changes in their expression leading to gene-pesticide exposure interactions.

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P119. CRISPR/Cas9-mediated mutation of the trehalase gene *SlTRE1* for enhanced thermotolerance in tomato (*Solanum lycopersicum* cv Micro-Tom).

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Introduction: Extreme heat events caused by climate change severely affect tomato (*Solanum lycopersicum*) productivity during reproductive stages. Trehalose is an osmoprotectant involved in abiotic stress tolerance, regulated by the TPS/TPP/TRE pathway. We hypothesized that loss-of-function mutation in *SlTRE1*, the tomato ortholog of *AtTRE1*, would increase endogenous trehalose accumulation and enhance thermotolerance in Micro-Tom plants. The aim of this work was to generate and molecularly characterize SlTRE1-edited lines using a dual-gRNA CRISPR/Cas9 system.
Materials and Methods: The *AtTRE1* ortholog in tomato was identified via proteome comparison using OrthoVenn3, reciprocal BLASTP, Clustal Omega, and InterProScan. Two gRNAs targeting early exons of *SlTRE1* were designed using CRISPOR and assembled into the pGGK7-AtCas9 vector using Golden Gate cloning. The resulting construct was introduced into *Agrobacterium tumefaciens* EHA105 used for the transformation of Micro-Tom cotyledon and hypocotyl explants. Explants were regenerated on selective medium supplemented with trans-zeatin, IBA, and kanamycin. Cas9 integration and mutations in the *SlTRE1* locus were confirmed in T0 plants by PCR and Sanger sequencing.
Results: Solyc08g082860.3 was identified as the functional ortholog of *AtTRE1* and containing the conserved GH37 catalytic domain. The dual-gRNA CRISPR/Cas9 construct was successfully assembled and validated by sequencing. Micro-Tom explants was successfully regenerated under trans-zeatin/IBA and kanamycin selection. PCR genotyping confirmed Cas9 integration in regenerated T0 plants. Sanger sequencing of the target locus revealed edited lines carrying indels at the expected CRISPR/Cas9 cleavage sites.
Discussion: Together, these results confirm the feasibility and efficiency of dual-gRNA CRISPR/Cas9 system to generate targeted mutations in *SlTRE1* in tomato. Molecular characterization confirmed Cas9 integration and the presence of mutations at the target locus in T0 plants. These lines provide the foundation to evaluate physiological and reproductive responses under controlled heat stress to determine the role of trehalose in thermotolerance.

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P120. Modulation of DNA modifications affects Heterochromatin Function and Transposable Element expression in differentiated cells.

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Introduction: Transposable elements (TEs) constitute a substantial portion of the mammalian genome, and their uncontrolled transcriptional activation is a potential trigger of genomic instability. Under normal conditions, the silencing of these elements is ensured by epigenetic mechanisms, including DNA methylation, which are maintained by key chromatin proteins such as DNMTs, TETs, and OGT. While these mechanisms have been studied in undifferentiated cells, it remains unclear how this dynamic turnover of epigenetic marks influences the control of repetitive regions during cellular differentiation processes, such as myogenesis. This work aims to evaluate how selective inhibition of this subgroup of epigenetic regulators impacts heterochromatin functions and the expression of genes and transposable elements.
Materials and Methods: We used the C2C12 cell model to recapitulate the myogenic differentiation program, culturing cells with selective inhibitors for key epigenetic proteins controlling DNA modifications. The impact of catalytic inhibition on different transposable element families, including LINEs and SINEs, was assessed at the transcriptional level using RT-qPCR, while changes at protein levels were measured by Western blot analysis.
Results: We found that the inhibition of expression regulators of DNA modifications affects specific TE subfamilies, suggesting the involvement of distinct regulatory mechanisms controlling different TE families, which together make up half of the mammalian genome. Remarkably, we also detected the expression of some TE-derived proteins by Western blot following treatments with these epigenetic regulators of DNA modification pathways. Finally, we determined the consequences of alterations in DNA modification patterns on cellular identity.
Discussion: Together, these findings evidence the critical role that DNA modifications play in the maintenance of heterochromatin integrity, the control of repetitive element expression, and cellular identity. This also reveals the necessary crosstalk between different chromatin complexes to maintain the epigenetic landscape in mammalian cells.
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P121. IRE1/XBP1/BDNF axis role in the interaction between neurons and glioblastoma cells during brain cancer progression.

