ABSTRACT BOOK

IV National Biosciences Congress 2025

III Argentina – Uruguay Binational Meeting

XIX Uruguayan Society for Biosciences (SUB) Meeting

XV Society for Biochemistry and Molecular Biology Meeting

XXI Uruguayan Society for Neurosciences Meeting

VIII Uruguayan Society for Genetics Meeting

IV Uruguayan Society for Microscopy and Imaging Meeting

I Uruguayan Limnology Meeting

May 28 – 30, 2025

Radisson Montevideo Victoria Plaza Hotel

Montevideo, URUGUAY


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SUMI
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SUM
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Inmunología (SUI)


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SZU

WELCOME

With great joy, the Uruguayan Society for Biosciences (SUB) celebrates this year the addition of two new sections, representing such diverse and fundamental areas as Ecology and Bioinformatics. Far from being nascent communities, these new sections formalize the recognition of groups with a rich history and an active role in national research, which have been pillars in positioning biological research in our country.

In turn, the Uruguayan Society of Limnology consolidates its membership in the SUB, adding its own activities that enrich the academic content of the congress and broaden the representation of the knowledge that constitutes us as a community. Along with these additions, the traditional meetings of the established sections continue, covering broad topics and bringing together a large portion of our members and other associates.

In this context, the congress is organized under the theme "Convergence and Diversity of Knowledge," a true reflection of our current composition as a society and of a trend that we consider not only inevitable but also deeply desirable: interdisciplinarity. We understand that we grow stronger when we generate synergies from our respective areas of expertise, addressing complex and relevant topics from multiple perspectives.

This growth and diversity present us with the challenge of organizing a comprehensive and inclusive congress that represents the plurality of knowledge and is, at the same time, valuable and enriching for all participants.

As the Scientific Committee, we are committed to designing a congress that is academically sound, creating "cross-cutting" spaces dedicated to topics of general interest such as the microbiome, water, artificial intelligence, open science, bioprinting and biomaterials, and genomics and bioinformatics. These topics aim to bridge disciplines, reflecting the increasingly blurred boundaries between the various scientific fields that represent us.

The congress is also enriched by the participation of partner societies, whose ongoing support has complemented the knowledge represented in the SUB, expanding opportunities for interaction, synergy, and collaboration.

The Organizing Committee set out to offer an inclusive, equitable, representative, and sustainable congress, where freedom, respect, and environmental stewardship are paramount.

We prioritize the presentation of work in progress or unpublished research, fostering exchange spaces designed for researchers in the early stages of their careers.

None of this would be possible without the continued support of institutions and private companies, to whom we express our sincere gratitude. And, above all, we thank our partners and scientific friends for their participation and for generously sharing their knowledge with the Uruguayan scientific community.

We wish all participants an excellent congress!

Maria Eugenia Francia

President of the SUB

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ORAL COMMUNICATIONS

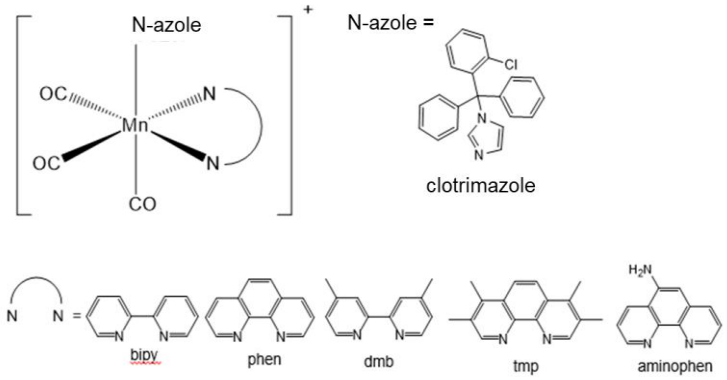
Elucidation of Mechanisms of Action and Omic Studies of Organometallic Mn(I) Compounds with Antiparasitic Activity

Del Mármol Carolina[1,2], Scalese Gonzalo[1], Machado Ignacio[3], Lima Analía[4], Pérez Díaz Leticia[2] and Gambino Dinorah[1]

[1]Área Química Inorgánica, DEC, Facultad de Química, Universidad de la República; [2]Programa de Posgrado de la Facultad de Química, Universidad de la República; [3]Área Química Analítica, DEC, Facultad de Química, Universidad de la República; [4]Unidad de Bioquímica y Proteómica Analíticas, Institut Pasteur de Montevideo; [5]Sección Genómica Funcional, Facultad de Ciencias, Universidad de la República

Abstract: Neglected tropical diseases such as Chagas disease and visceral leishmaniasis, caused by the trypanosomatid parasites *Trypanosoma cruzi* and *Leishmania infantum*, severely impact the Latin American population.

In the search for metal-based drugs against these diseases, our group has developed a family of organometallic compounds of the formula fac-[MI(CO)$_3$(CTZ)(NN)](PF$_6$), where M=Mn or Re, CTZ=clotrimazole, and NN=bioactive polypyridyl ligands. They presented a promising activity on *T. cruzi* trypomastigotes (0.25-4.46 μM) and *L. infantum* promastigotes (0.80-2.91 μM), and moderate selectivities. Working on elucidating possible mechanisms of action of the new Mn compounds, it was evidenced the inhibition of the parasitic enzyme lanosterol 14-α-demethylase, key enzyme on the biosynthetic pathway of ergosterol in parasites, and the photoinduced release of CO. Metalomic studies of the most promising Mn compound, *fac*-[Mn(CO)$_3$(CTZ)(tmp)](PF$_6$), showed a bigger uptake on *T. cruzi* trypomastigotes than its Re analogue, and preferential association to soluble proteins. Proteomic analysis on *T. cruzi* epimastigotes revealed that the parasite incubated with *fac*-[Re(CO)$_3$(CTZ)(tmp)] (PF$_6$) presented a significantly bigger number of modified proteins in their abundance (*vs* control), while for the Mn analogue, the number was much smaller, suggesting that both compounds exert their antiparasitic action by different mechanisms. Together, the result emphasises the potential of Mn(I) tricarbonyl compounds as promising candidates for the development of antiparasitic agents.



Keywords: Metal-based drugs, organometallic compounds, new Mn compounds.

Therapeutic Ultrasound in Epilepsy: Advances and Perspectives

Garay Badenian Natalia[1] and Simini Franco[1]

[1]*Núcleo de Ingeniería Biomédica de las Facultades de Medicina e Ingeniería, Universidad de la República*

Abstract: Epilepsy affects 0.9% of the population in Uruguay, with 30% of cases being refractory to medication. Surgery is an available treatment option, but it is not always feasible. Neuromodulation with implantable stimulators has been shown to reduce seizures by up to 70% of cases, although with varying degrees of invasiveness. Ultrasound is thus emerging as a non-invasive therapeutic alternative with potential for neuromodulation and ablation of epileptic foci. A search of scientific literature and patents was conducted. Research articles, clinical case reports, and relevant patents were analyzed. Preclinical studies in animal models and patented ultrasonic neuromodulation devices were also considered. Significant advances were identified, including the first clinical trial demonstrating the efficacy of transcranial ultrasonic neuromodulation in reducing epileptic seizures in patients. A clinical case with positive results and the development of a patented ultrasound device for detecting and inhibiting epileptic foci were found. An ongoing clinical trial using focused ultrasound for temporal lobe epilepsy was also identified. The findings highlight the potential of ultrasound as a therapeutic tool in epilepsy, with modulatory effects on neuronal activity and the possibility of precise targeting. However, technical challenges remain, along with the need for controlled studies involving larger patient populations. This review confirms the relevance of our research, which focuses on ultrasound on brain phantoms and biological tissue, as a developing technology for optimizing stimulation parameters and analyzing anatomical access pathways.

Keywords: Epilepsy, neuromodulation, ultrasound.

Description of Copy Number Variants in Sporadic Breast Cancer in Uruguay

Brignoni Lucía[1,2], Cappetta Mónica[1], Pereyra Silvana[1], Artagaveytia Nora[2] and Bertoni Bernardo[1]

[1]*Unidad Académica de Genética, Facultad de Medicina, Universidad de la República;* [2]*Unidad Académica Básico de Medicina, Hospital de Clínicas, Facultad de Medicina, Universidad de la República*

Abstract: In Uruguay, breast cancer is highly prevalent, with 1,800 women diagnosed each year. Sporadic breast cancer accounts for 85–90% of all cases, and point mutations do not explain its development. Considering that breast cancer risk varies among populations, and the Uruguayan population is trihybrid, it is difficult to extrapolate results from other populations, making it essential to determine risk biomarkers specific to our population. For this purpose, Copy Number Variants (CNVs) are highly diverse at the individual and population levels, and their association with breast cancer is relevant. In this study, we analyzed the impact of CNVs using peripheral blood DNA from 24 patients and 13 controls. Using bioinformatic analysis of site-specific methylation microarray data, we detected three differential CNVs between patients and controls (FDR < 0.05) located in the 6p21.31, 10p12.31, and 10q26.13 regions. These results were evaluated by real-time PCR in a larger sample (45 patients and 45 controls) using a Bayesian statistical approach, validating the three CNVs as candidate biomarkers for breast cancer in our population. Furthermore, using the absence of heterozygosity detection analysis based on low-coverage whole-genome sequencing (4x), we obtained new differential CNVs between patients and controls.

These results open up new possibilities for contributing to the state of knowledge on the relevance of these types of variants in the development of sporadic breast cancer in Uruguay.

Keywords: Breast cancer, copy-number variation, biomarkers.

The Gut Microbiome as a New Target in Biomedicine

Riera Nadia[1]

[1]*Microbial Genomics Laboratory, Institut Pasteur de Montevideo. Montevideo, Uruguay*

Abstract: In recent years, a link has emerged between the microorganisms that live in close association with our bodies, collectively known as the microbiome, and human health. There is growing evidence associating the microbiome with diseases, ranging from gastrointestinal and metabolic disorders to neurological conditions and different types of cancer.

Driven by this, we have studied the role of the gut microbiota in the response to checkpoint immunotherapy in patients with advanced cancer. For this, we collected fecal matter from 22 patients and 23 individuals without a cancer diagnosis, and identified biomarkers associated with cancer. Using high-depth shotgun sequencing and proximity ligation analysis, we identified six bacterial species differentially present in those individuals diagnosed with cancer. We evaluated differences in the gut microbiota between responder and non-responder patients, and identified limitations in using predictive biomarkers previously described for other countries.

In parallel, in another research line, we are studying the gut microbiome of children with Autism Spectrum Disorder (ASD). For this, we selected 50 Uruguayan families with children diagnosed with ASD and their non-diagnosed siblings, all children within the 4-10 year age range. In collaboration with doctors and nutritionists, this cohort was characterized based on their clinical profile, food consumption frequency, and gastrointestinal symptoms. Using full-length 16S rRNA gene amplification with Oxford Nanopore sequencing technology and shotgun metagenomics, we characterized the bacterial profiles of these children. This ongoing work aims to identify new microbial biomarkers associated with ASD that can help complement clinical diagnosis.

Keywords: Microbiome, autism, cancer immunotherapy.

Sequencing of the Gene Clusters Responsible for the Biosynthesis of the O-specific Antigens of *Escherichia Coli* SC-UY1 and SC-UY4

Cuchman, Sylvia[1,2], Gianneechini Edgardo[3], Rivero Rodolfo[3], Benítez-Galeano María José[4], Rodriguez-Osorio Nélida[4], Corvo Ileana[5] and Fontana Carolina[1]

[1]*Laboratorio de Química Orgánica, Departamento de Química del Litoral, CENUR Litoral Norte, Universidad de la República, Paysandú, Uruguay;* [2]*Programa de Posgrados de la Facultad de Química, Universidad de la República, Montevideo, Uruguay;* [3]*División Laboratorios Veterinarios "Miguel C. Rubino", MGAP, Paysandú, Uruguay;* [4]*Unidad de Genómica y Bioinformática, Departamento de Ciencias Biológicas, CENUR Litoral Norte, Universidad de la República, Salto, Uruguay;* [5]*Laboratorio de I+D Moléculas Bioactivas, Departamento de Ciencias Biológicas, CENUR Litoral Norte, Universidad de la República, Paysandú, Uruguay.*

Abstract: The O-specific antigen (O-Ag), the outermost region of the Lipopolysaccharide (LPS), defines the 182 officially recognized *Escherichia coli* serogroups. While most *E. coli* strains are harmless, certain pathogenic variants can cause severe diseases, such as fulminant diarrhea in calves, leading to economic losses and decreased livestock productivity. The rising prevalence of antibiotic-resistant strains underscores the importance of identifying virulence-associated serogroups and prioritizing them in vaccine development.

In this study, *E. coli* strains SC-UY1 and SC-UY4 were isolated from mesenteric lymph nodes of calves during necropsies. The O-Ags were structurally characterized using Nuclear Magnetic Resonance (NMR) spectroscopy, revealing unique chemical structures, expanding the known diversity of *E. coli* O-antigens and bacterial surface glycans. These antigens exhibited features associated with two distinct biosynthetic pathways: a linear heteropolysaccharide typical of the flippase/polymerase-dependent pathway and a polysaccharide with a backbone composed of D-rhamnose residues, indicative of the ABC transporter-dependent pathway.

To elucidate the genetic basis of these structures, the O-Ag biosynthesis gene clusters were amplified and sequenced using Nanopore Technology (MinION). The resulting sequences (16,120 bp for SC-UY1 and 20,100 bp for SC-UY4) fall within

the typical size range reported for *E. coli* O-Ag gene clusters (6–20 kbp). Functional annotation of the genes was performed through BLAST analysis, in combination with structural insights from NMR data.

Functional annotation of the encoded proteins was performed using BLAST analysis, integrated with structural information derived from the polysaccharides.

Keywords: O-specific antigen, Lipopolysaccharide, pathogenic variants.

Response of Turbidity in Paso Severino to Flood Events: How Density Currents Modulate Water Quality

Ríos Agustín[1], Santoro Pablo[1] and Pedocchi Francisco[1]

[1]*Instituto de Mecánica de los Fluidos e Ingeniería Ambiental, Universidad de la República, Montevideo, Uruguay*

Abstract: ***Introduction:*** This study examines the influence of hydro-thermodynamic processes on the distribution of substances in the Paso Severino reservoir, focusing on flood events and their effect on turbidity.

Hypothesis: The fate of the materials supplied by the Santa Lucía Chico River (SLCh) during flood events depends on the hysteresis in the concentration–discharge curve (due to the lag between the peak of the hydrograph and that of each substance in the river) and on the formation of density currents within the reservoir.

***Materials and Methods*:** The methodology integrates a 3D hydro-thermodynamic numerical model with the analysis of subdaily discharge series (DINAGUA) and turbidity data (OSE). The calibrated and validated model was used to simulate a conservative tracer. Boundary conditions were derived from SLCh turbidity measurements, and model results were validated against turbidity observations at the reservoir's outflow.

***Results*:** Data show that incoming turbidity peaks occur during the rising limb of the hydrograph, generating clockwise hysteresis loops. These peaks are not always reflected in the turbidity measured at the reservoir's outlet. Model simulations indicate that flood events generate different density currents depending on the season. Tracer experiments that incorporate both hysteresis loops and density currents successfully reproduce the observed turbidity dynamics in the reservoir. Discussion and Conclusions. These findings highlight the importance of characterizing the inflow C–Q curve and accounting for density currents when evaluating the retention or export of substances in Paso Severino. Moreover, the model provides key information on variables critical for primary production, such as light climate, vertical mixing, and temperature.

Keywords: Numerical modelling, reservoirs, density currents.

Anti-inflammatory and Antiatherogenic Properties of Cannabis Sativa

Bruno Musetti[1,2], Marcel Donze[1], Alejandra Kun[3], David Menchaca[4], Alejandra Rodríguez-Haralambides[4], Javier Varela[5], Edward Moreira-Bahnson[2] and Leonor Thomson[1]

[1]*Laboratorio de Enzimología, Instituto de Química Biológica, Facultad de Ciencias, Universidad de la República, Uruguay;* [2]*Department of Cell Biology & Physiology, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA;* [3]*Laboratorio Biología Celular del Sistema Nervioso Periférico-DPAN-IIBCE, Instituto de Investigaciones Biológicas Clemente Estable, Sección Bioquímica, Facultad de Ciencias, Uruguay; CIBERNED-España;* [4]*Química Bioanalítica, Instituto Polo Tecnológico de Pando, Facultad de Química, Universidad de la República, Uruguay;* [5] *Laboratorio de Química Orgánica y Medicinal, Facultad de Ciencias, Universidad de la República, Uruguay.*

Abstract: Cardiovascular diseases, and atherosclerosis in particular, are the leading cause of death worldwide. The initial stages in the development of atheroma plaque are characterized by the invasion of the subendothelium by inflammatory

cells, and the accumulation of foam cells, laden with oxidized LDL (LDLox). Based on previous reports on the anti-inflammatory and antioxidant effects of phytocannabinoids, we set out to explore the effect of extracts rich in these compounds on atheroma plaque triggers. To this end, extracts from three Cannabis sativa cultivars with different relative cannabinoid composition were selected. The extracts obtained, analyzed by UPLC, showed THC(A)/CBD(A) ratios of 16 (intoxicant), 0.5 (intermediate), and 0.04 (fiber). All three extracts, regardless of their relative compositions, prevented LDL oxidation and transformation of LDLox-exposed murine macrophages into foam cells, as demonstrated by conjugated diene analysis and confocal microscopy, respectively. The inhibitory effect of cannabis extracts on the LDLox internalization process was accompanied by decreases in scavenger receptors, OLR1, and CD36. In addition, the extracts decreased the expression of mediators of pro-inflammatory differentiation (IL-1β, pIKBα, and NOS2), and induced a shift towards a pro-resolving phenotype, with increased expression of HO-1, in both oxLDL and LPS/INFγ-challenged macrophages. These results support the anti-inflammatory and antiatherogenic potential of cannabis extracts and support further research into the therapeutic use of medicinal cannabis in the cardiovascular field.

Keywords: Atherosclerosis, LDL oxidation, foam cells, cannabinoids, inflammation.

Microalgal Biomass Production as a Productive and Sustainable Alternative in Agroindustry

Ramírez Mérida[1] and Luis Guillermo[1]

[1]Technological University of Uruguay (UTEC), Water Engineering and Sustainable Development, ITR-CS, Francisco Antonio Maciel s/n esq. Luis Morquio CP 97000 Durazno, Uruguay

Abstract: The agroindustry is seeking sustainable and resilient alternatives in the face of growing demand and the challenges of climate change. Microalgal biomass production is emerging as an innovative solution with a triple impact: productive, environmental, and climate. Microalgae, efficient photosynthetic microorganisms, convert CO_2, light, and nutrients into valuable biomass for biofuels, biofertilizers, bioplastics, nutraceuticals, food, and animal feed, among others.

The development of microalgae-based biotechnological processes offers significant sustainability advantages by requiring less land and water than traditional agriculture, and can even utilize unconventional resources such as wastewater. Its ability to capture CO_2 contributes to mitigating climate change, while the resulting biofertilizers reduce dependence on polluting chemical inputs.

In the context of climate change, microalgal biomass strengthens the resilience of the agroindustry. It diversifies income sources, improves soil health with biofertilizers, and biofuel production reduces the sector's carbon footprint.

While there are challenges in strain optimization, scalability, and costs, the opportunities for technological innovation and integration into agroindustrial value chains are significant. Microalgal biomass represents a crucial tool for a more productive, sustainable agroindustry that is adapted to the challenges of the future. Its development and large-scale implementation are essential for a greener and more resilient agrifood sector.

Keywords: Microalgae, sustainable production, climate change, bioeconomy, CO_2 capture.

Genetics in Action: From the Book to the Laboratory

Cappetta Mónica[1] and Pereyra Silvana[1]

[1]Departamento de Genética, Facultad de Medicina, Universidad de la República

Abstract: Scientific thinking is an essential tool for developing appropriately in today's society. It is important to bring scientific practice closer to the classroom, to encourage young people's interest in science, and to democratise its access to the general population. In Uruguay, academic curricula have recently been updated, with an increased presence of genetics mainly in higher secondary education. This has generated an increase in interest and motivation among teachers to incorporate genetics activities in their classrooms. We have created the ‘Genetics in the Classroom’ programme, with the aim of

carrying out and facilitating the implementation of innovative DNA-based activities in the classroom. Successful experiences in the teaching and dissemination of genetics among children and adolescents in Uruguay, as well as among their teachers, are presented. Workshops were held at educational centres, seeking to encourage students' critical thinking and bring them closer to scientific work, especially research in genetics. In the workshops, we discussed laboratory practices, appropriate experimental designs, and the importance of genetic analysis in human health. For most of the students, this is their first close interaction with researchers, as well as with methodologies inaccessible in their schools. The main goal of the interventions is to stimulate interest in science among young people, encourage their curiosity, and democratize access to scientific knowledge, as well as to highlight the role of women in scientific research.

Keywords: Education, genetics, public engagement.

Telling, Drawing, and Performing Science: Interventions That Transform Classroom Education

Arredondo Daniela[1,2,3]

[1]Laboratorio de Microbiología y Salud de las Abejas, Departamento de Microbiología, Instituto de Investigaciones Biológicas Clemente Estable, Ministerio de Educación y Cultura; [2]Comicbacterias; [3]Bardocientífico

Abstract: The social appropriation of science entails more than just access to scientific information: it means that people can understand it and integrate it into their lives. This is especially important in the classroom, where the foundations of a critical and informed citizenry are built. However, when it comes to teaching abstract or invisible concepts, such as algorithms, molecules, nucleic acids, and microorganisms, the challenges increase. At ComicBacterias, a collective comprising mainly scientists and artists, we have developed a series of comics and playful resources to teach microbiology in an accessible and entertaining manner. Through our comics, we address complex topics in bacteriology, virology, vaccination, and biotechnology using a combination of adventure, humor, and science. In parallel, at Bardo Científico, a diverse group of researchers and educators use monologues as an educational format, promoting critical thinking and the enjoyment of science by incorporating tools from stand-up comedy, theater, and storytelling. The results of these interventions have demonstrated high receptivity from children, teenagers, and adults alike, facilitating an understanding of key concepts and fostering a more positive attitude toward science. For these reasons, both initiatives have led workshops for teachers and students in secondary and higher education. In these workshops, we provide tools that can be used in the classroom. The intersection of science, art, and education not only captures attention but also transforms the way knowledge is built. We thus propose a more inclusive, creative, and participatory science education.

Keywords: Outreach, science communication, science storytelling, microbiology.

Perennial Grain Crops: *Tinopiro* in Uruguay

Locatelli Andrés[1], Picasso Valentín D[2,3], Speranza Pablo R[2] and Gutiérrez Lucía[2,3]

[1]CENUR Litoral Norte – Departamento de Ciencias Veterinarias y Agrarias, Est. Exp. Mario A. Cassinoni, Universidad de la República, Paysandú, Uruguay; [2]Facultad de Agronomía, Universidad de la República, Montevideo, Uruguay; [3]Department of Plant and Agroecosystem Sciences, University of Wisconsin – Madison, Madison, USA

Abstract: Annual crops have historically constituted the foundation of human food systems. However, the predominant production systems that support them have been associated with various issues, most notably the significant degradation of natural resources. Perennial crops such as *Thinopyrum intermedium* (commonly known as Intermediate Wheatgrass (IWG) or Kernza) offer several agronomic and environmental advantages over annual species, including enhanced soil erosion control, greater water and nutrient use efficiency, increased soil carbon sequestration, and higher resilience to both biotic and abiotic stresses.

Currently, more than forty institutions worldwide are engaged in the development of perennial grain crops, including rice, sunflower, sorghum, and IWG species. Based on controlled-environment trials and field experiments with half-sib families, our objectives were to: (1) investigate agronomic constraints, particularly vernalization requirements, affecting IWG cultivation; (2) assess its agronomic performance as a dual-purpose crop (grain + forage) under Uruguayan conditions; and (3) initiate the development of germplasm with baseline agronomic adaptation to our region.

Moderate vernalization requirements were observed, along with significant genetic variability within the evaluated germplasm. Forage performance was agronomically promising, whereas grain yield will require improvement for IWG to be considered a viable dual-purpose crop. The high additive genetic variance estimated for most key agronomic traits, along with the identification of candidate traits for indirect selection under dual-purpose management, highlight the potential for genetic improvement and regional agronomic adaptation of this species.

Keywords: Perennial grains, sustainable agriculture, perennial breeding crops.

The Effect of Prepartum Shearing in Corriedale Ewes on Placental and Lamb Development and Neonatal Behaviour

Scaglione-Sanson Fiorella[1], Neimaur-Fernández Karina[2], Cantou-Mayol Inés[2], Abreu-Palermo Cecilia[3], Rodríguez-Gamarra Pablo[4], González-Montaña José[5] and Cal-Pereyra Luis[3]

[1]Unidad Académica Salud de Rumiantes, Departamento de Producción Animal y Salud de los Sistemas Productivos, Facultad de Veterinaria, Universidad de la República, Montevideo, Uruguay; [2]Unidad Académica Ovinos, Lanas y Caprinos, Departamento de Producción Animal y Salud de los Sistemas Productivos, Facultad de Veterinaria, Universidad de la República, Montevideo, Uruguay; [3]Unidad Académica Patología, Departamento de Patobiología, Facultad de Veterinaria, Universidad de la República, Montevideo, Uruguay; [4]Unidad de Planeamiento y Evaluación Institucional, Facultad de Veterinaria, Universidad de la República, Montevideo, Uruguay; [5]Departamento de Medicina Veterinaria, Cirugía y Anatomía. Facultad de Medicina Veterinaria, Universidad de León, León, España.

Abstract: The study aims to evaluate the effects of early and late pre-partum shearing of Corriedale ewes carrying single fetuses on placental and lamb development and neonatal lamb behaviour. At 70 days of gestation, 37 multiparous Corriedale ewes with known gestation dates were randomly allocated into three groups: S70 (n = 12) and S110 (n = 12), shorn at Days 70 and 110 of gestation, and US (n = 13), which were not shorn pre-partum. Gestation length, lambing duration, placental expulsion time, placental weight, number and weight of cotyledons, and placental efficiency (lamb weight/placental weight) were determined. At birth, body temperature, weight, morphometric measurements, ponderal index (lamb weight/lamb crown–rump length), and behaviour were recorded, with weight remeasured 72 hours later. Four male lambs per group were slaughtered immediately after parturition, and organ weight, perirenal brown fat weight, and energy content were recorded. Pre-partum shearing, regardless of timing, increased total dried placental weight per ewe. Pre-partum shearing at Day 70 of gestation increased the number and mean weight of the > 2 to ≤ _3-cm cotyledons, while pre-partum shearing at Day 110 of gestation increased only the weight of these cotyledons. At birth and at 72 hours, lambs from ewes shorn either at 70 days of gestation (birth: 5.5 (95% CI = 4.6–6.4) kg, p = 0.001; 72 hours: 6.4 (95% CI = 6.1–6.8) kg, p = 0.002) or at 110 days of gestation (birth: 5.4 (95% CI = 4.4–6.4) kg, p = 0.001; 72 hours: 6.5 (95% CI = 5.9–7.1) kg, p = 0.001) were heavier than lambs from unshorn ewes (birth: 4.0 (95% CI = 3.3–4.8) kg; 72 hours: 4.8 (95% CI = 3.5–6.1) kg). Lambs born to S70 and S110 ewes suckled sooner (31.5 (95% CI = 14.5–48.5) minutes, p = 0.001; and 39.3 (95% CI = 23.7–55.0) minutes, p = 0.001, respectively) than lambs born to the US group (70.3 (95% CI = 38.6–102.1) minutes). There was no evidence for an effect of pre-partum shearing on gestation length, parturition length, time of placental expulsion, placental efficiency, weight, energy of perirenal brown fat, and lamb temperature at birth. In conclusion, shearing ewes pre-partum may lead to placental changes affecting lamb development and behaviour, and is associated with higher survival.

Keywords: Pregnancy, placenta, body weight.

Development and Evaluation of Biomass-derived Compounds as Anti-UV and Antioxidants Agents

Sanders-Pons Agustina[1], Pallas Guillermina[1], López, Miriam[1], Tassano, Tiago[2], Porcal, Williams[2,3], López Gloria V[2,3], de la Sovera Victoria[2] and Hernández Paola[1]

[1]Departamento de Genética, Instituto de Investigaciones Biológicas Clemente Estable, Ministerio de Educación y Cultura, Montevideo, 11600, Uruguay; [2]Laboratorio de Síntesis Orgánica y Desarrollo de Fármacos, Institut Pasteur de Montevideo, Montevideo, 11400, Uruguay; [3]Departamento de Química Orgánica, Facultad de Química, Universidad de la República, Montevideo, Uruguay

Abstract: Ultraviolet (UV) radiation induces DNA damage and oxidative stress, contributing to photoaging and increasing skin cancer risk. Petroleum-based filters used nowadays have adverse effects on human and environmental health. Recent studies describe the photoprotective properties and safety of biomass-derived compounds that make them promising substitutes for common UV filters. The aim of this work is the synthesis and biological evaluation of novel molecules derived from lignocellulosic biomass platforms, synthesized following green chemistry principles, as photoprotective agents against UV radiation. In this regard, we evaluated a chemical library of more than 30 compounds, selecting those capable of absorbing in the UV range and maintaining photostability. The cytotoxicity, antioxidant activity, and protection against DNA damage were assessed in HaCaT cell cultures. Furthermore, the estrogenic effect was determined *in silico* and *in vitro*. Six of the studied compounds were photostable in the UV region, showed no cytotoxicity, and outperformed the photoprotective effect of the reference compound avobenzone. In summary, the evaluated biomass-derived compounds are potential filters against UV radiation.

Keywords: Ultraviolet, DNA damage, oxidative stress.

From Raw Reads to Pseudochromosomes: Accessible Genome Assemblies in Neotropical Fishes

Almansa Villa[1], Diego Alejandro[1], Benítez-Galeano[1], María José[1] and Rodríguez Osorio Nélida[1]

[1]Unidad de Genómica y Bioinformática, Departamento de Ciencias Biológicas, CENUR Litoral Norte, Universidad de la República, Uruguay

Abstract: The construction of reference genomes for non-model species remains a challenge in Latin America, where financial and infrastructure constraints directly impact bioinformatics decisions. This study compares different genome assembly approaches applied to two ecologically and economically important Neotropical fish species.

For *Pseudoplatystoma magdaleniatum* (striped catfish), genome assemblies were constructed from Illumina and ONT reads (7X and 20X) using hybrid approaches with the software tools Platanus-Alle, DBG2OLC, Flye, NGSEP, and NextDenovo. The impact of short read polishing with (Pilon) and structural improvement through Hi-C data integration was assessed, ultimately resulting in a highly contiguous assembly scaffolded to the pseudochromosome level.

In *Prochilodus magdalenae* (bocachico), a previously published female genome assembly was improved from the contig level to pseudochromosomes using Hi-C data. Additionally, a new assembly was generated from a male individual using PacBio HiFi and ONT long reads, assembled with Hifiasm. Hi-C data from the female was used to improve the structural organization of the male assembly. As a result, a more contiguous and chromosomally organized assembly was obtained by integrating data from both sexes.

Assembly quality was then assessed using QUAST for contiguity metrics, and BUSCO and COMPLEASM for genome completeness. The results of the latter two were compared to identify differences in completeness estimation.

This work contributes to the development of efficient and reproducible assembly pipelines for structural genomics in wild species from the region.

Keywords: Non-model fish genomics, hybrid genome assembly, Hi-C scaffolding.

Dichloroacetate: Modulator of the Effect of Vincristine on the Ovary

Anesetti Gabriel[1], Toledo Agustina[1], Hernández Mir Karina[1] and Chávez-Genaro Rebeca[1]

[1]*UA Histología y Embriología, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay*

Abstract: The ovaries of female mammals have a limited number of follicles that decrease throughout their lives. Their reproductive potential depends on their ability to produce mature oocytes at the time of ovulation. Follicles are highly sensitive to the gonadotoxic effects of various chemotherapeutic drugs, but little is known about the effect of vincristine, widely used for the treatment of hemato-oncological diseases. Dichloroacetate is a PDH-kinase inhibitor that promotes oxidative metabolism. Its potential beneficial effect in the treatment of certain neuropathies and oncological diseases has been proposed. In this study, we analyzed the effects of vincristine on several reproductive parameters and the possible protective effects of dichloroacetate.

Vincristine administration altered cyclicity, increasing the activation of primordial follicles and inducing atresia in growing follicles. It also affected the ovulated oocyte, increasing its size and that of the meiotic spindle, and the percentage of fertilized oocytes was lower. Simultaneous administration of both drugs allowed the maintenance of cyclicity transiently, reduced the number of growing follicles while increasing atresia, and decreased AMH signaling. The number of ovulated oocytes decreased even further, although aspects such as spindle length and the percentage of fertilized oocytes returned to values similar to the control group.

This study confirms the gonadotoxic effect of vincristine and provides data on the simultaneous action of both drugs, which does not appear to be adequate for preventing gonadotoxic effects.

Keywords: Gonadotoxicity, oncofertility, follicular reserve.

BCL-2 Family Genes Expression in Ocular Squamous Cell Carcinoma in Hereford Cattle

Balemian Nariné[1], Fernández-Calero Tamara[2,3], Armstrong Eileen[1] and Pedrana Graciela[4]

[1]*Unidad Académica de Genética y Mejora Animal, Departamento de Producción Animal y Salud de los Sistemas Productivos, Facultad de Veterinaria, Universidad de la República;* [2]*Unidad de Bioinformática, Institut Pasteur de Montevideo, Uruguay;* [3]*Departamento de Ciencias Naturales y Exactas, Universidad Católica del Uruguay;* [4]*Unidad Académica de Histología y Embriología, Departamento de Biociencias Veterinarias, Facultad de Veterinaria, Universidad de la República*

Abstract: Bovine Ocular Squamous Cell Carcinoma (BOSCC) is a very common epithelial neoplasm in Hereford cattle. However, the main transcripts linked to apoptosis evasion, one of the main hallmarks of these tumors, have not yet been described. Therefore, we analyzed *BCL-2* (B-cell lymphoma 2) family genes with anti- or pro-apoptotic functions, such as *BCL2A1*, *BCL2L13*, *BCL2L15*, and *BNIP3* in BOSCC samples. Ocular tumor samples were obtained from depigmented Hereford cattle with BOSCC (n = 5) and control animals (n = 3) and stored in Trizol at -80°C until RNA extraction and sequencing. The obtained reads were analyzed in R, and differential expression was analyzed with edgeR, using the ARS-UCD1.2/bosTau9 reference genome. Genes with a False Discovery Rate (FDR) < 0.05 and Fold Change (FC) > 2 were selected. The results indicate that *BCL2A1*, *BCL2L15*, and *BNIP3* were overexpressed in tumor samples, while *BCL2L13* was underexpressed. This is consistent with previous studies in other tumor types demonstrating that *BCL2A1* exhibits anti-apoptotic functions in tumor tissues. However, *BCL2L15* is considered pro-apoptotic. On the other hand, *BCL2L13* and *BNIP3* may exhibit either anti- or pro-apoptotic functions depending on the tumor type. In lung tumors, *BNIP3* overexpression is linked to aggressive tumors with increased metastasis. We suggest that BNIP3 in BOSCC regulates ocular tumour progression in bovines. We conclude that most of the BCL-2 family apoptosis-related genes are overexpressed in bovine ocular tumors.

Keywords: Ocular tumor, beef cattle, anti-apoptosis, pro-apoptosis.

Diversity and Ancestry of the Genome of a Sample of the Uruguayan Population

Pereyra Silvana[1], Cappetta Mónica[1], Brignoni Lucia[1,2], Bonilla Carolina[3] and Bertoni Bernardo[1]

[1]UA de Genética, Facultad de Medicina, Universidad de la República. Uruguay; [2]UA Básica de Medicina, Facultad de Medicina, Universidad de la República. Uruguay; [3]Departamento de Medicina Preventiva, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brasil

Abstract: The historical demographic process in Uruguay is characterized by distinctive features that differentiate it from the rest of the Americas. The forced colonization and conquest of the region resulted in a heterogeneous population characterized by a distinct directionality, with a maternal contribution that is predominantly of Native American descent (30-70%, varying by region) and a paternal contribution that is almost exclusively of European descent (95-99%). At the autosomal level, this translates into a European contribution ranging from 70% to 89%. These data are derived from genetic marker panels that have been meticulously designed for the purpose of ancestry calculation. The objective of this study is to analyze the genomic structure and its variation by chromosomal region with respect to the population's mean values. In this study, we utilized the low-coverage sequencing technique to sequence 30 women from the Uruguayan population, thereby developing an analysis protocol. Following the filtration process, which entailed the removal of SNPs exhibiting MAF>5% and linkage disequilibrium, a total of 593,500 SNPs were subjected to comparative analysis with data from all populations present in the 1000 Genomes project. Principal component analysis demonstrated a discernible distribution in a hybrid population, exhibiting a robust association with European populations. This finding aligns with the conclusions of previous studies that employed ancestry markers as a means of genetic analysis. Conversely, when analyzing variability across the genome, chromosomal regions with divergent ancestry patterns were identified. The identification of local ancestry blocks in the genome of the Uruguayan population will facilitate the search for indications of recent natural selection and the investigation of its potential association with diseases.

Keywords: Low pass sequencing, ancestry, Uruguay.