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P122. Electrophysiological characterization of ALMT channels of *Arabidopsis thaliana* in *Xenopus laevis* oocytes.

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Introduction: Aluminum-activated Malate Transporters (ALMTs) are plant anion channels involved in ion homeostasis and adaptation to abiotic stress. Although the ALMT12, ALMT13, and ALMT14 channels belong to the same phylogenetic clade, their functional properties remain poorly characterized. This study aimed to characterize the electrophysiological properties of these channels and determine the subcellular localization of AtALMT12.
Materials and Methods: AtALMT12, AtALMT13, and AtALMT14 were heterologously expressed in Xenopus laevis

oocytes by mRNA microinjection. Anion channel activity was evaluated using the Two-Electrode Voltage Clamp technique under different anion conditions. For AtALMT12, current-voltage relationships, nitrate concentration dependence, and sensitivity to niflumic acid were determined. Functional interactions were evaluated by co-expressing AtALMT12 with AtALMT13 or AtALMT14. AtALMT12 localization was analyzed using an AtALMT12-GFP fusion expressed in Allium cepa cells and visualized by confocal microscopy.
Results: AtALMT12 produced large voltage-dependent anionic currents, whereas AtALMT13 and AtALMT14 showed minimal or undetectable activity under the conditions tested. AtALMT12 displayed the highest current amplitudes in the presence of nitrate, and increasing $NaNO_3$ concentration enhanced current amplitude, with the highest response observed at 100 mM. Treatment with 1 mM niflumic acid reduced AtALMT12-mediated currents by approximately 45%. Co-expression with AtALMT13 markedly reduced or abolished AtALMT12 activity, while co-expression with AtALMT14 did not significantly affect the current. Confocal microscopy confirmed the predominant localization of AtALMT12-GFP at the plasma membrane.
Discussion: These results reveal functional heterogeneity among ALMT12, ALMT13, and ALMT14 and support a prominent role for AtALMT12 as a voltage-dependent anion channel. Its plasma membrane localization and nitrate sensitivity provide relevant insights into ALMT function and plant ion regulation. .

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P123. How does the Arabidopsis embryo respond to iron-induced oxidative damage?
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Introduction. Reactive oxygen species play a dual role in plant development, acting as signaling molecules while becoming potentially harmful when their production exceeds cellular antioxidant capacity. Iron (Fe) is particularly relevant to this balance due to its redox activity, which can promote oxidative damage under conditions of excess. Protein carbonylation represents an irreversible oxidative modification and provides a useful marker of oxidative protein damage. While mechanisms controlling Fe acquisition under excess conditions have been extensively characterized in roots, how developing embryos respond to excessive Fe availability remains poorly understood. The aim of this work is to study Fe accumulation and Fe induced oxidative damage in developing embryos.
Materials and Methods. Isolated Arabidopsis Col-0 embryos at the bent-cotyledon stage were incubated for 72h with different Fe-EDDHA concentrations. Protein carbonylation was assessed by DNPH derivatization followed by immunodetection. Ponceau staining was used as a protein-loading control. Fe accumulation under Fe concentrations was independently assessed by Perls/DAB histochemical staining.
Results. Protein carbonylation progressively increased with increasing Fe-EDDHA concentrations, showing a marked accumulation of oxidatively modified proteins at the highest Fe treatment. Histochemical staining showed Fe accumulation in embryos exposed to high-Fe conditions, indicating that Fe continues to accumulate under conditions associated with oxidative protein damage.
Discussion. The embryo Fe accumulation and protein carbonylation raises the possibility that Fe acquisition in embryos is regulated differently from that described in roots or that its regulatory capacity becomes saturated under Fe excess. These findings provide a basis for investigating the protein-mediated mechanisms underlying Fe sensing, homeostasis, and tolerance to iron-induced oxidative stress during embryo maturation.