In Vivo CRISPR/Cas9-mediated Mutagenesis of the *CV1* Promoter to Enhance Drought Tolerance in Plants

Briano Selene[1], Fernández Joaquín[1], Fleitas Andrea Luciana[1] and Vidal Sabina[1]

[1]Plant Molecular Biology Laboratory, Institute of Biological Chemistry, Faculty of Sciences, Universidad de la República, Montevideo, Uruguay

Abstract: Soybean is a drought-sensitive crop that is frequently exposed to water-deficit conditions. Previous studies have shown that drought-induced *CV1* expression is negatively correlated with stress tolerance across different soybean genotypes. *CV1* encodes a protein involved in chloroplast dismantling during stress-induced senescence. Experiments using transgenic Arabidopsis expressing the GUS reporter gene under the control of the soybean native *CV1* promoter (proCV1:GUS) demonstrated that promoter activity increases upon water deficit and other abiotic stress conditions, but not during natural senescence.

This study aims to develop a strategy to reduce *CV1* expression in plants by introducing mutations in specific regions of the promoter using the CRISPR/Cas9 system. Eight constructs were designed to express CRISPR/Cas9 and simultaneously target two specific sites within proCV1 in transgenic Arabidopsis, with the goal of removing key cis-regulatory regions. The constructs were introduced into Arabidopsis, generating a variety of edited lines currently under characterization. Recent results reveal a decrease in promoter activity in several lines carrying deletions in proCV1.

Alongside this, we are currently analyzing the contributions of two NAC transcription factors (TFs) in the regulation of proCV1 under stress and senescence conditions, using the same proCV1:GUS reporter model. Transgenic lines with conditional expression of these TFs were generated, and promoter activity was evaluated in the presence or absence of the expression of these genes.

Collectively, these findings contribute to the development of strategies for enhancing drought stress tolerance in plants and deepen our understanding of the regulatory architecture of proCV1.

Keywords: CRISPR/Cas9, water deficit, *CV1*.

Wastewater-based Epidemiology: A Promising Tool for Advancing Public Health

Cancela Florencia[1], Lizasoain Andrés[2], Panzera Yanina[3], Fernández-López Elena[4], Lozano Joaquín[4], Calleros Lucia[3], Grecco Sofia[3], Marandino Ana Eugenia[3], Cortinas. María Noel[5], Masachessi Gisela[6,7], Nates Silvia[6], Icasuriaga Romina[1], Colina Rodney[2], Smyth Davida[8] and Mirazo Santiago[1]

[1]Laboratorio de Ecología Viral y Virus Zoonóticos, Unidad Académica Bacteriología y Virología, Instituto de Higiene, Facultad de Medicina, Universidad de la República; [2]Laboratorio de Virología Molecular, Departamento de Ciencias Biológicas, Centro Universitario Regional Litoral Norte, Universidad de la República, Salto; [3]Sección Genética Evolutiva, Departamento de Biología Animal, Instituto de Biología, Plataforma Genómica, Facultad de Ciencias, Universidad de la República; [4]BIKO S.A. [5]Unidad Genómica, Departamento de Laboratorios de Salud Pública, Ministerio de Salud Pública, Montevideo 11600, Uruguay; [6]Instituto de Virología Dr. J. M. Vanella, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba, Enfermera Gordillo Gómez s/n, Ciudad Universitaria, Córdoba X5000, Argentina; [7]Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Godoy Cruz 2290, CABA C1425FQB, Argentina. [8]Department of Life Sciences, Texas A&M University-San Antonio, San Antonio, Texas, Estados Unidos

Abstract: Wastewater-Based Epidemiology (WBE) is currently considered a reliable and cost-effective prediction tool to evaluate infection trends at a community scale in order to mitigate the impact of epidemic waves or outbreaks.

This approach has generated more interest since the COVID-19 pandemic and is currently being used globally. In this context, we previously carried out the first WBE surveillance of SARS-CoV-2 in Uruguay, allowing us to study the (re)emergence and prevalence of SARS-CoV-2 variants of concern/interest at different stages of the epidemic outbreak.

Recently, we conducted a study to evaluate the performance of a commercial targeted enrichment panel for respiratory viral pathogens through next-generation sequencing (Respiratory Pathogen ID/AMR enrichment panel -RPIP- Illumina, Inc., USA) in wastewater samples from the 2023 winter season, with the aim to determine its suitability to develop WBE programs in Uruguay.

This RPIP panel was able to detect and characterize several viral pathogens, including Influenza A-H1N1, SARS-CoV2 and Coxsackievirus A.

Even though this panel requires high sequencing coverage, our results suggest its applicability as a complementary tool for more comprehensive genomic WBE studies of respiratory enteric pathogens.

Keywords: Wastewater-based epidemiology, targeted enrichment sequencing, enteric and respiratory viruses, Uruguay.

Deciphering the Contribution of Vault Non-coding RNAs to Tumorigenesis

Duhagon, María Ana[1,2], Fort Rafael[1,3], Oliveira-Rizzo Carolina[1], Colantuono Lucía[1,2], Sheppard Jake[1], Coitiño Evangelina[1], Ladra Camila[1], Victorica Felipe[1], Kislinger Thomas[4,5] and Stanley Liu[4,6,7]

[1]Sección Genómica Funcional, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [2]Unidad Académica de Genética, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay; [3] Departamento de Genómica, Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay; [4] Department of Medical Biophysics, University of Toronto, Toronto, Canada; [5]Princess Margaret Cancer Centre, University Health Network, Toronto, Canada.; [6]Department of Radiation Oncology, University of Toronto, Toronto, Canada; [7]Odette Cancer Research Program, Sunnybrook Research Institute, Toronto, Canada

Abstract: Vault RNAs (vtRNAs) are a class of 84–141 nt non-coding RNAs transcribed by RNA polymerase III and originally named for their association with the enigmatic vault particle. In humans, vtRNA1-1, vtRNA1-2, and vtRNA1-3 are clustered at a single locus, while vtRNA2-1 is a divergent paralogue located separately. All share a conserved hairpin structure that enables direct interaction with proteins such as PARP, P62, PKR, and OAS1, modulating a variety of cellular processes, including nucleocytoplasmic transport, multidrug resistance, proliferation, apoptosis, autophagy, lysosomal activity, differentiation, motility, and innate immunity. However, the differential targets and functional roles of each individual vtRNA remain poorly defined.

While investigating small non-coding RNAs deregulated in human cancer, we focused on vtRNAs and found that vtRNA2-1 and vtRNA1-2 are epigenetically regulated in multiple cancers. Using gain- and loss-of-function models and bioinformatic analyses of large multiomics cancer datasets, we demonstrated that vtRNA2-1/nc886 functions as a tumor suppressor gene in prostate cancer through the modulation of cell proliferation, apoptosis, invasion, and epithelial immune responses. In contrast, our data suggest that vtRNA1-2 has oncogenic potential across cancer types, with preliminary findings indicating its distinctive involvement in epithelial cell proliferation and differentiation.

Additionally, we and others have shown that vtRNAs can serve as precursors of small RNAs. We characterized svRNA2-1-3p, a fragment with microRNA-like activity that contributes to tumor suppression in prostate cancer. Our emerging data now support a broader role for vtRNA-derived fragments in gene regulation across both normal and tumor tissues.

Keywords: Vault RNAs, divergent paralogue, cellular processes.

Behavioral, Biochemical, and Microbiome-related Approaches to Investigate the Effect of Cocaine in Rats

Fabius, Sara[1], Urbanavicius, Jessika[1], Fernández-Ciganda Sofia[2], Lozano Joaquin[2], Piccini Claudia[2], Zunino Pablo[2] and Scorza Cecilia[1]

[1]Departamento de Neurofarmacología Experimental, Instituto de Investigaciones Biológicas Clemente Estable; [2]Departamento de Microbiología, Instituto de Investigaciones Biológicas Clemente Estable

Abstract: Changes in the Gut Microbiota (GM) have been linked to the consumption of psychostimulants, suggesting the involvement of the bidirectional Microbiota–Gut–Brain (MGB) axis in the response to drugs of abuse. Preclinical evidence has shown that cocaine induces changes in the GM and that antibiotic pretreatment enhances its stimulating and reinforcing behavioral effects. Recently, we have demonstrated that repeated exposure to volatilized cocaine alters the structure and diversity of the GM in rats, leading to the hypothesis that modulating the GM may attenuate cocaine's effects. In this study we explored the effects of the GM modulation through oral administration of a multi-strain bacterial formulation in rats repeatedly exposed to volatilized cocaine through three approaches: (1) Behavioral, by assessing locomotor sensitization and anxiety-like behaviors; (2) Biochemical, through the measurement of short-chain fatty acids and plasma cytokines; and (3) Microbiological, *via* analysis of fecal microbiota. For 28 days, animals received either the multi-strain formulation or

vehicle, and during the final 7 days, they were exposed to volatilized cocaine. The results showed that GM modulation did not attenuate the locomotor effects induced by cocaine but rather sustained them until the end of the experiment. In addition, significant alterations in GM structure and changes in relevant bacterial components were observed in animals exposed to cocaine and pretreated with the formulation. These findings reinforce the importance of the MGB axis in the effects of cocaine and highlight the need to identify specific bacterial strains to mitigate its impact.

Keywords: Cocaine, MGB axis, probiotic, short-chain fatty acids, cytokines.

Differences in CYP Gene Variant Frequencies in Uruguayan Patients with Schizophrenia: Implications of Ancestry on Clozapine Metabolism

Gonzales Sofía[1], Menéndez Clara[2], Blanco Valentina[3], Badano José L.[2], Cayota Alfonso[3,4], Olmos Ismael[5], Ricciardi Carina[6], Guevara Natalia[7], Vázquez Marta[7], Acuña Sabrina[7], Maldonado Cecilia[7], Mato Mauricio[5], Toledo Mauricio[8], Cárdenas-Rodriguez Magdalena[2] and Spangenberg Lucía[1]

[1]Bioinformatics Unit, Institut Pasteur de Montevideo, Montevideo, Uruguay; [2]Human Molecular Genetics Laboratory, Institut Pasteur de Montevideo, Montevideo, Uruguay; [3]Functional Genomics Laboratory, Institut Pasteur de Montevideo, Montevideo, Uruguay; [4]Department of Basic Medicine, Hospital de Clínicas, Universidad de la República, Montevideo, Uruguay; [5]Clinical Pharmacology Unit, Vilardebó Hospital, ASSE, Montevideo, Uruguay; [6]Outpatient Clinic, Vilardebó Hospital, ASSE, Montevideo, Uruguay; [7]Department of Pharmaceutical Sciences, Faculty of Chemistry, Universidad de la República, Montevideo, Uruguay; [8]CLAEH University Institute – School of Medicine, Montevideo, Uruguay

Abstract: Genomic variant frequencies vary across populations with different ancestral backgrounds, potentially affecting drug responses such as to Clozapine (CZP). Most genetic databases are predominantly European, limiting their applicability to admixed Latin American populations. This study analyzed 50 Uruguayan patients with treatment-resistant schizophrenia undergoing CZP therapy. Haplotypes and SNPs were characterized for the genes *CYP1A2*, *CYP2D6*, *CYP2C19*, and *CYP3A4*, which are involved in CZP metabolism.

Next-Generation Sequencing (NGS) was performed using customized panels, followed by bioinformatic analysis with GATK, PLINK2, ANNOVAR, ShapeIT, Aldy, and RFMix v1. Haplotype frequencies were compared with the PharmFreq database, and SNP frequencies with 1000 Genomes and gnomAD (global, European, and Latin American) using exact binomial tests.

More than 70 SNPs and several haplotypes per gene were identified. *CYP1A2* showed a high frequency of the 30 haplotype (associated with tobacco-induced metabolism). *CYP2C19* and *CYP2D6* displayed notable functional diversity, with *CYP2D6* showing elevated frequencies of 39, 56, and 106 haplotypes compared to European databases. *CYP3A4* was dominated by the normal-function 1 haplotype. Allelic frequencies of several SNPs also differed from reference populations. These differences suggest that European ancestry alone does not fully explain the observed patterns. Further local ancestry analysis is recommended to explore potential genetic contributions to CZP metabolism in this population.

Keywords: Clozapine metabolism, pharmacogenomics, CYP haplotypes, Latin American population.

Toxic Cyanobacteria *Microcystis Aeruginosa*: Adaptive Growth Responses to Nutrient Availability in Laboratory Cultures and Río Negro Reservoirs

González-Etchebehere L[1], Galvanese E[1], Haakonsson S[1], Olano H[1], De Giacomi S[1], Bonilla S[1] and Aubriot L[1]

[1]*Sección Limnología, Instituto de Ecología y Ciencias Ambientales, Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay*

Abstract: The toxic cyanobacteria *Microcystis* form extensive blooms in freshwater systems worldwide, generating negative environmental impacts. In Uruguay, the Río Negro reservoirs (Bonete, Baygorria, and Palmar) consistently show eutrophic conditions and frequent toxic cyanobacterial blooms, capable of being transported downstream to the Río de la Plata estuary and the adjacent Atlantic coast. This study aimed to identify how nutrient availability, phosphorus (P) and nitrogen (N), contributes to cyanobacterial growth and to understand how dominant species persist under suboptimal conditions. Although P is often the main limiting nutrient for growth, when present in excess, it can shift the balance of nutrients, potentially leading to N limitation or co-limitation. A complementary approach was adopted, combining bioassays using water samples taken from the reservoirs to evaluate the cyanobacterial response to variations in phosphorus and nitrogen additions, and by evaluating the interaction between isolated strains of *Microcystis* and *Dolichospermum* (N-fixer) under N-limited and N-deprived conditions. *Microcystis* and *Dolichospermum* were observed to co-occur in the reservoirs during the warmest periods, with *Microcystis* producing the highest biovolumes. Bioassays using reservoir samples showed that the chlorophyll *a* increased in treatments supplemented with N and with both N and P additions. Therefore, N is the limiting nutrient in reservoirs and the primary driver of exponential cyanobacterial growth, while available P influences the total biomass produced. In culture-based bioassays, *Microcystis* withstands long-term N starvation and subsequently recovers growth after N is reintroduced into the medium. Biovolume calculations and the interspecific interaction index revealed that *Microcystis* exhibited greater growth in mixed cultures with *Dolichospermum*, suggesting facilitation rather than resource competition. Ammonium concentrations increased during the experiment in monocultures of *Dolichospermum* and mixed cultures, indicating that *Dolichospermum* could contribute N to the medium through N-fixation, supporting *Microcystis* growth and survival. Altogether, the results suggest that the increase in N availability explains blooms during warm periods, and that *Dolichospermum* may enhance *Microcystis* survival under N-limiting conditions. In contrast, the total biomass that can be achieved depends on phosphorus availability. This suggests that if phosphorus levels in the reservoirs were lower, increases in nitrogen would not lead to substantial growth of cyanobacterial biomass. The results highlight the importance of nutrients in controlling massive blooms and the role of interspecific interactions in explaining their persistence in the environment, both key factors to consider in eutrophication management strategies.

Keywords: Cyanobacteria, nitrogen, phosphorus, bioassays.

Emerging Contaminants in Aquatic Systems: Current Situation and Scientific Challenges

Griffero Luciana[1]

[1]*Microbial Ecology of Aquatic Systems, Interdisciplinary Department of Coastal and Marine Systems, Regional University Center East (CURE), Universidad de la República, Uruguay*

Abstract: Recent environmental research has revealed the presence of chemical compounds in aquatic ecosystems that, although found in low concentrations, raise concerns due to their potential ecological impact and health risks. Emerging Contaminants (ECs) include chemical substances and biological agents that continuously enter aquatic ecosystems. While they may not exhibit significant acute toxicity like some traditional pollutants, they exert subtler effects—for example, through endocrine disruption. Untreated wastewater and effluents from treatment plants not designed to remove them are key sources of ECs. As a result, a significant portion of these contaminants and their metabolites reaches surface and groundwater bodies, commonly used for drinking water supply. ECs possess chemical properties and can undergo transformations both in treatment plants and the environment, posing challenges for their detection and for the assessment of their associated ecotoxicological risk. In this context, advanced analytical technologies have been developed, allowing for the identification

of transformation products and suspect compounds through non-targeted analyses. Additionally, environmental risk-based prioritization strategies have been implemented to define priority areas for monitoring and remediation. However, significant gaps remain in current regulatory frameworks, which often fail to adequately address the presence or removal of these contaminants. This presents a challenge for integrated management of water quality and the protection of public and environmental health.

Keywords: Emerging contaminants, aquatic ecosystems, ecotoxicological risk.

Phytoplankton Blooms in the Paso Severino and Canelón Grande Reservoirs as a Response to the 2023 Water Deficit in the Santa Lucía River Basin (Uruguay)

Nogueira Lucía[1], González-Madina Lucía[1], Tesitore Giancarlo[1], Deambrosis María José[1] and Brusoni Mariana[1]

[1]*Planta potabilizadora de Aguas Corrientes, Administración de las Obras Sanitarias del Estado (OSE), Canelones, Uruguay*

Abstract: The lack of rainfall in the Santa Lucía river basin in 2023 led to the most severe water deficit in the past 75 years. As a consequence, the reservoirs used as raw water sources for drinking water treatment—Paso Severino (PS) and Canelón Grande (CG)—reached their minimum water levels, while total nitrogen rose to historic peaks in both systems (PS: 3.2 mg/L and CG: 5.2 mg/L). Once the water volume recovered, there was no immediate response from the primary producer community to these disturbances. However, the following summer, both reservoirs experienced nearly simultaneous phytoplankton blooms, registering the highest cyanobacterial biomass values for the period 2014-2025 (PS: 4.61 mm^3/L and CG: 88.2 mm^3/L). The Canelón Grande reservoir exhibited a cyanobacterial bloom of the genus *Dolichospermum*. In Paso Severino, a bloom involving multiple cyanobacterial genera occurred, with dominance shifting over time, beginning with Raphidiopsis, followed by *Planktothrix* and *Microcystis*. Both systems recorded odor-causing metabolites (2-methylisoborneol and/or geosmin) but no cyanotoxins. Downstream, there was no high cyanobacterial biomass, and the raw water quality at the Aguas Corrientes treatment plant was unaffected. All of the above underscores the importance of robust, continuous, and interdisciplinary water-quality monitoring programs, since aquatic systems do not typically respond immediately to major disturbances. This, combined with projected high variability in precipitation regimes due to climate change, makes such programs even more pertinent.

Keywords: Phytoplankton bloom, water deficit, reservoirs.