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P124. Morphological and histological characterization of *Hermetia illucens* larval tissues as a baseline for recombinant protein expression.
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Introduction: The black soldier fly (BSF, *Hermetia illucens*) is an edible insect used in animal nutrition that has become a key organism in biotechnology. Despite its growing potential as a biofactory, detailed knowledge regarding the morphological changes throughout its larval development remains limited. ByBug Synthetics® is a biotechnology company that seeks to revolutionize animal pharmaceuticals with therapeutic proteins derived from the BSF; the objective of this work was to establish a reference histological map of key tissues such as the gut, fat body, muscle, and cuticle across different larval stages, in order to understand and contrast the morphology of the larva during its industrial use.

Materials and Methods: BSF larvae at different developmental stages were collected, fixed, and processed using standard histological techniques. For this, 2nd, 3rd, and 5th instar larvae were used in triplicate. Tissue sections were stained using routine hematoxylin-eosin staining to evaluate cellular organization, tissue differentiation, and structural modifications associated with growth and nutrient accumulation.
Results: Morphological analyses revealed progressive structural changes in the digestive tract, accompanied by marked hypertrophy and cellular accumulation of lipid and protein reserves in the fat body as the larvae mature towards the prepupal stage. Furthermore, modifications in cuticle thickness and overall cellular organization were documented.
Discussion: These results provide a detailed histological framework of native BSF ontogeny. This cellular cartography establishes a fundamental baseline to understand the normal development of the larva, which will allow the ByBug Synthetics® platform to obtain a gold standard during therapeutic protein expression. This makes it possible to isolate variables, identify the tissue localization of transgenic expression, and accurately evaluate any physiological impact derived from recombinant protein production.

P125. Establishment of a neuronal cad cell model to investigate svct2 mitochondrial localization and response to β-amyloid.
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Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disorder in which β-amyloid (Aβ) accumulation, oxidative stress, and mitochondrial dysfunction contribute to neuronal damage. Vitamin C is an important antioxidant in the central nervous system, and its cellular uptake is primarily mediated by the sodium-dependent vitamin C transporter 2 (SVCT2). Although SVCT2 has traditionally been characterized as a plasma membrane transporter, its presence in mitochondrial compartments has been reported, raising questions regarding its potential role in neuronal responses to cellular stress.
The aim of this study is to establish a neuronal cell model based on CAD cells to investigate SVCT2 expression and mitochondrial localization, and to evaluate its response to conditions associated with Alzheimer's disease. CAD cells are differentiated under serum-deprivation conditions to obtain a neuron-like phenotype, which is characterized through morphological and neuronal features. SVCT2 expression is subsequently evaluated, and subcellular fractionation is performed to obtain mitochondrial-enriched fractions and investigate the presence of SVCT2 in this compartment.
Preliminary results demonstrate the establishment of a differentiated CAD neuronal model and the detection of SVCT2 in these cells. Subcellular fractionation provides preliminary evidence of SVCT2 in mitochondrial-enriched fractions, supporting further investigation of its mitochondrial localization in the neuronal model. The established neuronal model is being used to investigate the cellular response to β-amyloid oligomers, including changes in SVCT2 expression and mitochondrial localization, together with cellular oxidative stress. These approaches provide a cellular platform to further investigate the potential role of SVCT2 in neuronal responses associated with Alzheimer's disease.
Materials and Methods: CAD (Cath.a-differentiated) cells were differentiated under serum-deprivation conditions and characterized by immunocytochemistry and Western blot using β-III tubulin and MAP2 as neuronal markers. SVCT2 expression and mitochondrial localization were evaluated by immunocytochemistry, Western blot, and subcellular fractionation using COXIV as a mitochondrial marker. The neuronal model is being used to investigate the cellular response to β-amyloid oligomers, including changes in SVCT2 and oxidative stress.
Results: Serum deprivation induced a neuronal phenotype in CAD cells, evidenced by characteristic morphological changes and increased β-III tubulin expression. SVCT2 expression increased during neuronal differentiation, while immunocytochemistry showed colocalization of SVCT2 with the mitochondrial marker COXIV. Subcellular fractionation further supported the presence of SVCT2 in mitochondrial-enriched fractions.
Discussion: Together, these findings establish a neuronal CAD model and support the presence of SVCT2 in the mitochondrial compartment, providing a platform to investigate its potential role in neuronal responses to β-amyloid-induced stress.

P126. Four universal modules for decoding the amplitude and frequency of Ca^{2+} signals in plants.
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Introduction: Calcium (Ca^{2+}) is the most universal second messenger in cell biology, yet how plant cells decode its signals, whether transient or oscillatory, remains largely a black box, partly because a unifying theoretical framework linking the microscopic thermodynamics of ion binding to observable physiological behaviour has been missing. The aim of this work was to build such a bridge from first principles and derive general rules describing how Ca^{2+}-binding proteins (CBPs) transduce the amplitude and frequency of Ca^{2+} signals into physiological activity.

Materials and Methods: We developed a bottom-up mathematical model starting from the thermodynamics of Ca^{2+} binding to the EF hands of a CBP, deriving at steady state an expression for CBP activity as the ratio of two quadratic polynomials, equivalent to the widely used Hill equation. We extended this framework into four universal modules describing activation and inactivation steps of a target protein by a CBP, valid across the three known molecular architectures (integrated EF-hand domain, catalytic modulation, direct binding), and solved analytically the temporal dynamics of each module under Ca^{2+} pulses, validating the solutions numerically against realistic Gaussian signals.
Results: The four modules generate distinct amplitude and frequency activation islands, explaining why the same Ca^{2+}-dependent kinase can show markedly different sensitivities depending on the substrate. The module combinations predicted mathematically match real protein complexes described in plants, such as CBL-CIPK and CaM-CNGC, and the framework generalizes beyond Ca^{2+} to other regulatory ligands such as ABA and Zn^{2+}.
Discussion: This work establishes a rigorous analytical bridge between molecular thermodynamics and systems biology, providing closed-form solutions that can guide the design of new experiments and support the construction of predictive computational models of cell signalling in plants.

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P127. Individual knockout of U5 snRNA variants produces variant-specific transcriptional and phenotypic responses in BT-549 triple-negative breast cancer cells.
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Introduction: Pre-mRNA splicing is frequently dysregulated in cancer, including triple-negative breast cancer (TNBC). U5 snRNA is a core spliceosome component encoded by multiple loci that generate variants traditionally considered functionally redundant. Whether individual U5 variants contribute to functionally specialized spliceosomes that shape cancer-associated transcriptional programs and phenotypes remains unknown. Resolving this question could reveal a previously underappreciated layer of spliceosome regulation in cancer. Here, we systematically assessed the phenotypic and transcriptional consequences of individually deleting the five major U5 variants (U5A, U5B, U5D, U5E, and U5F)
Materials and Methods: U5 snRNA variant-specific knockout (KO) pools were generated in BT-549 cells using eSpCas9 and two sgRNAs per target. Transcriptomic profiles were analyzed by RNA-seq to identify differentially expressed genes (DEGs) and cancer-associated signatures. Selected U5A-KO RNA-seq findings were independently validated by RT-qPCR in two KO pools generated using distinct sgRNA sets. Cancer-associated phenotypes were assessed using wound-healing, colony-formation, and doxorubicin-response assays.
Results: RNA-seq revealed variant-specific transcriptional profiles: EMT- and angiogenesis-related signatures were enriched in U5A, U5D, and U5F-KO cells, whereas an interferon α/γ signature emerged in U5E-KO cells. RT-qPCR confirmed reproducible changes in selected EMT- and chemoresistance-associated transcripts across independent U5A-KO pools. Phenotypically, U5E-KO showed reduced migration, whereas the other KO cells exhibited migration comparable to that of control cells. U5A-KO cells uniquely formed larger and more dispersed colonies. U5E-KO cells showed doxorubicin sensitivity comparable to control cells, whereas the other KO cells exhibited increased doxorubicin resistance.
Discussion: These findings support functional differences among U5 snRNA variants in TNBC, with the loss of individual variants producing distinct transcriptional and phenotypic responses. Replication across independently generated U5A-KO pools supports the robustness of selected U5A-associated transcriptional changes and warrants further investigation of the mechanisms underlying U5 variant-specific functions.