Pericyte Panx1 Channels Regulate Cerebral Capillary Dynamics and Support Learning and Memory

Mai-Morente Sandra[1] and Abudara Verónica[1]

[1]*Laboratorio de Interacciones Neuro-glio-vasculares, Unidad Académica de Fisiología, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay*

Abstract: At the blood–brain barrier, contractile pericytes play a critical role in regulating capillary resistance and cerebral blood flow to match the brain's metabolic demands, although the molecular mechanisms underlying these functions remain poorly understood. Here, we demonstrate that cerebral pericytes in mice express functional Pannexin1 (Panx1) channels, which mediate ATP release — a key signal promoting pericyte contraction and capillary constriction. In hippocampal slices, we found that Panx1 activity in pericytes controls changes in capillary diameter in response to variations in extracellular ATP and glutamatergic synaptic activity, which has been reported to underlie neurovascular coupling. Selective deletion of Panx1 in pericytes impairs capillary dilation during learning tasks and compromises memory performance, as assessed by novel object and location recognition tests. Pericyte Panx1 is modulated by glutamatergic (NMDA/AMPA) and purinergic

(ionotropic P2X7 and metabotropic P2Y6) receptors, which adjust ATP efflux and perivascular extracellular ATP levels through variations in Panx1 channel activity, ultimately regulating pericyte intracellular calcium and capillary diameter. These findings identify Panx1 in pericytes as a key physiological modulator of capillary dynamics, essential for cognitive function, and highlight it as a potential therapeutic target for cognitive deficits associated with cerebrovascular dysfunction.

Keywords: Pericytes, pannexin1, ATP, capillary diameter, memory.

Livestock Genetic Improvement: Towards Low-Methane-Emissions Production Systems

Navajas Elly[1], De Barbieri Ignacio[2], Peraza Pablo[1], Carracelas Beatriz[1] and Ciappesoni Gabriel[1]

[1]Instituto Nacional de Investigación Agropecuaria, Sistema ganadero, Canelones, Uruguay; [2] Instituto Nacional de Investigación Agropecuaria, Sistema ganadero, Tacuarembó, Uruguay

Abstract: Genetic selection for lower Methane Emissions (ME) in cattle and sheep is one of the strategic tools to achieve national mitigation commitments, given its moderate heritability, with effects that are cumulative and permanent. In response to this opportunity, phenotyping platforms for feed intake, feed efficiency, and methane emissions have been implemented in the genetic evaluation nuclei of Hereford cattle and Corriedale, Texel, Merilín, Australian Merino, and Dohne sheep. The magnitude of ME is phenotypically and genetically associated with feed intake level, which is also linked to animal productivity. Optimizing ME reduction without compromising the economic and environmental sustainability of livestock production requires knowledge of heritabilities and genetic and phenotypic correlations among these traits. To optimize investment in phenotyping for its application in R&D&I, data are collected from animals that are either included in genetic evaluations or are genetically connected to them. Genotyping these animals turns the information nuclei into reference populations for genomic selection, enabling faster genetic progress. Results indicate that contributing to mitigation targets is feasible, with the expansion of databases being key to achieving more accurate estimates of synergies and antagonisms. This is complemented by new protocols for measuring ME under grazing conditions and the integration of rumen microbiome data to identify biomarkers and their effect on the prediction of genetic merit for ME.

Keywords: Sustainability, methane mitigation, selective breeding, sheep, cattle.

Genetic Variants Influencing Glucocorticoid Response and Toxicity in Patients with Hematological Diseases

Palermo Carla[1], Da Luz Julio[2], LaLuz Florencia[3], Soler Ana[2] and Corvo Ileana**[1]**

[1]Laboratorio de Moléculas Bioactivas, Departamento de Ciencias Biológicas, CENUR LN, Universidad de la República; [2]Laboratorio de Genética Molecular Humana, Departamento de Ciencias Biológicas, CENUR LN, Universidad de la República; [3]Servicio de Hemato Oncología, Hospital de Paysandú

Abstract: Glucocorticoids (GCs) are integral components of standard treatment regimens for a variety of diseases. In hematological disorders, high-dose and/or prolonged GC administration is commonly employed in conditions such as Acute Lymphoblastic Leukemia (ALL)—the most prevalent pediatric cancer—and in adults with Immune Thrombocytopenic Purpura (ITP) and warm antibody-mediated Autoimmune Hemolytic Anemia (AIHA). The metabolic pathway of GCs involves multiple genes and genetic polymorphisms that can influence both therapeutic efficacy and the risk of adverse effects. This study aims to investigate allelic variants of genes involved at different stages of the GC pathway, in order to establish their association with treatment response and toxicity in patients diagnosed with ALL, ITP, and AIHA. Initial focus was placed on the IKZF gene family—which encodes a transcription factor linked to GC responsiveness—and the GST gene family, which is involved in GC metabolism.

To this end, optimized molecular protocols were developed to detect:

- Deletions in IKZF genes using multiplex PCR, - Presence or deletion of GSTT1 and GSTM1 genes via multiplex PCR,

- Two Single-Nucleotide Polymorphisms (SNPs) in GSTP1 (rs1695 and rs1138272), using PCR-RFLP and PCR-sequencing, respectively.

Analysis of the Laboratorio de Genética Molecular Humana genomic DNA bank of ALL patients revealed individuals with deletions in the IKZF gene (pending further characterization), as well as both homozygous and heterozygous deletions in GSTT1 and GSTM1. Additionally, all three genotypes of the GSTP1 SNPs were observed. The next steps include completing genotyping of the ALL DNA samples and expanding the study to incorporate genomic DNA from patients with AIHA and ITP. This will enable association studies between specific genotypes and both therapeutic response and GC-related adverse effects.

Keywords: Glucocorticoids, acute Lymphoblastic Leukemia, polymorphisms, PCR, IKZF, GST.

Preclinical Models to Study the Link Between Depression and Alcohol Use

Ruiz Paul[1], Colombo Micaela[1] and Pautassi Ricardo[2]

[1]Departamento de Biociencias, Facultad de Veterinaria, Universidad de la República, Uruguay; [2]INIMEC-CONICET-UNC, Facultad de Psicología-UNC, Argentina

Abstract: Depression is the most prevalent mental illness worldwide, and alcohol is the main associated drug. Preclinical models have made fundamental contributions to understanding the etiologies and treatments of this psychopathology. There are pharmacological, behavioral, and genetic preclinical models that largely reproduce human depression symptoms. In this presentation, we address two models (pharmacological and behavioral), discussing the construct validity of each one in modeling the relationship between depression and alcohol, seen in depressed individuals. The pharmacological model is based on the reserpine administration (a monoamine-depleting agent), and the behavioral model is based on emotional contagion (animals that live with depressed peers tend to become depressed). We show how behavioral and neurophysiological variables seen in depressed individuals are modeled in both models, focusing mainly on the relationship between depression and alcohol consumption. The reserpine-based model modeled what has been seen in humans, where depressed individuals consume more alcohol, accompanied by a central depletion of monoamines. Meanwhile, even though the behavioral model generates a central monoamine decrease, not increase alcohol consumption, although the animals seem to be more resistant to the alcohol aversive effects. In summary, both models are useful for studying different dimensions of the relationship between alcohol consumption and depression seen in humans.

Keywords: Depression, alcohol, rats.

Diversity and Conservation of Antarctic Invertebrates: A Comprehensive Academic Approach

Volonterio Odile[1]

[1]Sección Zoología de Invertebrados, Facultad de Ciencias, Universidad de la República, Uruguay

Abstract: Despite more than two centuries of research, much remains to be uncovered about the current characteristics of Antarctic fauna. Understanding these aspects is critical, as Antarctic animals face increasing pressures from climate change and human activity on the continent. Effective conservation strategies require comprehensive data on species diversity, abundance, biological traits, and vulnerability to environmental changes. Moreover, proactive measures are essential to prevent the introduction of non-native species that could disrupt the fragile balance of Antarctic ecosystems. In response to these challenges, and with the support of the Uruguayan Antarctic Institute and the Scientific Committee on Antarctic Research, a line of study was launched in 2007, focused on generating essential data on invertebrate groups that are often overlooked due to their relatively low visibility and a shortage of taxonomic expertise. As part of this effort, the presence of the non-native dipteran *Trichocera maculipennis* was documented on King George Island. Additionally, new species

have been described, and previously unrecorded taxa in the region have been identified. The knowledge gained through this research has been integrated into undergraduate and postgraduate courses, the training of early-career researchers, and the development of a sustained outreach program centered on Antarctic science. Looking ahead, this ongoing work will continue to document Antarctic biodiversity and aims to adopt an ecological perspective to support the long-term monitoring of biotic changes.

Keywords: Biodiversity, climate change, maritime antarctic, non-native species.

Exercise as a Circadian Entrainer

Marchesano Mariana[1]

[1]*Grupo de Investigación Cronobiología, CSIC, Universidad de la República*

Abstract: The light-dark cycle is the primary temporal cue for the circadian system; however, the photic signal has been weakened by urban living conditions (darker days, brighter nights). This mismatch between solar and social clocks disrupts our biological rhythms, with consequences for health, work, and education. Recent research has shown that physical exercise performed at specific times of the day can elicit circadian phase shifts independent of light exposure. Moreover, early and late chronotypes exhibit distinct daily profiles of motor performance. In this sense, exercise scheduled in alignment with individual circadian phases may facilitate the adjustment of our ancestral biological clocks to challenging situations, improving both performance and recovery in athletes and dancers. In this talk, we will review some studies that explore the temporal dimension of exercise and its impact on sleep habits, cognitive performance, and motor performance. Finally, we will discuss recent findings on exercise profiles and circadian rhythms in the Uruguayan population.

Keywords: Light-dark cycle, circadian system, solar and social clocks.

Poster Communications

Cellular Plasticity in scRNA-seq Data: Characterization of the Th17 Transcriptional Landscape

D'Anatro, Antonella[1,2,3], Olivera Daniela[1,2], Russo Sofía[1,2], Vázquez Gustavo[4], Hill Marcelo[1,2], Segovia Mercedes[1,2] and Rego Natalia[3,5]

[1]Immunobiology Department, Faculty of Medicine, Universidad de la República; [2]Laboratory of Immunoregulation and Inflammation, Institut Pasteur de Montevideo; [3]Bioinformatics Unit, Institut Pasteur de Montevideo; [4]Informatics Department, Universidad Católica del Uruguay; [5]Laboratory of Evolutionary Genomics, Faculty of Sciences, Universidad de la República

Abstract: Plasticity is an essential property of immune cells, which allows them to transition between different physiological and phenotypical environments in response to pathogens and environmental stimuli. This property gives them the capacity of acquiring a series of states in a high-dimensional "transcriptional landscape", where each point represents a unique gene expression profile. Data obtained through single-cell RNA sequencing (scRNA-seq) allows the characterization of dynamic populations without imposing rigid cell-type restrictions. The aim of this project is to develop a bioinformatics pipeline in order to quantify cellular plasticity through metrics that explore many of the landscape's aspects, including transcriptional diversity, geometric space, network connectivity, lineage trajectory, metabolic activity, and relevant gene selection through a machine learning module. This pipeline will be implemented to study mouse-derived wild-type and Tmem176b$^{-/-}$ Th17 cells. Tmem176b$^{-/-}$ is an ionic channel that modulates immune regulation and has been recently linked to the plasticity of this particular cell lineage. This approach intends to reveal whether the absence of Tmem176b$^{-/-}$ hinders the capability of Th17 to acquire a more regulatory phenotype, especially in the context of autoimmune diseases. In order to achieve this, we will also make use of public datasets, in which Th17 cells are integrated with other cell types. At present, the project is taking its initial steps by preparing data and implementing the diversity module.

Keywords: Plasticity, environmental stimuli, physiological.

Virtual Audience in Cichlids: A Possible Tool to Study Social Modulation of Intersexual Aggression

Salustri Chiara[1], Brasca Mariano[1], Pozzi Andrea[2,3] and Scaia María Florencia[1]

[1]Laboratorio de Neuroendocrinología del Comportamiento Social, Instituto de Fisiología, Biología Molecular y Neurociencias – CONICET, Ciudad Autónoma de Buenos Aires, Argentina; [2]Instituto de Biodiversidad y Biología Experimental y Aplicada – CONICET, Ciudad Autónoma de Buenos Aires, Argentina; [3]Laboratorio de Neuroendocrinología y Comportamiento en Peces y Anfibios, Departamento de Biodiversidad y Biología Experimental, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Ciudad Autónoma de Buenos Aires, Argentina

Abstract: The question of how aggressive behaviors across different vertebrate groups can be shaped by the social environment can be addressed through the Audience Effect. Social behavior is based on individuals perceiving the environment and communicating with each other through signals, and the presence of an observer may influence the behavior of interacting individuals. While the Audience Effect has been reported in intersexual encounters in fish, this was assessed in reference to courtship but not to agonistic behavior. In the Neotropical cichlid fish *Cichlasoma dimerus*, aggressive behavior has been reported in intersexual dyadic encounters. To evaluate how the presence of an audience can modify intersexual aggression and the neural correlates of this behavior, a virtual stimulus may be used as an audience. The aim of this study is to design and validate the use of a virtual stimulus that will then allow assessing the Audience Effect. For this, a focal fish was placed in an aquarium and presented to a screen on one side, playing a video of a smaller subordinate conspecific. Two experimental setups were used: one with the opposite side empty, and another one showing a second screen with a

video of an empty aquarium. An ethogram was performed, and agonistic behavioral displays were quantified to assess temporal dynamics. Validating the virtual stimulus as an audience will allow future experiments to evaluate brain activation patterns associated with this behavioral paradigm, particularly within the Social Decision-Making Network (SDMN), to better understand how social context modulates aggression in intersexual encounters.

Keywords: vertebrate groups, social behavior, audience effect.

Differences in Cellular Architecture and Microenvironmental Responses in Pre-tumoral and Tumor Cell Models Exposed to Coverslip-induced Hypoxia

Hochmann Jimena[1], Millán Magdalena[2], Parietti Felipe[2], Lamela Florencia[1], De Rossi María Cecilia[3], Benítez Belén[4], Levi Valeria[3], Domingues Manoela[5], Bologna-Molina Ronell[1] and Arocena Miguel[2]

[1]Departamento de Diagnóstico en Patología y Medicina Oral, Facultad de Odontología, Universidad de la República, Uruguay; [2]Departamento de Biología Odontológica, Facultad de Odontología, Universidad de la República, Uruguay; [3]Instituto de Química Biológica de la Facultad de Ciencias Exactas y Naturales (IQUIBICEN), Facultad de Ciencias Exactas y Naturales, CONICET-Universidad de Buenos Aires, Buenos Aires, Argentina; [4]Instituto de Fisiología, Biología Molecular y Neurociencias (IFIBYNE), Facultad de Ciencias Exactas y Naturales, CONICET-Universidad de Buenos Aires, Buenos Aires, Argentina; [5]Departamento de Odontología Conservadora, Facultad de Odontología, Universidad do Rio Grande do Sul, Brasil

Abstract: The tumor microenvironment is an altered environment that imposes multiple selective pressures leading to the survival and dissemination of aggressive tumor cell subpopulations. The response of pre-tumoral and tumor cells to changes in their microenvironment will determine subsequent tumor evolution. In this study, we subjected pre-tumoral and tumor cells to coverslip-induced hypoxia, which recapitulates the intracellular hypoxia and extracellular acidification characteristic of the early tumor microenvironment, and used a combination of quantitative phase microscopy and epifluorescence to analyze various responses to this altered environment. Under normoxia, tumor cells displayed differences in nuclear organization, as evidenced by decreased foci of the nuclear heterochromatin marker, HP1, and under hypoxia, significant changes in nuclear architecture were observed, with tumoral cells showing significantly increased numbers of high-density dry mass foci in the nucleus compared to pre-tumoral and non-tumor cells. In contrast, compared with pre-tumoral and normal cells, mitochondrial ATP levels decreased markedly in tumor cells under hypoxia, whereas activation of executioner caspases increased only in tumor cells under this condition. Thus, in terms of cellular organization, metabolic changes, and activation of cell death processes, tumor cells showed more dramatic responses to an altered microenvironment than their pre-tumor and normal counterparts, responses that in turn could play pivotal roles in shaping tumor development.

Keywords: Hypoxia, tumor microenvironment, nuclear architecture.

Assessment of Harmful Algal Blooms and Fecal Contamination in Substrates and Water at Arazatí Beach

Leites Lucía[1], Piccini Claudia[1] and Kruk Carla[2,3]

[1]Department of Microbiology, Clemente Estable Institute of Biological Research. Avenida Italia 3318, Montevideo 11600, Uruguay; [2]Limnology Section, Institute of Ecology and Environmental Sciences, Faculty of Sciences, Universidad de la República. Iguá 4225, Montevideo 11400, Uruguay; [3]Statistical Data Modeling and Artificial Intelligence, Regional University Center of the East, Universidad de la República. National Route No. 9, intersection with Route No. 15, Uruguay

Abstract: The Río de la Plata and its beaches face significant environmental issues, among which fecal contamination and blooms of the Microcystis aeruginosa complex stand out. Although water fecal contamination is regularly monitored, the capacity of microorganisms to form and inhabit biofilms is not taken into account. This lifestyle allows them to survive adverse environmental conditions, associate with other organisms, and persist in the environment. One of the most studied fecal microorganisms is Escherichia coli, a species capable of forming biofilms on various substrates. This study focuses on analyzing the abundance and persistence of fecal coliforms in substrates and water at Arazatí beach (San José), located on the Río de la Plata, as well as the interaction between this contamination and the presence of toxic blooms of the Microcystis Aeruginosa Complex (MAC). The methodology employed includes the analysis of coliform abundance in water and on various substrates present on the beaches, using the membrane filtration method, while the presence of toxic MAC is determined through qPCR targeting the mcyE gene. Preliminary results show that, although the coliform load in the water was within regulatory limits, there is a high abundance of coliforms attached to substrates such as stones, shells, sand, and fish scales, suggesting that they could act as reservoirs of fecal contamination. This persistence on substrates could have implications for human health, especially in recreational areas. This research is particularly relevant due to the future installation of a drinking water treatment plant in the area.

Keywords: significant environmental issues, fecal contamination, microcystis aeruginosa complex.

Development of a *Caenorhabditis Elegans* Assay to Evaluate the hERG Potassium Channel Inhibitory Activity of Ibogaine Analogs

Mena Natali[1], Mesa Juan Manuel[2], Carrera Ignacio[2], Flames Nuria[3], Romanelli Laura[4] and Carrera Inés[1]

[1]Pharmacology Area, Laboratory of Animal Experimentation, Department of Pharmaceutical Sciences, Facultad de Química, Universidad de la República; [2]Laboratory of Organic Synthesis, Department of Organic Chemistry, Facultad de Química, Universidad de la República; [3]Neurodevelopment Unit, Institute of Biomedicine of Valencia, Spain; [4]Laboratory of Worm Biology, Institut Pasteur de Montevideo

Abstract: Ibogaine is a naturally occurring alkaloid with therapeutic potential in the treatment of substance use disorders. However, its clinical application is limited by its ability to block the Human Ether-à-go-go-Related Gene (hERG) potassium channel, which is essential for cardiac repolarization and can lead to potentially fatal arrhythmias. In this context, we aim to develop a screening assay using *Caenorhabditis elegans* to investigate the relationship between the chemical structure of iboga alkaloids and their activity as hERG channel blockers, seeking to design safer analogs. For this purpose, we employ a transgenic *C. elegans* strain that expresses a gain-of-function mutant chimeric hERG channel, resulting in worm paralysis—a phenotype that can be reversed by hERG-blocking compounds. We are currently developing an automated motility assay using reference hERG blockers such as dofetilide and clofilium to determine assay sensitivity and reproducibility. Preliminary results show that these compounds selectively restore motility in hERG-expressing worms, but not in non-transgenic controls. In parallel, we are assessing the effect of ibogaine, which will serve as a reference for screening a chemical library of structural analogs. Initial findings demonstrate dose-dependent responses to the reference hERG blocker clofilium, supporting the utility of this model. This assay may become a cost-effective, scalable, and accessible tool for early-stage screening of hERG-blocking liability in drug candidates prior to clinical development.

Keywords: Ibogaine, *Caenorhabditis elegans*, hERG.

Characterizing the Transcription Factor FpaD of *Aspergillus Nidulans*

Dourron, Juliette[1], Svoboda Thomas[2], Sanguinetti Manuel[1], Amillis Sotiris[3], Scazzocchio Claudio[4,5], Strauss, Joseph[2] and Ramón Ana[1]

[1]Sección Bioquímica, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [2]Department of Agricultural Sciences, Institute of Microbial Genetics, BOKU University, Vienna, Austria; [3]Department of Biology, National and Kapodistrian University of Athens, Greece; [4]Department of Life Sciences, Imperial College London, London, United Kingdom; [5]CEA, CNRS, Institute for Integrative Biology of the Cell (I2BC), Université Paris Saclay, Gif-sur-Yvette, France

Abstract: In the absence of primary carbon and/or nitrogen sources, *Aspergillus nidulans* can use alternative sources (e.g., amino acids). This requires the synthesis of specific transporters and enzymes for their metabolism. A mutant, *fpaD43*, isolated for its resistance to Fluorophenylalanine (FPA) and D-Serine (D-Ser)—toxic analogs of Phe and L-Ser, respectively—shows altered transport capacity for these and other amino acids. FpaD is predicted to be a transcriptional repressor, with two nuclear localization signals and two different types of DNA-binding domains (a homeodomain and three Zn fingers). The *fpaD43* mutation introduces an Ala388Asp change in one of the Zn fingers. The nuclear localization of msGFP2-FpaD was verified by fluorescence microscopy. Through ChIP-seq assays, we found that FpaD binds to its own Coding Sequence (CDS) and its upstream region. Additionally, it binds to the CDS and upstream region of *cpcA*—an activator of genes involved in amino acid biosynthesis— as well as to the CDS of several genes implicated in stress responses or predicted to be regulators. Based on RNA-seq results comparing the mutant strain to the wild type, we found that several differentially expressed genes are involved in amino acid metabolism.
Our results suggest that FpaD is indeed involved in regulating the expression of transporters (and other genes related to amino acid metabolism), though likely through an indirect and more complex mechanism than initially proposed.

Keywords: *Aspergillus nidulans*, amino acid transport, transcription regulation.

Differential Responses Between Control Keratinocytes and Pretumoral Keratinocytes Exposed to a Hypoxic Microenviroment

Millán Magdalena[1], Arocena Miguel[1] and Hochmann Jimena[2]

[1]Department of Dental Biology, School of Dentistry, Universidad de la República, Uruguay; [2]Department of Diagnosis in Pathology and Oral Medicine, School of Dentistry, Universidad de la República, Uruguay

Abstract: During carcinogenesis, cancer cells acquire certain characteristics: uncontrolled proliferation, angiogenesis, altered metabolism, hypoxia, invasion, and metastasis. To evaluate some of these characteristics, we used human keratinocytes transduced with HPV-18 viral oncogenes (E5/E6/E7-18) as a pretumoral model subjected to a hypoxic microenvironment. We hypothesized that there are differences in the expression of proteins associated with carcinogenesis and cellular stress between control and pre-tumor keratinocytes.

Spontaneously immortalized human keratinocytes, HaCaT (control) and HaCaT with HPV-18 oncogenes (E5/E6/E7), were used. These were exposed to a hypoxic microenvironment using the hypoxia induction method with coverslips. Protein extractions were performed and quantified using Bradford. Commercial arrays of proteins associated with carcinogenesis and cellular stress were used. Protein levels were quantified using ImageQuant TL software. Immunocytochemical assays were performed using specific antibodies for the detection of phosphorylated mTOR, EpCAM, and HIF-1α. The results were visualized with a ZEISS 800 confocal microscope and quantified using ImageJ software.

Significant differences were observed in the levels of some proteins between control HaCaT cells and HaCaT E5/E6/E7-18 cells under normoxic and hypoxic conditions. Increased expression of the proteins EpCAM, galectin-3, and EGF-R was observed in HaCaT E5/E6/E7-18 cells under hypoxia. We observed increased expression of EpCAM and HIF-1α, and a slight decrease in phosphorylated mTOR expression, in both cell lines under hypoxia.

In conclusion, differences were observed in the levels of proteins associated with carcinogenesis and cellular stress, particularly under hypoxic conditions.

Keywords: Carcinogenesis, HPV-18, hypoxic microenvironment.

Comparative Evaluation of the Efficiency of Three Tardigrade Extraction Techniques in Urban Microenvironments of Montevideo (Uruguay)

Silveira Angela[1], Ponce de León Rodrigo[1] and Volonterio Odile[1]

[1]Sección de Zoología de Invertebrados, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay

Abstract: Tardigrades, with more than 1,460 species, inhabit terrestrial, marine, and limnic ecosystems. Their ability to adapt to extreme conditions makes them key bioindicators of ecological health and environmental quality, especially in urban settings. The aim of this study was to evaluate the efficiency of three extraction techniques and to test the taxonomic identification of tardigrades in urban microenvironments of Montevideo. Three extraction methods were tested: direct fishing, Tullgren funnels, and flotation, with various modifications (sample size, sample type, extraction period, lighting, and sugar solution concentration).

A moss sampling was conducted, recording environmental parameters such as light intensity (lx), wind speed (m/s), temperature (°C), and humidity (%). The samples were transported to the laboratory, hydrated for 12 hours, and then processed using different extraction methods to obtain tardigrades, moults, and eggs.

The most efficient technique was direct fishing, using an extraction period of 8 hours and 2 grams of sample. The Tullgren method was the least efficient, while flotation, although better than Tullgren, was still less effective than direct fishing. It was observed that moss mat samples contained more tardigrades than those that included soil.

Adult individuals (gravid and non-gravid), juveniles, moults, and eggs were found, and four genera were identified: Macrobiotus, Paramacrobiotus, Milnesium (Eutardigrada), and Echiniscus (Heterotardigrada).

This study highlights the importance of optimizing tardigrade extraction techniques for local conditions, contributing to their use as bioindicators of environmental status.

Keywords: Bioindicators, environmental quality, taxonomy of urban tardigrades.

Neuroplasticity in Danio Rerio Under Different Lighting Conditions

Berrosteguieta, Inés[1,2], Silva Stephanie[1], Herrera Laura[1,3], Rosillo Juan Carlos[1,4], Casanova Gabriela[5] and Fernández Anabel[1,6]

[1]Laboratorio de Neurobiología Comparada, Departamento de Neurociencias Integrativas y Computacionales, Instituto de Investigaciones Biológicas Clemente Estable (IIBCE). Facultad de Ciencias, Universidad de la República. Uruguay; [2]Unidad Curricular ESFUNO, Facultad de Enfermería, Universidad de la República. Montevideo, Uruguay; [3]Sección Fisiología y Nutrición, Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay; [4]Departamento de Histología y Embriología, Facultad de Medicina, Universidad de la República. Montevideo, Uruguay; [5]Unidad de Microscopía Electrónica, Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay; [6]Laboratorio de Neurociencias, Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay

Abstract: Neuroplasticity refers to the nervous system's ability to adapt and reorganize in response to internal and external changes, enhancing an organism’s chances of survival and reproduction in dynamic environments. Light is a key modulator

of this process, capable of influencing cell proliferation in both the retina and the brain. Teleost fish offer an exceptional model for studying neuroplasticity due to their sustained capacity for neural cell proliferation throughout life.

Danio rerio, a widely used model species, typically inhabits clear, shallow freshwater streams in Asia. This study investigated cell proliferation in the retina and in brain regions involved in olfaction and vision in adult zebrafish exposed to different light regimes, aiming to demonstrate adaptive neuroplasticity.

Two groups were established (n = 5 per group): one group was maintained in constant darkness (0 lux) for 16 days, while the control group experienced a photoperiod of 14 hours of light (500 lux) and 10 hours of darkness. On day 8, all individuals received an intraperitoneal injection of 5-ethynyl-2'-deoxyuridine (EdU), a thymidine analog used to label proliferating cells. After 16 days, animals were euthanized and perfused for tissue fixation.

Results revealed increased cell proliferation in the retina and olfactory bulb, and decreased proliferation in the optic tectum, in the dark-exposed group compared to controls. These findings provide evidence of environmentally induced neuroplasticity, suggesting that neural proliferation may shift to prioritize sensory modalities most relevant under specific environmental conditions.

Keywords: Neuroplasticity, cell proliferation, light conditions, *Danio rerio*, sensory systems.

Characterization of Very Low Birth Weight Infants' Gut Microbiome at Pereira Rossell Children's Hospital

Vera Josefina[1], Vaz Ferreira Catalina[2], Moraes Mario[2] and Riera Nadia[1]

[1]Microbial Genomics Lab, Institut Pasteur de Montevideo. Montevideo, Uruguay; [2]Centro Hospitalario Pereira Rossell, School of Medicine, Universidad de la República. Montevideo, Uruguay

Abstract: Prematurity has increased globally in recent years, driven by older maternal age and the use of assisted reproductive techniques, significantly contributing to infant and neonatal mortality. In Uruguay, this trend is alarming, as prematurity accounts for 30% of infant mortality and up to 70% of neonatal mortality. The study of microbiota in early life stages has revealed that dysbiosis, or alteration in bacterial colonization profiles, influences neonatal health. Nutritional exposures, such as breastfeeding, can modify the microbiota of newborns and their risk of diseases throughout life. This study aims to characterize the gut microbiota of Very Low Birth Weight (VLBW) infants in Uruguay, evaluating its relationship with predominant Mother's Own Milk (MOM) feeding. For this purpose, an observational, prospective, analytical, and single-center study was designed, which will analyze meconium samples from 100 VLBW newborns during 2025-2026, using 16S rRNA gene sequencing with Oxford Nanopore Technology (ONT). The cohorts will include VLBW newborns fed expressed human milk and those with mixed feeding at two time points. To date, we have completed sequencing for 20 patients, and the results show differences in the microbiological profiles at the different time points evaluated, as well as the predominance of potentially pathogenic bacteria, such as *Klebsiella pneumoniae* and *Escherichia coli*, which has already been observed in studies with similar characteristics. In the future, we plan to extend the preliminary analyses by expanding the information on the clinical variables collected.

Keywords: Gut microbiota, very low birth weight infants, mother's own milk.

Identifying Novel Biomarkers and Bacterial Strains Relevant to Gut Health for Individuals with Autism

Peñalba Florencia[1], Rusiñol Camila[2], Lamberti Lucia[2], Garrido Gabriela[2], Florencia Konick[3], Guisande Andrea[4], Iglesias Claudio[4], Mendive Paula[3], Parada Andres[1,5] and Riera Nadia[1]

[1]Microbial Genomics Lab, Instituto Pasteur de Montevideo, Montevideo, Uruguay; [2]Academic Unit of Pediatric Psychiatry, Faculty of Medicine, Universidad de la República, Montevideo, Uruguay; [3]School of Nutrition, Universidad de la República, Montevideo, Uruguay; [4]Department of Pediatric Gastroenterology, Hepatology and Nutrition, Pereira Rossell Hospital Center, Montevideo, Uruguay; [5]Department of Ecology and Evolution, Faculty of Sciences, Universidad de la República, Montevideo, Uruguay

Abstract: Autism Spectrum Disorder (ASD) is a group of neurodevelopmental disorders frequently associated with various conditions, including gastrointestinal problems. Microorganisms present in the gut can produce and modulate metabolites that can directly influence the host's nervous system, affecting cognitive and social processes. In this study, fecal samples were collected from children diagnosed with autism and their neurotypical siblings, aged between 4 and 10 years. In addition, data on gastrointestinal health, Food Frequency Questionnaires (FFQ), and the child's clinical history were gathered. A total of 76 fecal samples were obtained, out of which 53 were processed for DNA extraction and purification. From these samples, long-read sequencing of the 16S ribosomal RNA (16S rRNA) gene, using Oxford Nanopore Technology (ONT), was performed. A total of 22 pairs (ASD/Neurotypical) were analyzed, and individually, 4 children had autism, and 3 did not have a diagnosis. Considering the obtained results, the intestinal bacterial community profile of each child was characterized. Using Linear Discriminant Analysis Effect Size (LEfSe), significant differences in the abundance of various bacterial species were identified. In children with autism, a higher abundance of species such as *Faecalitalea cylindroides*, *Lactobacillus sp.*, *Mediterraneobacter sp.*, *Clostridium colinum*, and *Erysipelatoclostridium ramosum* was observed. In contrast, neurotypical children showed a higher abundance of bacteria such as *Blautia hydrogenotrophica*, *Ruminococcus lactaris*, and *Haemophilus parainfluenzae*. These results suggest that the composition of the gut bacterial community may be associated with autism, which might offer new perspectives for early diagnosis and the design of more precise therapeutic strategies.

Keywords: Autism spectrum disorder, microbiota, 16S rRNA.

Complete Protocol for the Generation of Drug-Resistant Mutants in the Amastigote Form of *Trypanosoma Cruzi*

Sanz-Rodríguez Carlos E.[1,2] and Robello Carlos[1,2]

[1]Laboratorio de Interacciones Hospedero-patógeno — UBM, Institut Pasteur de Montevideo, Montevideo, Uruguay; [2]Unidad Académica de Bioquímica, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay

Abstract: *Trypanosoma cruzi* is the etiological agent of Chagas disease, the main parasitic disease in the Americas. Its life cycle is complex and includes two hosts in three stages: epimastigote, which is replicative but not infectious and occurs within the insect vector (family Reduviidae); trypomastigote, which is infectious but not replicative; and finally, amastigote, an intracellular replicative and infectious stage whose persistence in the vertebrate host is associated with disease development. The traditional approach to infection is chemotherapy to eliminate amastigotes. Existing treatments (Benznidazole and Nifurtimox), developed over half a century ago, have significant side effects. For the development of new drugs, precise knowledge of the mechanism of action that the candidate compound may have during preclinical trials is required. In recent years, the *in vitro* evolution of drug-resistant mutants, combined with sequencing and comparison of genomes sequenced with second- and third-generation technologies, has allowed the deciphering of several mechanisms of action. This work presents, for the first time, a complete protocol for generating drug-resistant mutants in the amastigote form, using mutagenic agents. For the proof of concept, three ketoconazole-resistant strains were generated using this protocol. The genomes of these strains were sequenced using Oxford Nanopore Technology to study the changes related to their resistance to the drug.

Keywords: Mode of action, amastigote, drug-resistance, comparative genomics.

The Neural Basis of the Descending Electromotor Command for the Emission of the Chirp-Type Subordination Electric Signals in *Gymnotus Omarorum*

Píriz Antony[1], Comas Virginia[1] and Borde Michel[1]

[1]*UA Fisiología, Laboratorio de Neurofisiología Celular y Sináptica, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay*

Abstract: South American electric fish (Gymnotiformes) emit electric discharges through the activation of a myogenic peripheral effector in response to a command generated by a medullary Pacemaker Nucleus (PN).

The PN is a medial nucleus composed of a dorsal subnucleus of pacemaker cells (PM-cells) and a ventral subnucleus of relay cells (R-cells). R-cells receive the command generated by the PM-cells and project to the spinal components of the electromotor system. Characteristically, the orderly activation of the effector results in rhythmic and stereotyped discharges, whose waveforms are critical for sensory exploration of the environment. During agonistic encounters in *Gymnotus omarorum*, subordinate individuals replace this stereotyped pattern with high-frequency, low-amplitude bursts of discharges known as CHIRPs, which are proposed to function as communication signals.

In this study, we advanced in the characterization of CHIRPs and the identification of PN neurons that generate the descending command for these signals by specifically labeling their cell bodies. We found that CHIRPs (n = 107), analyzed across 10 individuals, result from suprathreshold and relatively synchronous activation of a specific subpopulation of R-cells. These cells represent between 16% and 31% of the total R-cells population, project to caudal segments of the spinal cord, and are preferentially located within the dorsal 60% of the R-cells subnucleus.

These results reveal the functional heterogeneity within the R-cells population and highlight their hierarchical contribution to the functional configuration of the PN for electrocommunication.

Keywords: Neuroethology, electrocommunication, electroreception, pacemaker, gymnotiformes.

Blooming at the Palmar Dam During the Summer of 2024-2025 (Río Negro, Uruguay): Local Alert

Carballo Carmela[1], Cuevas Julieta[1], De Giacomi Sol[1], González-Piana Mauricio[1] and Guillermo Chalar[1]

[1]*Sección de Limnología, Instituto de Ecología y Ciencias Ambientales (IECA), Universidad de la República*

Abstract: The increase in cyanobacterial blooms is one of the greatest concerns for the ecology of aquatic ecosystems and human health. They can produce potent toxins affecting human and animal health. In recent decades, bloom events have been recurrent in the reservoirs of the Río Negro, seriously compromising their ecosystem functions. Particularly during the last summer season, the Palmar dam showed high biomasses of cyanobacteria with high spatial variability, mostly accumulated on the coast. The following work analyzes the cyanobacterial bloom event (Microcystis spp.) that occurred between December 2024 and January 2025 in Palmar. Toxin levels (Microcystin-LR) in water, chlorophyll a *in vivo*, and by extraction were quantified. Analyses indicated the presence of Microcystin-LR in Palmar in December 2024 and January 2025. During December, the concentration in open waters, where there was no accumulation of cyanobacteria, was 0.12 mg/L of Microcystin-LR. In January, concentrations of 0.96 and 4.00 mg/L of Microcystin-LR were recorded in open waters and on the coast, respectively. Considering that the alert values for recreational waters according to the U.S. Environmental Protection Agency (EPA) are lower than those recorded, the situation has raised great public concern. In turn, the bloom generated exposure of residents to unpleasant odors, loss of recreational uses in beach areas, a decrease in local tourism, and uncertainty about the quality of water for human consumption. This led to the formation of a social group, made up of different users of the dam, with the aim of demanding that the authorities implement management measures.

Keywords: *Microcystis* spp., citizen participation, risk management.