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P128. Effect of ECE1c-bearing extracellular vesicles derived from malignant colorectal cancer cells on the modulation of epithelial-mesenchymal transition and migration in recipient less-malignant colorectal cancer cells.
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Introduction: Colorectal cancer (CRC) is the second leading cause of death worldwide. Its tumor microenvironment can be reprogrammed by extracellular vesicles (EVs). These EVs, secreted by tumor cells, can promote epithelial-mesenchymal transition (EMT) and, consequently, facilitate cell migration. The Endothelin-Converting Enzyme-1c (ECE1c) promotes aggressiveness in colorectal, glioblastoma and lung cancers. ECE1c remains stable following phosphorylation at its N-terminal Ser18/Ser20 residues. This phosphorylation leads to a malignant phenotype. Furthermore, ECE1 has been found within CRC-derived EVs. Therefore, the aim of this work was to determine whether EVs bearing phosphomimetic mutant of ECE1c isolated from DLD-1 (Duke C) malignant CRC cells may affect expression of EMT-associated proteins and promote migration of SW480 (Duke B) and HT29 (Duke B/C) less-malignant CRC cells.
Materials and Methods: EVs were isolated from the DLD-1 cells, which overexpresses the ECE1c protein with phosphomimetic ($ECE1c^{DD}$) and phosphoresistant ($ECE1c^{AA}$) mutations at its N-terminus. Characterization was performed using NTA and Western blot. Expression of genes associated with EMT was evaluated by Western blot and RT-qPCR, as well as a Transwell assay to measure cell migration.
Results: Characterization of the particles isolated from DLD-1 cells revealed a population of small vesicles. Traditional markers indicate an enrichment in EVs. SW480 and HT29 cells, which were stimulated for 48 hours with different EVs derived from ECE1c mutant expressing DLD-1 cells, exhibited changes in genes associated with EMT, such as Slug and Twist. The effect on the modulation of proteins associated with EMT is observed in the migratory phenotype after 16 hours of stimulation with EVs.
Discussion: It is well known that EVs derived from tumor cells enhance phenotypes associated with tumor malignancy in recipient cells. Here, we observed that EVs derived from ECE1c mutant expressing DLD-1 clones do indeed modulate migration and, in turn, cause changes in EMT traits. We propose to study this phenomenon at shorter times to determine whether there are higher changes in the proteins studied.

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P129. Induction of pathogen resistance mediated by *ICS2* during sulfur deficiency in *Arabidopsis thaliana.*
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Introduction: Sulfur (S) is an essential macronutrient required for plant growth and metabolism. In *Arabidopsis thaliana* the response against this stress is regulated by the transcription factor SLIM1, which regulates genes involved in S uptake and homeostasis. Interestingly, S deficiency also affects plant immunity. Previous studies have shown that acute S deprivation induces the expression of the *PATHOGEN RELATED 1(PR1)* gene and enhances resistance to pathogens. *PR1* is used as a marker of salicylic acid (SA)-dependent immunity, and SA is a key phytohormone that promotes defense against *Pseudomonas syringae*. These observations suggest that changes in S nutritional status may modulate pathogen resistance through the activation of SA-associated defense pathways. Pathogen-induced SA biosynthesis mainly depends on *ISOCHORISMATE SYNTHASE 1* (*ICS1*), whereas *ICS2* makes only a minor contribution. Interestingly, bioinformatic analysis revealed putative SLIM1-binding sites in the *ICS2* promoter, suggesting a possible link between S-deficiency signaling and SA biosynthesis. We therefore hypothesized that S deprivation promotes defense responses through the induction of *ICS2*, contributing to enhanced resistance against *Pseudomonas syringae*.
Materials and Methods: *A. thaliana* Col-0 seedlings were grown *in vitro* under S-sufficient conditions and subsequently transferred to media containing sufficient or deficient S. Expression of *ICS2* and defense-related genes was evaluated by RT-qPCR. To assess pathogen resistance, plants were inoculated with *Pseudomonas syringae* and bacterial growth was quantified
Results: Following transfer to S-deficient medium, plants showed a significant induction of *ICS2*, but not *ICS1*, together with increased expression of defense-related genes such as *PR1* and *PR5*. Consistent with this transcriptional response, plants exposed to S deficiency display enhanced resistance to *P. syringae*, showing reduced bacterial growth compared with plants maintained under S-sufficient conditions.
Discussion: Together, these experiments demonstrate that in an *in vitro* system, acute stress of S deprivation induces a better defense response and expression of genes of interest.