Study of Bioflocculation with Filamentous Fungi for the Harvesting of Microalgae Producing Bioactive Molecules with Potential Use in Animal Supplementation

Pagglianno Camila[1], Parentelli Constanza[1] and Umpiérrez-Failache Mariana[1]

[1]*Biotechnology Laboratory, School of Engineering, Universidad ORT Uruguay*

Abstract: Population growth and the scarcity of natural resources threaten food security, requiring sustainable alternatives. Microalgae, due to their high nutritional value, represent a promising option, but their high harvesting costs limit their application. Bioflocculation appears as a promising technique to reduce costs, optimize their use, and promote sustainability.

This work aims to determine the bioflocculant capacity of different fungal strains and analyze the efficiency of bioflocculation in co-cultures of microalgae and filamentous fungi as a possible harvesting method, considering their potential for incorporation into animal feed.

Fungi and microalgae were tested and cultured separately and then combined in bioflocculation assays. Biomass recovery efficiency was measured, and its nutritional properties were analyzed using Bradford (proteins), Folch (lipids), and ABTS (antioxidant capacity) assays. In addition, astaxanthin production in *H. pluvialis* was induced by reducing the nitrogen source in the culture medium.

The results showed recovery rates of 62–100% in 22–28 hours, depending on the co-culture. The protein content was 20–30%, while the lipid content ranged from 0.11 to 0.21 g/L, lower than values reported in the literature for the studied algae. The biomass showed antioxidant activity (312–822 mg ascorbic acid equivalent/100 g of dry biomass). In addition, astaxanthin was identified by HPLC-DAD in both its free and esterified forms.

The results showed that bioflocculation is a viable and sustainable strategy for microalgae harvesting, with potential applications in animal supplementation.

Keywords: Population growth, natural resources, bioflocculation.

Water Quality Assessment of the Yí and Salsipuedes Rivers (Uruguay) Between 2009 and 2024

De Giacomi Sol[1], Carballo Carmela[1], Cuevas Julieta[1], González-Piana Mauricio[1] and Chalar Guillermo[1]

[1]*Limnology Section, Institute of Ecology and Environmental Sciences, Faculty of Sciences, Universidad de la República, Uruguay*

Abstract: The global challenge of drinking water scarcity is also affecting Uruguay, where extended droughts and deteriorating water quality have become increasingly frequent. This study evaluates the water quality of two major tributaries of the Negro River — the Yí and Salsipuedes Rivers — which drain basins with differing levels of anthropogenic impact. The Yí River basin covers 13,622 km² and is subject to more intensive agricultural and livestock activities, as well as residential wastewater discharges. In contrast, the Salsipuedes River basin spans 1,937 km² and maintains a higher proportion of natural land cover with lower human disturbance.

Data were collected through collaborative agreements between the Faculty of Sciences (Universidad de la República) and UTE from 2009 to 2024. Water quality was evaluated based on physicochemical parameters and their temporal trends.

According to mean phosphorus concentrations over the study period, the Yí River is classified as eutrophic, while the Salsipuedes River is mesotrophic. Based on nitrogen levels, both rivers fall within the mesotrophic category. Statistically significant differences were observed between the rivers in total phosphorus concentrations, with means of 133.94 ± 48.60 μg L^{-1} for the Yí and 65.38 ± 36.58 μg L^{-1} for the Salsipuedes. Significant differences were also found for turbidity, total suspended solids, nitrate, ammonium, and phosphate, all of which had higher average values in the Yí River. These differences in water quality are likely attributable to the greater intensity of human activities in the Yí River basin compared to the more preserved Salsipuedes basin.

Keywords: Eutrophication, rivers, water quality, uruguay.

Chlorophyll-a Estimation in Rio Negro Reservoirs Using Data-based Models

Díaz Micaela[1], Luján Pilar[1] and Duque Johan[1]

[1]*Artificial Intelligence Applications Research Group, Environmental Data Modeling and Analysis Laboratory, Department of Environmental Sustainability, Agro-Environmental Engineering, Universidad Tecnológica del Uruguay ITR-CS*

Abstract: Understanding water quality status is important given the escalating eutrophication of freshwater resources designated for human consumption. Computational modeling systems enable data-driven estimation of complex water quality parameters, such as chlorophyll-a, in advanced eutrophication scenarios. This study evaluates the performance of two machine learning algorithms, Multi-Layer Perceptron (MLP) and Long Short-Term Memory (LSTM) neural networks, for estimating chlorophyll-a concentrations in Uruguay's Río Negro reservoirs (Rincón de Bonete, Baygorria, and Palmar). Using historical data (2009–2023) from Uruguay's National Environmental Observatory, predictive models employed total phosphorus, total nitrogen, dissolved oxygen, water temperature, and pH as inputs. The methodology comprised three phases: preprocessing and exploratory data analysis, model application, and performance evaluation of the models using Root Mean Square Error (RMSE) and coefficient of determination (R^2). Results demonstrate the MLP model's superior performance, achieving RMSE values below 2% and an R^2 of 90%. While the LSTM model exhibited higher RMSE (exceeding 10% in some instances), it attained exceptional R^2 values surpassing 95%. Collectively, these findings underscore the efficacy of neural networks in estimating complex parameters such as chlorophyll-a.

Keywords: Machine learning, artificial neural network, water quality.

Effects of Undernutrition During Gestation and Lactation on Spatial Memory and Hippocampal Morphology in 365-Day-Old Rats

Genovese Patricia[1], Herrera Emiliano[1], Genovese Eva[1], Duque Martín[1], Bielli Alejandro[1] and Ruiz Paul[2]

[1]*Unidad Académica de Histología y Embriología, Departamento de Biociencias, Facultad de Veterinaria, Universidad de la República;* [2]*Unidad Académica de Fisiología, Departamento de Biociencias, Facultad de Veterinaria, Universidad de la República*

Abstract: This study investigated the resolution time and the number of errors made to solve a multiple T-maze by 365-day-old male Wistar rats that were born to dams fed either ad libitum (GC) or undernourished (50% food restriction during gestation; GT). After parturition, all dams were fed ad libitum; litters from the control group (GC) were kept with 8 pups, and those from the undernourished group (GT) were kept with 14. Pups were weaned at 25 days after birth. At 1 year of age, we evaluated spatial memory by placing the animals in a maze (L) for 5 consecutive days, recording their resolution time and number of errors. Subsequently, the animals were euthanized. We measured Body Weight (BW), Brain Weight (BrW), and Encephalon Weight (EnW), as well as the thickness and length of different hippocampal regions (CA1, CA2, CA3, Dentate Gyrus). The treatment negatively affected BW (GC 579.9 ± 34.1* vs GT 532.8 ± 25.5), EnW (GC 2.3 ± 0.1** vs GT 2.1 ± 0.08), and BrW (GC 1.6 ± 0.06* vs GT 1.5 ± 0.09). Among morphometric variables, we found differences only in the thickness of CA1 of Ammon's horn, which was greater in GT (GC 181.7 ± 15.0 vs GT 239.0 ± 22.5*). Neither the time spent in the maze nor the number of errors was different between groups. In conclusion, under our experimental conditions, undernutrition during early life stages affected body and brain development and slightly modified hippocampal morphometry, but did not affect spatial memory.

Keywords: Resolution time, multiple T-maze, spatial memory.

Characterizing Phosphorus Fractions in Eutrophic Reservoir Sediments: Quantification, Mobility Assessment, and Implications for Water Column Dynamics

Chalar Guillermo[1], Garreta Celina[1], De Giacomi Sol[1], Cuevas Julieta[1] and González-Piana Mauricio[1]

[1]*Limnology Department, Institute of Ecology and Environmental Sciences, Faculty of Sciences, Universidad de la República*

Abstract: Sediments can store substantial amounts of phosphorus that may be re-released into the water column, becoming bioavailable. This study was conducted in three interconnected eutrophic reservoirs primarily utilized for hydroelectric power generation. The goal was to quantify the sedimented phosphorus and identify the processes that mobilize it and return it to the water column in a bioavailable form. The methodology involved analyzing phosphorus species through sequential fractionation and short-term sediment incubation experiments under hypoxic conditions. The phosphorus fractions identified in the sediments were correlated using Generalized Linear Models with the organic and mineral composition (Al, Fe, Mn, and Ca) of the sediments. The findings suggest that iron would be the main modulator of P movement between the water column and sediments. Additionally, phosphorus bound to sedimented organic matter represents a significant mobile fraction. The sedimentation of organic matter, primarily from cyanobacterial bloom senescence, provides a source of organic P, which, upon mineralization, replenishes other inorganic phosphorus fractions. On the other hand, P associated with aluminum oxides and hydroxides serves as an important immobilized form of P in sediments, representing a non-bioavailable P source. The accumulated P in the study reservoirs is quantitatively significant and should be considered in management plans aimed at improving water quality and reducing eutrophication.

Keywords: Eutrophication, phosphorus fractions, internal load, reservoir ecology.

Canine Distemper in Uruguay: Epidemiological and Clinical Characterization of Diagnosed Cases (2021–2023)

Iribarnegaray Victoria[1], Godiño Guillermo [2], Verdes José Manuel [2] and Puentes Rodrigo[1]

[1]*Unidad Académica de Microbiología, Departamento de Patobiología, Facultad de Veterinaria, Universidad de la República;* [2]*Unidad Académica de Patobiología, Departamento de Patobiología, Facultad de Veterinaria, Universidad de la República.*

Abstract: Canine Distemper Virus (CDV) is a highly contagious viral infection that causes immunosuppression and affects both domestic and wild canids, with high mortality rates. This study retrospectively analyzed CDV-diagnosed cases submitted to the Microbiological Diagnostic Laboratory of the Faculty of Veterinary Medicine, Universidad de la República (Montevideo, Uruguay), between 2021 and 2023. A total of 251 samples were processed, mostly from Montevideo (85%), with CDV detected in 119 cases by RT-qPCR. No significant differences were observed by sex, and dogs under two years of age were more susceptible (71.4%). Sixty percent of the cases were unvaccinated, while 28% had a complete vaccination schedule, suggesting possible vaccine failures. Mixed-breed dogs were the most affected, although CDV was detected in several breeds. The main clinical signs were neurological, followed by respiratory, digestive, and dermatological signs; 24% presented combined symptoms. Phylogenetic analysis suggests a predominant CDV lineage in Uruguay, along with some divergent strains. Understanding the epidemiology and clinical presentation of CDV in Uruguay is essential for improving prevention, diagnostic, and treatment strategies.

Keywords: Canine distemper virus, epidemiology, phylogenetic analysis.

Cyanobacteria Monitoring Program at Montevideo Beaches, Uruguay

Islas Ma. Belén[1], Fernández Sofía[1], Risso Jimena[2], Sienra Daniel[2], D'Alessandro Bruno[2], Urban Analía[2], Hernández Tania[2], Haakonsson Signe[1] and Bonilla Sylvia[1]

[1]Sección Limnología, Instituto de Ecología y Ciencias Ambientales, Facultad de Ciencias, Universidad de la República; [2]Unidad de Calidad de Agua, Servicio de Evaluación de la Calidad y Control Ambiental, Departamento de Desarrollo Ambiental. Intendencia de Montevideo.

Abstract: Cumulative cyanobacterial blooms are frequent in coastal ecosystems such as the beaches of Montevideo (Río de la Plata estuary, Uruguay). These events threaten water quality and pose a high risk to human and animal health. Since 2010, the Municipality of Montevideo (IM) has been carrying out a visual monitoring program of cyanobacteria on the beaches of Montevideo in collaboration with the lifeguard service. Three stages are established for visual monitoring: 0 (absence of blooms), 1 (presence without scums/incipient bloom), and 2 (scums foam/developed bloom). This study examined the IM historical database for the period 2011-2024 at 21 beaches on the coast of Montevideo. Variables such as phytoplankton chlorophyll *a* concentration, total microcystin concentration, visual observations, and abiotic factors, including temperature and salinity, were analyzed. The consistency of visual monitoring with the categories established in World Health Organization (WHO) guidelines was evaluated, and Bayesian logistic regression models were fitted to predict the three visual stages according to water temperature and salinity. Preliminary results from these studies indicated a high agreement of category 2 with WHO guidelines (chlorophyll *a* and microcystin) with the level 2 of the visual monitoring. Visual monitoring is presented as a robust tool that can generate valuable data for long-term modelling of bloom occurrence dynamic.

Keywords: Cumulative cyanobacterial blooms, coastal ecosystems, human and animal health.

Maternal Undernutrition During Different Stages of Gestation Mildly Affects Testicular Morphology in Adult Male Rats

Kelland Nicolás[1], Herrera Emiliano[1], Núñez Belén[1], Duque Martín[1], Bielli Alejandro[1] and Genovese Patricia[1]

Unidad Académica de Histología y Embriología, Departamento de Biociencias, Facultad de Veterinaria, Universidad de la República

Abstract: Using a 2 x 2 design, the following experimental groups were generated: undernourished during the first half of gestation (TCC), during the second half of gestation (CTC), during the entire gestation (TTC), and controls fed ad libitum (CCC). At 120 days after birth, the following variables were measured: body weight (BW), testicular weight (TW), seminiferous tubule diameter (DTS), absolute volume of seminiferous epithelium (VASE), number of Sertoli cells per seminiferous tubule cross-section (NCSC), and total number of Sertoli cells per testis (NCST). BW was negatively affected by the treatment at any gestational moment, with a greater effect in the groups undernourished during the first half or during the entire gestation (CCC 575.6 ± 11.7a; TTC 549.4 ± 19.2bc; TCC 532.6 ± 10.5b; CTC 561.1 ± 21.9ac). Similarly, TW was lower in the undernourished groups (CCC 1.7 ± 0.1a; TTC 1.4 ± 0.2b; TCC 1.4 ± 0.2b; CTC 1.5 ± 0.2ab). We found no differences in DTS (CCC 216.5 ± 14.1; TTC 203.1 ± 8.6; TCC 205.8 ± 17.8; CTC 203.2 ± 16.1). Both the TTC and CTC groups presented a reduction in VASE (CCC 73.4 ± 2.3ac; TTC 71.4 ± 1.6ac; TCC 70.7 ± 2.4a; CTC 74.0 ± 2.6bc), and a similar pattern was observed in NCSC (CCC 29.6 ± 1.6a; TTC 26.3 ± 1.2b; TCC 28.7 ± 1.6ac; CTC 27.5 ± 0.5bc). However, we found no differences in NCST (CCC 26.5 ± 5.3; TTC 21.2 ± 2.3; TCC 22.8 ± 3.7; CTC 25.2 ± 3.9). In conclusion, under our experimental conditions, maternal undernutrition during different stages of gestation mildly affects testicular morphology in adult male rats, with more pronounced effects in pups whose mothers were undernourished during the entire gestation.

Keywords: Body weight, volume of seminiferous epithelium, undernourished.

Ibogaine-induced c-Fos Immunoreactivity in the Brain of Adult Rats

Lima de Almeida Lucía[1], Mesa Juan Manuel[2], Romero Camila[3], Verdes José[3], Rossi Francesco Mattia[1], Carrera Ignacio[2] and Prieto José[1]

[1]Neuroscience Laboratory, School of Science, Universidad de la República; [2]Department of Organic Chemistry, School of Chemistry, Universidad de la República; [3]Department of Pathobiology, School of Veterinary Medicine, Universidad de la República

Abstract: Ibogaine is a psychedelic alkaloid found in the root bark of *Tabernanthe iboga*. Anecdotal reports regarding its anti-addictive potential have led to clinical and preclinical research that provide supporting evidence for its therapeutic potential. However, its security profile, as well as its actions in the Central Nervous System (CNS) underlying the described effects, are not yet fully elucidated.

This work analyzes the effects of acute ibogaine treatment on the protein expression of the early immediate early gene *c-fos* as an indicator of neuronal activity in the CNS of adult rats. Particularly, we focused on the Medial Prefrontal Cortex (mPFC), a region involved in processes such as reward and behavioral inhibition, which can be affected by ibogaine.

Adult male Wistar rats received an intraperitoneal injection of ibogaine (40 mg/kg) or its vehicle. Immediately afterwards, behaviors associated with the serotonergic syndrome, characteristic of psychedelic substances, were quantified for 30 minutes in an open field. 90 minutes later, the animals were anesthetized, and their brains were fixed and frozen. Coronal sections at the level of the mPFC were then obtained and processed for c-Fos immunohistochemistry.

Ibogaine induced distinctive behaviors associated with serotonergic syndrome, mainly characterized by high levels of tremor. Increased immunoreactivity to c-Fos was observed in all mPFC subregions analyzed (cingulate, prelimbic, and infralimbic cortex). These findings suggest the involvement of the mPFC in the early acute actions of ibogaine and provide relevant information on its differential effects on the CNS.

Keywords: Ibogaine, anti-addictive potential, central nervous system.

Chronobiological Profile and Clock Gene Variants in the Uruguayan Population

Marchesano Mariana[1], Spangenberg Lucía[2], Silva Ana[1,3] and Tassino Bettina[1,4]

[1]Grupo de Investigación Cronobiología, CSIC, Universidad de la República; [2]Unidad de Bioinformática, Instituto Pasteur – Montevideo; [3]Laboratorio de Neurociencias, Facultad de Ciencias, Universidad de la República; [4]Sección Etología, Facultad de Ciencias, Universidad de la República

Abstract: Circadian rhythms are endogenous biological rhythms of approximately 24 hours, mainly entrained by the daily light-dark cycle. The Cronobiología group (CSIC, Universidad de la República) investigates the environmental and social factors that modulate these rhythms in challenging everyday scenarios such as school and work shifts, exposure to different photoperiods, exercise, or motherhood. These studies have yielded a wealth of data through objective measures (sleep-activity patterns, light exposure, hormone levels) and self-report questionnaires (chronotype, circadian preference, sleep quality, mood). A striking finding is the tendency toward nocturnality across different age groups of the Uruguayan population. Late chronotypes are considered a risk factor for various health disorders, and often experience difficulties stemming from the misalignment between biological and social clocks. However, they exhibit flexibility in adjusting to environmental changes. Recent genomic studies, mostly conducted in European populations, have identified associations between genetic variants of clock genes and chronotype. To our knowledge, there are no data regarding the frequency of genetic variants associated with the circadian system in the Uruguayan population. This is the first chronobiological study with a local population that includes genetic analysis. Here, we report preliminary findings from an experimental study aimed at identifying associations between individual chronobiological and genetic profiles in a sample of 91 young participants.

Keywords: Circadian system, late chronotype, Uruguayan genome.

Molecular Characterization of Autochthonous Strains with Enological Potential

Giménez Sofía[1], Soler Gabriela[2], Garmendia Gabriela[1], Gonzalez Paula[2] and Vero Silvana[1]

[1]Microbiology Area, Department of Biosciences, Faculty of Chemistry, Universidad de la República; [2]Biochemistry Area, Department of Biosciences, Faculty of Chemistry, Universidad de la República

Abstract: The molecular characterization of enological yeasts enables the identification of strains with distinctive value and potential to reflect local microbial identity. In this study, two autochthonous strains were analyzed: *Saccharomyces cerevisiae* T-19-3FS and *Starmerella bacillaris* T-19-3MS, previously selected for their enological performance, including resistance to metabisulfite and ethanol, fermentation kinetics, β-glucosidase activity, and killer phenotype. The objective was to genetically type these strains and compare them with ten other strains of the same species from different origins.

For *S. cerevisiae* T-19-3FS, PCR of interdelta regions was performed using primers δ1-δ2 and δ12-δ2, while *S. bacillaris* T-19-3MS was analyzed by RAPD-PCR using the primer $(GTG)_3$. Amplification products were separated on 1.5% agarose gels and visualized under UV light after GelRed staining.

The resulting profiles clearly differentiated the autochthonous strains from those isolated from other origins, showing marked intraspecific genetic variability. These results highlight the usefulness of both methodologies for strain-level discrimination in these two species. The identification of a distinct genetic profile is essential for their traceability in winery fermentations. As a future perspective, the fermentative performance of both strains will be evaluated in different grape musts to validate their behavior under diverse technological conditions.

Keywords: Molecular characterization, microbial identity, autochthonous strains.

Undernutrition During Different Stages of Gestation Affects the Proportion of Binucleated Hepatocytes at Puberty in Male Rats.

Núñez Belén[1], Rodríguez Leandro[1], Kelland Nicolás[1], Duque Martín[1], Herrera Emiliano[1], Bielli Alejandro[1] and Genovese Patricia[1]

[1]Unidad Académica de Histología y Embriología, Departamento de Biociencias, Facultad de Veterinaria, Universidad de la República

Abstract: An experimental 2 x 2 design was used in order to generate the following four experimental groups: undernutrition during the first half of gestation (TCC), the second half of gestation (CTC), the entire gestation (TTC), and control animals that were fed *ad libitum* (CCC). At 40 days post-partum, the following variables were measured: Body Weight (BW), Body Length (BL), Liver Weight (LW), proportion of binucleated hepatocytes around the centrilobular veins (%BCL), and around the portal areas (%BEP). BW was negatively affected by undernutrition at any stage of gestation. All variables were expressed as means ± SD. Both the CTC and TTC groups were the most affected as compared to their controls (CCC 207.2±6.8a; CTC 164.7±5.3b; TCC 182.3±8.8c; TTC 152.3±9.6b). No differences were found in BL. Similarly, LW in the CTC and TTC groups was reduced as compared to the CCC and TCC groups (CCC 9.1±0.5a; CTC 6.3±0.5b; TCC 8.2±0.8a; TTC 5.9±0.7b). The %BCL in the CTC, TTC, and TCC groups increased relative to the control group, although the TCC animals were the least affected among the treated groups (CCC 4.7±1.7a; CTC 12.5±3.5b; TCC 10.4±3.3ab; TTC 13.6±3.2b). Finally, undernutrition at any stage of gestation increased %BEP (CCC 4.3±0.8a; CTC 9.5±2.0b; TCC 7.6±1.6ab; TTC 7.8±1.8b). In summary, under our experimental conditions, undernutrition during different stages of gestation affects liver morphology by increasing the proportion of binucleated hepatocytes.

Keywords: Undernutrition, undernutrition, TCC animals.

Impact of Intranasal Melanin-Concentrating Hormone on Anxiety-related Behavior and Hypothalamic-Pituitary-Adrenal Axis Activation in Rats

Perini Valentina[1], Bai Florencia[1], Martínez Gaby[1], Scorza Cecilia[1] and Urbanavicius Jessika[1]

[1]*Departamento de Neurofarmacología Experimental, Instituto de Investigaciones Biológicas Clemente Estable*

Abstract: The hypothalamic neuropeptide Melanin-Concentrating Hormone (MCH) modulates the activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis and anxiety-related behavioral responses, although evidence remains contradictory. We have previously shown that acute intracerebral administration of MCH induces a pro-depressive effect in the rat forced swim test. Recently, we demonstrated that acute and repeated intranasal administration of MCH induced an anhedonic effect (a hallmark symptom of depression) in the rat sucrose preference test. However, the underlying mechanisms remain to be elucidated. Given that stress is a major risk factor for depression and the high comorbidity with anxiety disorders, we hypothesized that the anhedonic effect induced by MCH is accompanied by an anxiogenic response and an increase in corticosterone levels. In this study, adult male rats received acute intranasal administration of MCH (15 or 30 μg/30 μl), and anxiety-related behavior was assessed in the open field and elevated plus maze. Subsequently, plasma corticosterone levels were measured using ELISA. Additionally, to determine whether MCH reaches the brain after intranasal administration, we used MCH conjugated to the fluorophore Rhodamine (MCH-ROD). Results showed no significant effects of MCH on anxiety-related behavior or plasma corticosterone levels. MCH-ROD was found to be widely distributed in the brain, from the prefrontal cortex to brainstem nuclei. Further experiments are ongoing to evaluate the effect of MCH on anxiety-related behavior and HPA axis activation, including corticotropin-releasing factor expression and corticosterone levels, after repeated MCH regimen. These studies will contribute to a better understanding of the mechanisms underlying the pro-depressive action of MCH.

Keywords: Anhedonia, elevated plus maze, corticosterone.

Characterization of an *In Vitro* Model for the Study of the MAO-A-Inflammation Axis in Alzheimer's Disease

Valiente Victoria[1], Porcal Williams[2], Duarte Pablo[1], Savio Eduardo[1], Arredondo Florencia[1] and Dapueto Rosina[1]

[1]*Área I&D Biomédico, Departamento de Radiofarmacia, Centro Uruguayo de Imagenología Molecular, Uruguay;* [2]*Departamento de Química Orgánica, Facultad de Química, Universidad de la República*

Abstract: Alzheimer's Disease (AD) is the leading cause of dementia in older adults. Its development is associated with the accumulation of Amyloid-Beta (Aβ) plaques and neurofibrillary tangles of hyperphosphorylated tau protein, along with inflammatory processes and oxidative stress that damage synapses and promote neurodegeneration.

One of the first changes observed in AD is the exacerbated activation of glial cells, which contributes to chronic inflammation and neuronal deterioration. In this context, the expression of the enzyme Monoamine Oxidase A (MAO-A) is associated with Aβ accumulation and AD. Previous studies suggest that MAO-A inhibitors can decrease neuroinflammation by modulating NF-κB, TNF-α, and the NLRP3 inflammasome, thereby reducing glial activation. We hypothesize that modulating the MAO-A-inflammation axis is a valuable strategy for the treatment of AD. This work aims to characterize an *in vitro* cellular model that recapitulates the interaction of glial cells with neurons in an inflammatory context. We will evaluate the effect of MAO-A inhibition on NLRP3 and NF-κB activation in primary microglia cultures, as well as its effects on astrocytes and primary neurons' viability.

Preliminary results in LPS/ATP-treated cultures show increased expression of NLRP3, TNF-α, and IL-1β, and NF-κB activation, demonstrating that this model is suitable for studying the modulation of neuroinflammation in AD.

Keywords: Alzheimer´s disease, glial cells, MAO-A, inflammation.

Evaluation of Brain Metabolism in Rats After Intravenous Administration of Ibogaine: Functional Study with [^{18}F]Fluorodeoxyglucose

Bentura Manuela[1], Reyes Laura[1], Falasco German[1], Urrutia Leandro[1], Paolino Andrea[1], Gonzalez Bruno[2], Mesa Juan Manuel[2], Arredondo Florencia[1], Carrera Ignacio[2] and Savio Eduardo[1]

[1]Department of Radiopharmacy, Uruguayan Center for Molecular Imaging, Montevideo, Uruguay; [2]Department of Organic Chemistry, Faculty of Chemistry, Universidad de la República, Montevideo, Uruguay

Abstract: Ibogaine, a psychedelic alkaloid extracted from the shrub Tabernanthe iboga, has shown prolonged anti-addictive properties in preclinical models and observational clinical studies. This effect is long-lasting, persisting beyond the pharmacokinetic elimination of ibogaine and its active metabolite (noribogaine) from the body. Although its mechanisms of action have not been fully elucidated, its prolonged effects suggest the induction of neuroplasticity processes.

In this study, changes in brain metabolism induced after intravenous administration of ibogaine in rats were investigated. Male Wistar rats aged 3 months received ibogaine at a dose of 10 mg/kg (n = 8). Using a nanoScan® PET/MRI3T (Mediso), four imaging acquisitions were performed: before treatment, during compound administration, 1 week post-treatment, and 4 weeks post-treatment.

The results showed significant differences in brain metabolism compared to controls, with variations depending on the post-treatment time. In particular, alterations were observed in the motor and entorhinal cortices, cingulate cortex, and the striatum, regions involved in sensory integration, modulation of emotional and cognitive responses, and reward circuits. These findings are consistent with previously described effects and suggest the possible induction of neuroplasticity processes following ibogaine administration.

Keywords: Neuroplasticity, ibogaine, PET, brain metabolism.

Characterization of the Role and Expression of *Higd2a* During Zebrafish Development

Cúparo Mikaela[1,2], Sosa Ileana[1,3], Zolessi Flavio R.[4] and Bedó Gabriela[1]

[1]Sección Genética Evolutiva, Instituto de Biología, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [2]Departamento de Neurofisiología Celular y Molecular, Instituto de Investigaciones Biológicas Clemente Estable, Ministerio de Educación y Cultura, Montevideo, Uruguay; [3]Laboratorio de Genética Molecular Humana, Institut Pasteur de Montevideo, Montevideo, Uruguay; [4]Sección Biología Celular, Instituto de Biología, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay

Abstract: The *hig-1* gene was described for its expression in response to hypoxic conditions. This gene encodes a small protein located in the inner mitochondrial membrane. Later, a family of HIG domain proteins was described, renaming the gene as *higd1a*. Its expression is related to cell protection, differentiation, mitochondrial function, and responses to different types of stress. The zebrafish is an animal model that has a fully sequenced genome, is easy to maintain, and adult mating produces an abundant amount of eggs. Using this model, the laboratory has generated *higd1a knockout* mutant lines through gene editing by the CRISPR/Cas9 system. Recent studies have confirmed the presence of *higd2a* in zebrafish; *higd1a* and *hig2a* are paralogs and are located on different chromosomes. In this work, we characterized for the first time the expression pattern of *higd2a* using RT-qPCR at early stages of development. We extracted RNA from embryos starting at 4 hours post-fertilization. We found expression of this gene at all stages, with a significant increase at 4 days post-fertilization. We also performed a *knockdown* approach by injecting a morpholino against *higd2a*, observing a phenotype that preliminarily corresponds to a delay in normal development. We also developed guide RNAs with the aim of performing genome editing of *higd2a* using the CRISPR/Cas9 system. This strategy allows us to compare both loss-of-function assays and analyze their effect on various aspects of the phenotype.

Keywords: Development, gene editing, zebrafish.

Mechanical Defects During Primary Neurulation Lead to Live Cell Extrusion in the Chick Embryo

Bosch Roascio Santiago A.[1,2], Hernández Julio[1] and Zolessi Flavio R.[2,3]

[1]Sección Biofísica y Biología de Sistemas, Facultad de Ciencias, Universidad de la República; [2]Sección Biología Celular, Facultad de Ciencias, Universidad de la República; [3]Grupo de Biología Celular de Desarrollo Neural, Institut Pasteur de Montevideo

Abstract: During primary neurulation, the amniote embryo's initially flat neuroectoderm folds and fuses, giving shape to the neural tube, the precursor to the central nervous system. Proper development of this process requires contributions at different scales from both the neuroectoderm and adjacent tissues. To study these conditions, we focused on a specific defect induced by PMA treatment in chick embryos: the "expulsion" of neuroepithelial cells towards the apical side in a process known as "cell extrusion". Cell extrusion may be classified either as "apoptotic" or "live" depending on whether the extruded cell is destined for apoptosis. Previous results pointed to this particular case as being of the second kind and related to MARCKS, a protein capable of joining the plasma membrane to the cell cortex, thus suggesting a mainly mechanical underlying cause.

With the aim of understanding the origin of this defect, we took a combined approach, performing pharmacological experiments on chick embryos using PMA and the apoptosis inhibitor QVD-OPh, as well as *in silico* experiments on a mathematical model of epithelial cells.

We determined that the observed extrusion in this system occurs independently of apoptosis, indicating it is an example of live extrusion, possibly caused by mechanical instability in the tissue. Thanks to our model, we qualitatively reproduced the normal pseudostratified morphology of the epithelium and the occurrence of live extrusion, and were able to make quantitative predictions regarding the forces necessary for preventing it during normal development.

Keywords: Neuroepithelium, chick embryo, vertex models, mechanobiology, MARCKS.

Design of Novel Anthelmintic Agents Against *Haemonchus Contortus*: *In Silico* Analysis and Structure-Activity Relationship

Colobbio Maximiliano[1,2], Teixeira Ramiro[3], Duarte Gerardo[3], Nieves Magdalena[2,3], Melian Elisa[3], Munguía Beatríz[3], Ramos Juan Carlos[1] and Manta Eduardo[1,4]

[1]Laboratorio de Química Fina, Instituto Polo Tecnológico de Pando (IPTP) / Departamento de Química Orgánica (DQO), Facultad de Química, Universidad de la República; [2]Graduate Program in Chemistry, Facultad de Química, Universidad de la República, Montevideo, Uruguay. [3]Área Farmacología, Departamento de Ciencias Farmacéuticas (CIENFAR), Facultad de Química, Universidad de la República, Montevideo, Uruguay; [4]Laboratorio de Química Farmacéutica, Departamento de Química Orgánica (DQO), Facultad de Química, Universidad de la República, Montevideo, Uruguay.

Abstract: *Haemonchus contortus* is a highly pathogenic gastrointestinal nematode that significantly affects sheep production, causing substantial economic losses. The extensive use of anthelmintic drugs has led to the prompt emergence of resistance among parasitic populations, highlighting the urgent need for novel compounds with innovative mechanisms of action against these parasites. In this framework, Structure-Activity Relationship (SAR) analysis using *in silico* approaches enables the identification of candidates with enhanced anthelmintic potential. To address this challenge, hybrid compounds were designed and synthesized by integrating the structural features of commercial anthelmintics with novel pharmacophores. The physicochemical properties and drug-likeness parameters were predicted using the SwissADME platform, complementing the biological assays conducted on the adult stage of *H. contortus*. A clear trend emerged between lipophilicity and polarity, suggesting that these are key physicochemical features associated with antiparasitic efficacy. Although Lipinski's rule of five serves as a general guideline for drug discovery, compliance with these criteria is not strictly required to achieve effective intraparasitic concentrations or elicit an anthelmintic response. The combined use of *in silico* analysis

and biological evaluation offers a more comprehensive understanding of the behavior of compounds. These findings support the notion that certain physicochemical profiles are favorable for anthelmintic activity, guiding the rational design of new therapeutic candidates. This multidisciplinary strategy provides a promising avenue for developing effective agents against *H. contortus*.

Keywords: Anthelmintics, drug resistance, molecular hybrids, *Haemonchus contortus*, SAR.

Seasonal Variation of Zooplankton Community Structure Between Two Subtropical Reservoirs of Contrasting Hydraulic Retention Time

Cuevas Julieta[1], Chalar Guillermo[1], De Giacomi Sol[1], González-Piana Mauricio[1] and Carballo Carmela[1]

[1]*Sección Limnología, Instituto de Ecología y Ciencias Ambientales, Facultad de Ciencias, Universidad de la República*

Abstract: Reservoirs significantly alter aquatic ecosystems by modifying flow regimes and creating artificial water bodies. This study examines seasonal variations in zooplankton community structure in two Uruguayan reservoirs in cascade—Bonete and Baygorria—with a focus on the effect of water residence time. Bonete, located upstream, has a long average residence time (~140 days), while Baygorria, downstream, has a short residence time (~ 3 days). Between 2018 and 2023, twenty-four sampling campaigns were conducted in summer, autumn, winter, and spring, recording physical and chemical variables, identifying zooplankton species, and estimating their biomass. Community structure was analyzed using Redundancy Analysis (RDA), and co-occurrence networks were constructed based on presence/absence correlations, incorporating environmental variables as nodes. Results revealed marked seasonal variation in the zooplankton community, with temperature as the main explanatory variable. Water residence time also played a structuring role in both reservoirs. Bonete showed higher zooplankton biomass and was dominated by larger, slow-developing species, while Baygorria was dominated by smaller, fast-reproducing species. Our study highlights the importance of temperature and water residence time in shaping zooplankton community structure in reservoirs. Generating further knowledge about these systems and their organisms is key to developing effective management strategies adapted to their complexities.

Keywords: Neotropical, freshwater, reservoirs, zooplankton community, water residence time.

Proteome of Outer Membrane Vesicles of Uropathogenic *Escherichia Coli* and *Proteus Mirabilis*

González María José[1], Navarro Martínez Nicolás[1], Cruz Jorge Erlen Yizenia[1], Robino Luciana[2], Lima Analía[3], Scavone Paola[1]

[1]*Departamento de Microbiología, Laboratorio de Biofilms Microbianos, Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay;* [2]*Departamento de Bacteriología y Virología Universidad de la República, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay;* [3]*Unidad de Bioquímica y Proteómica Analíticas, Institut Pasteur de Montevideo & Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay*

Abstract: *Escherichia coli* and *Proteus mirabilis* are the main pathogens responsible for urinary tract infections. These Gram-negative bacteria produce Outer Membrane Vesicles (OMVs), which are structures that export biomolecules such as DNA, RNA, lipids, proteins, and toxins. The OMVs are involved in biofilm formation, nutrient acquisition, bacterial communication, immune evasion, and the transport of virulence factors.

This study analyzed the protein composition of OMVs from two uropathogenic strains isolated from clinical samples: *E. coli* U144 and *P. mirabilis* 2921, grown in Luria-Bertani (LB) broth and Artificial Urine (AU). The OMVs were purified and characterized by filtration, ultracentrifugation, and mass spectrometry. In LB, *E. coli* OMVs measured 185.5 nm and in

AU 257.6 nm; in *P. mirabilis*, 267.6 nm and 320.4 nm, respectively. Proteomic analysis identified 282 and 353 proteins in OMVs from *E. coli* and *P. mirabilis* grown in LB, and 215 and 103 proteins when grown in AU, respectively, most of which were related to the cell envelope, motility, and adhesion.

The protein composition of the OMVs varies depending on the culture medium, with notable enrichment of proteins involved in zinc and iron uptake in AU, suggesting that the OMVs adapt to different environmental conditions. These differences may influence the pathogenicity and infection capacity of these bacteria, providing key insights for the development of therapeutic strategies.

Keywords: Outer membrane vesicles, uropathogens, UTI.

Morphological Characterization of *Arachis Villosa* Benth., A Wild Relative of Peanut *A. Hypogaea* L.