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P130. The effect of selenium deficiency and supplementation on HFD-induced cardiac ferroptosis.
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Introduction: Selenium deficiency (SD) is associated with increased oxidative stress and strongly linked to cardiovascular diseases (CVD). Higher serum selenium levels are associated with reduced mortality in heart failure patients, highlighting the importance of selenium in cardiac health. Under obesity or high-fat conditions, SD may exacerbate lipid peroxidation and tissue damage, potentially promoting ferroptosis, a distinct form of cell death. Mechanisms by which SD could contribute to cardiac ferroptosis remain unclear. This work aims to determine the effect of SD and supplementation on obesity-associated cardiac ferroptosis.
Materials and Methods: Adult male and female C57BL/6NJR mice were fed either a low-fat diet (LFD) or a high-fat diet (HFD) containing deficient (0 ppm) or sufficient (0.15 ppm) selenium for 12 weeks. At week 12, half of the animals were sacrificed, while the remaining mice continued on their respective LFD or HFD for an additional 6 weeks, with all groups receiving high selenium supplementation (0.40 ppm). Cardiac echocardiography was performed at baseline and at 12 and 18 weeks. Left ventricular tissue was collected for qPCR, Western blotting, and glutathione (GSH) measurements.
Results: Changes in mRNA and protein expression of ferroptosis markers (GPX4, TFR1, ACSL4, HO-1), mitochondrial biogenesis markers (TFAM, PGC1α), and antioxidant enzymes (SOD2 and CAT) varied according to Se and HFD status. Interestingly, these responses showed a marked sex dependence. Se supplementation restored the expression of most markers toward control levels. Free GSH levels also differed by sex, showing greater variability in males and overall higher levels in females.
Discussion: These results suggest that SD may promote or worsen a ferroptotic state under HFD conditions, with some responses differing between males and females. Se supplementation may ameliorate the effects of HFD and Se deficiency on ferroptosis and mitochondrial dysfunction, supporting selenium modulation as a potential strategy to limit cardiac lipotoxic damage.

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Regional universities as articulators of the territorial scientific, technological and innovation ecosystem: A case study from the University of Atacama and the application of an advanced triple-helix model

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Introduction: This study analyzes how a peripheral public university in a mining-dependent region such as the University of Atacama (UDA) in the Atacama Region can strengthen the articulation between academia, government institutions, industry and civil society under an advanced triple helix framework. This model can help to understand the different interactions in which science and innovation can have an impact within and between different actors. The aim of this research is to examine how a university can operate as articulators of the territorial science, technology and innovation (STI) ecosystems through a case study of the UDA in northern Chile.
Materials and Methods: This research uses a qualitative single-case-study design, in which we triangulate institutional diagnostics, municipal council sessions, focus groups, interviews, surveys and policy documents collected during 2024–2025 in the Atacama Region.
Results: This study reveals that the university possesses significant territorial research potential and impact within an advanced triple helix framework, but faces structural limitations related to fragmented governance, bureaucratic rigidity, weak technology-transfer mechanisms, limited postgraduate critical mass and insufficient territorial integration. Simultaneously, the territorial diagnosis identifies urgent regional challenges linked to water scarcity, environmental degradation, productive diversification and advanced human-capital retention, in which the UDA can play a role of articulation and impact through STI.
Discussion: The study argues that the UDA enabled the university to reposition itself as a strategic intermediary within the regional STI ecosystem, acting as articulator of the triple helix framework (academia, public and private sector) while also exposing the institutional transformations required for sustained territorial impact and evidence-based regional development.

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