Franco Camila, Da Rosa Natalia, Bonfiglio Maria De Los Ángeles, Tadich Ian, Naya Ignacio, Da Luz Claudia, Nuñez Nicolás, Vidal Rafael and Vaio Magdalena

Departamento de Biología Vegetal, Facultad de Agronomía, Universidad de la República

Abstract: Uruguay is part of the center of diversity of cultivated peanut (*Arachis hypogaea*) due to the diversity of landraces and because it harbors the main distribution area of *Arachis villosa,* a wild relative. *A. villosa* shares the A genome with peanut and exhibits traits of interest, such as disease resistance and nutritional quality. The aim of this study was to evaluate and characterize the morphological diversity of a collection of *A. villosa* and identify priority areas for its conservation. For this, 16 populations collected from different regions of Uruguay were analyzed, ranging from the northern end of the Uruguay River coast (Bella Unión) to the coastal regions of the Río de la Plata (San José). For each population, three seedlings from the same mother plant were grown. Seedlings were transferred to tubes and kept in a greenhouse for 20 days. They were then transplanted into 10-liter pots filled with a sand and soil mix. The experimental design was a completely randomized block design with three replicates. Five descriptors were used for phenotypic characterization: leaflet area, length, and width, as well as plant height and width. In all cases, measurements were taken on the right apical leaflet following the first flower, using a scanner and the Plimanshiny package. Preliminary results reveal phenotypic variability among populations; all descriptors, except leaflet length, showed significant differences. This variability highlights the importance of conserving *Arachis villosa* diversity. The information generated will contribute to identifying key areas for *A. villosa* conservation and will support future research.

Keywords: *Arachis villosa*, diversity, conservation, genetic resources.

MV14: A New Therapeutic Approach for Bladder Cancer

López Miriam[1,6], Varela, María[6], Machado Tesa[1], Ingold Mariana[6], Perelmuter Karen[2], Bollati-Fogolín Mariela[2], Fernández Marcelo[3], Fontes Florencia[3], Breijo Martin[3], Reyes Laura[4], Bentura Manuela[4], Savio Eduardo[4], Ramírez Juan[5], Yozzi Victoria[5], Romero Camila[5], Verdes José Manuel[5], López Gloria V.[6,7] and Hernández Paola[1]

[1]Departamento de Genética, Instituto de Investigaciones Biológicas Clemente Estable, MEC, Montevideo, CP. 11600, Uruguay; [2]Cell Biology Unit, Institut Pateur Montevideo, Montevideo, CP. 11400, Uruguay; [3]Unidad de Reactivos y Biomodelos de Experimentación (URBE), Facultad de Medicina, Universidad de la República, Montevideo, CP. 11800, Uruguay; [4]Centro Uruguayo de Imagenología Molecular (CUDIM), Montevideo, CP. 11600, Uruguay; [5]Unidad de Patología, Departamento de Patobiología, Facultad de Veterinaria, Universidad de la República, Montevideo, CP. 13000, Uruguay; [6]Laboratorio de Síntesis Orgánica y Desarrollo de Fármacos, Institut Pasteur Montevideo, Montevideo, CP. 11400, Uruguay; [7]Departamento de Química Orgánica, Facultad de Química, Universidad de la República, Montevideo, CP. 11800, Uruguay

Abstract: Bladder Cancer (BC) is a common neoplasm characterized by high recurrence rates and resistance to current treatments, highlighting the need to develop new therapeutic strategies. Nitric oxide-releasing agents have emerged as one of the most promising strategies for the treatment of BC. In this context, our research group identified the compound **MV14** from a library of nitric oxide-releasing molecules as a potential therapeutic agent, due to its high antiproliferative activity and selectivity toward bladder cancer-derived cells. In this study, we explored the potential mechanism of action of **MV14** and found that it modulates the levels of the transcription factor NF-κB, leading to a reduction in the expression of survivin, a key protein involved in BC development and progression. To assess its therapeutic potential *in vivo*, we developed an orthotopic murine model of BBN-induced BC and evaluated the antitumor activity of **MV14** *via* sequential intravesical instillations. The development of BC was monitored using Magnetic Resonance Imaging (MRI), and disease progression was analyzed through histopathological studies. The results revealed a decrease in urothelial disruption, indicating that **MV14** exerts an antitumor effect in this model of bladder cancer. Taken together, these findings support the potential of nitric oxide-releasing compounds as promising agents for the development of a new therapeutic strategy targeting the underlying mechanisms of BC development.

Keywords: Bladder cancer, nitric oxide donor, antitumor.

Antimicrobial Peptides in Peanut: A Comparative Analysis of *Arachis Hypogaea* Transcriptomes and Its Progenitors

Bonfiglio María de los Ángeles[1], Rodríguez-Decuadro Susana[2] and Vaio Magdalena[1]

[1]Laboratory of Plant Evolution and Domestication, Department of Plant Biology, Faculty of Agronomy, Universidad de la República; [2]Laboratory of Biotechnology, Department of Plant Biology, Faculty of Agronomy, Universidad de la República

Abstract: Peanut (*Arachis hypogaea*) is a tetraploid species that originated from the hybridization between *Arachis duranensis* and *Arachis ipaensis*. In this study, we conducted a comparative analysis of Antimicrobial Peptides (AMPs) present in the transcriptomes of *Arachis hypogaea* and its diploid progenitors. AMPs are key components of plant innate immunity and play a crucial role in peanuts, not only due to their antimicrobial properties but also because of their potential to trigger allergic reactions in humans upon consumption. Candidate AMP-encoding sequences were identified from *de novo*-assembled leaf and root transcriptomes (under control and drought conditions), generated for this study using raw sequencing data available in public databases. BLAST searches were performed using known AMP sequences as queries, and hits with an E-value below 10^{-3} and the characteristic cysteine motifs of each AMP family were retained. Genes from four AMP families, defensins, snakins, hevein-like peptides, and thionins, were analyzed. Peptidic variants were identified that were either exclusive to the diploid species, shared between the tetraploid and one or both diploids, or present in one diploid and the tetraploid but absent in the other diploid. These findings suggest that, during the evolutionary process of *A. hypogaea*, certain variants (orthologous genes) present in the diploid ancestors may have been lost or are not expressed in the analyzed tissues.

Cofilin-1 Modulation Restores High Levels of Plasticity in the Adult Visual Cortex

Hayek Emilia[1], Dapueto Agustina[2], Pannunzio Bruno[3], Acuña Alejo[1] and Rossi Francesco M[1]

[1]Laboratorio de Neurociencias "Unidad de Neuroplasticidad", Facultad de Ciencias, Universidad de la República; [2]Laboratorio de Mecanismos de Neurodegeneración y Neuroprotección, IIBCE; [3]Departamento de Histología y Embriología, Facultad de Medicina, Universidad de la República / Laboratorio de Neuroinflamación y Terapia Génica del Institut Pasteur de Montevideo

Abstract: Cofilin-1 is an actin-depolymerizing protein that has recently been identified as a potential regulator of brain plasticity. Here, we investigated the effects of modulating its activity on structural and functional plasticity processes in the mouse visual cortex.

Functional plasticity was assessed by measuring visual acuity, while structural plasticity was evaluated by analyzing dendritic spine density. Cofilin-1 activity was modulated in adult mice (P58) by administering either the phosphocofilin peptide (PCOF) or a control peptide (TAT). Monocular Deprivation (MD) was performed one day after peptide treatment by suturing the right eyelid for three days (P59–P62).

We found that MD reduced visual acuity in the deprived eye compared to the control eye by approximately 31% in adult mice treated with the PCOF peptide (control eye: 0.38 ± 0.01 vs. deprived eye: 0.27 ± 0.01, n = 8 mice, p < 0.05). Moreover, MD decreased dendritic spine density in the contralateral cortex compared to the ipsilateral side in PCOF-treated mice by about 40% (contralateral: 49.6 ± 3.5, n = 26 neurons vs. ipsilateral: 83.9 ± 8.7, n = 20 neurons, n = 7 mice, p < 0.05).

These results demonstrate that cofilin-1 plays a key role in experience-dependent plasticity in the mouse visual cortex, and that its modulation promotes the restoration of high levels of structural and functional plasticity in adulthood.

Keywords: Plasticity, phosphocofilin, cofilin-1, visual cortex.

Effects of Chronic Administration of Melanin-concentrating Hormone in an Experimental Model of Sporadic Alzheimer's Disease

Rodríguez Canclini Valentina[1], Ruiz-Viroga Vicente[1], Niño Sofía[1], Galeano Pablo[2] and Lagos Patricia[1]

[1]Unidad Académica de Fisiología, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay. [2]Laboratory of Brain Aging and Neurodegeneration, Fundación Instituto Leloir (IIBBA-CONICET), Buenos Aires, Argentina

Abstract: Melanin-Concentrating Hormone (MCH) is a neuropeptide produced by the hypothalamus and is involved in the regulation of energy metabolism and memory. MCHergic neurons project to several regions of the nervous system, including the hippocampus, which is a vital structure for memory processing and is one of the regions most severely affected in Alzheimer's Disease (AD). The aim of this study was to evaluate the effects of chronic MCH administration on memory processes and body weight in an experimental model of sporadic AD induced by intracerebroventricular (i.c.v.) administration of Streptozotocin (STZ). Male Wistar rats were divided into two groups: G1 and G2. The G1 received either chronic i.c.v. MCH administration via osmotic minipumps (4 μg/day) for 14 days or its vehicle (NaCl 0.9%). The G2 received chronic MCH administration with an i.c.v. pre-treatment with either STZ or its vehicle (artificial cerebrospinal fluid, aCSF). The Novel Object Recognition Test (NORT) was performed on days 14 and 30 post-minipump implantation, and body weight was measured throughout the experimental period. The results showed that chronic MCH administration impaired memory on day 14, an effect that persisted until day 30. Notably, STZ did not produce memory deficits at either time point and appeared to block the negative effect of MCH on memory. Chronic MCH administration led to a significant increase in body weight; this effect was paradoxically reversed by STZ pre-treatment. These findings suggest that MCH negatively impacts memory performance and that this effect may be modulated by the presence of STZ.

Keywords: Memory, Alzheimer's disease, melanin-concentrating hormone, Streptozotocin, minipumps.

Palladium Complexes with Thiosemicarbazones as Inhibitors of the Main Protease (M-pro) of SARS-CoV-2

Arandia Inés[1], Rostán Santiago[1], Fernández Mercedes[1], Clavijo Alexia[2], Bastidas Jonathan[3], Comini Marcelo[3], Mahler Graciela[2] and Otero Lucía[1]

[1]Area of Inorganic Chemistry, Estrella Campos Department, Faculty of Chemistry, Universidad de la República; [2]Pharmaceutical Chemistry Laboratory, Department of Organic Chemistry, Faculty of Chemistry, Universidad de la República; [3]Trypanosome Redox Biology Laboratory, Pasteur Institute of Montevideo

Abstract: The main protease (M-Pro) of SARS-CoV-2 is a cysteine protease widely accepted as one of the main molecular targets for the rational design of potential antiviral drugs. On the other hand, different derivatives of thiosemicarbazones and their metal complexes have been described as inhibitors of cruzipain, the main cysteine protease of the parasite *Trypanosoma cruzi*. Based on the above, in this work, we describe the preparation of two thiosemicarbazones derived from 5-bromo-salicyl-aldehyde (**L1** and **L2**, Fig. **1**) and their Pd(II) complexes of formulas [Pd(X)(**L1-L2)**] (X = Cl, PPh_3) and [PdCl(PPh_3)(**L1)**]. The inclusion of the different co-ligands (X) aims to modulate the stability and lipophilicity of the complexes, as well as the potential inhibition mechanism of M-pro. The results show that free thiosemicarbazones **L1** and **L2** are good inhibitors of M-pro (IC_{50} = 10 and 19 µM, respectively). For the complexes [Pd(PPh_3)(**L1-L2)**], a loss of inhibitory activity was observed, while the complexes [PdCl(**L1-L2)**] present an activity of the same order as the free ligands (IC_{50} = 8 and 16 µM for **L1** and **L2,** respectively). These results could be explained by the presence of a labile ligand, such as chloride, which could give rise to the covalent interaction of the metal with the cysteine present in the active site of M-pro. The complex [PdCl(PPh_3)(**L1)**] is transformed over time into [Pd(PPh_3)(**L1)**] in DMSO solution so it did not present inhibitory activity. Antiviral activity studies are underway for the most active compounds.

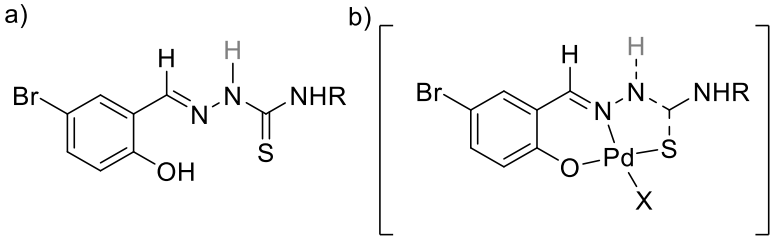


Fig. (1). (**a**) Thiosemicarbazones derived from 5-bromo-salicyl-aldehyde R = methyl (**L1**), R = ethyl (**L2**), (**b**) Palladium complexes evaluated [Pd(X)(**L1 - L2**)], X = Cl or PPh_3.

Keywords: M-pro inhibitors, thiosemicarbazones, palladium complexes.

Development of an Automated System for Plant Phenotyping Using Thermographic and Visible Spectrum Imaging

Casaretto Esteban[1], Bentancor Marcel[2], Muñoz Mercedes[3], Dagnino Esteban[2], Borsani Omar[1], Quero Gastón[1], Stewart Silvina[4], Ramírez Ignacio[5]

[1]Departamento de Biología Vegetal, Facultad de Agronomía, Universidad de la República; [2]Laboratorio de Biología Molecular Vegetal, Instituto de Química Biológica, Facultad de Ciencias, Universidad de la República; [3]Instituto de Computación, Facultad de Ingeniería, Universidad de la República; [4]INIA La Estanzuela; [5]Grupo de Tratamiento de Imágenes y del Núcleo de Teoría de la Información, Facultad de Ingeniería, Universidad de la República

Abstract: Thermal variations in a plant are mainly the result of changes in stomatal aperture. Stomata regulate most of the gas and water exchange between the plant and its environment. In response to water deficit, plants close their stomata to reduce water loss through transpiration. This decrease in transpiration leads to an increase in plant temperature, which can therefore be used as an indicator of stomatal aperture. Frequently, plant varieties that are more tolerant or resistant to a stress

factor exhibit a faster or earlier response compared to susceptible varieties. For this reason, it is of interest to analyze the plant phenotype using thermographic imaging, complemented by images captured in the visible spectrum. Based on the hypothesis that it would be possible to develop a low-cost and low-maintenance open-source phenotyping platform, a robotic system was successfully built. This system is capable of continuously acquiring thermal and visible-spectrum images of plants grown under controlled conditions. The platform uses a two-dimensional Cartesian motion system powered by stepper motors and controlled by a Raspberry Pi board. It is equipped with a 5MP color camera for image capture and a Lepton 3.5 module for thermal imaging. This platform will be used for phenotypic characterization of plants from conventional breeding programs or genetically modified experimental varieties developed in our laboratories.

Keywords: Thermal variations, phenotyping platform, raspberry Pi board.

Endophytic Fungi from Passiflora Caerulea and Ephedra Tweediana and Their Bioactive Potential

Riera Jazmín[1], Alonso Raquel[1] and Tiscornia Susana[1]

[1]*Sección Micología, Facultad de Ciencias, Universidad de la República*

Abstract: Endophytic fungi are microorganisms that inhabit the internal tissues of plants without causing visible disease symptoms. They are known for their ability to produce metabolites with potential antimicrobial, antioxidant, and phytotoxic activities. This study tested the hypothesis that *Passiflora caerulea* and *Ephedra tweediana*, two native plants of Uruguay, serve as reservoirs of diverse endophytic fungi capable of producing bioactive metabolites. The aim of this work was to identify endophytic fungi associated with *P. caerulea* and *E. tweediana* and to evaluate their ability to produce bioactive compounds. Samples of leaves, stems, and roots from healthy plants were collected. Endophytic fungi were isolated through cultivation techniques and identified based on morphological features and molecular analyses. Secondary metabolites were extracted, and their antimicrobial activity was assessed against phytopathogens such as *Erwinia sp., Colletotrichum sp., and Fusarium sp.* Additionally, the phytotoxicity of the extracts was evaluated on tobacco leaves. Fungi belonging to several genera were identified, including *Alternaria, Colletotrichum, and Fusarium*, some of which produced metabolites with antimicrobial activity against the tested pathogens. These findings underscore the relevance of exploring endophytic fungi from native plants as promising sources of new bioactive compounds with potential applications in biocontrol and the development of novel antifungal and antibacterial agents.

Keywords: Endophytic fungi, microorganisms, *P. caerulea*.

Characterization of Sleep, Cognition, and Functionality of Stroke Patients

Santoro Mateo[1], Roca Andrés[1], Pérez Camila[1], Rodríguez María José[1], Silveira Alicia[2], Abanonii Sttefano[2], Rivero Sebastián[2], Mariani Francesca[2], Estevan Ignacio[1] and Madriaga Cecilia[1]

[1]*Neuropsychology and Neurobiology, Institute of Foundations and Methods in Psychology, Universidad de la República;*
[2]*Neuropsychology Polyclinic, Hospital de Clínicas Dr. Manuel Quintela, Universidad de la República*

Abstract: ***Introduction*:** Stroke is the second leading cause of death worldwide and the third leading cause of disability. Evidence suggests that post-stroke cognitive impairments are common and that up to 70% of patients experience sleep disturbances. These cognitive and sleep-related alterations impact daily functioning, contribute to diminished quality of life, and increase disability burden.

***Method*:** This is a cross-sectional, non-experimental study aimed at characterizing aspects of cognition, sleep, and functionality in patients who have suffered a stroke and were evaluated at the Neuropsychology Polyclinic of the Hospital de Clínicas Dr. Manuel Quintela. The assessment included a comprehensive neuropsychological evaluation covering various cognitive

domains (Executive Functions, Attention, Memory, Language, Gnosias, Praxias, and Conceptual Functions), the Pittsburgh Sleep Quality Index, the WHODAS 2.0 disability severity scale, and the Beck Depression Inventory.

***Results*:** We present the characterization of six patients who experienced an ischemic stroke and attended the Clinic in 2024. The results indicate that the majority of patients (5 out of 6) exhibited sleep quality impairments. Moderate levels of disability and the presence of depressive symptoms were also reported. At the cognitive level, the most prominent difficulties were observed in the domains of attention and executive functioning.

***Discussion*:** Characterizing these aspects is essential for guiding comprehensive interventions that support improved recovery and adaptation in this population.

Keywords: Stroke, neuropsychological profile, sleep quality, disability.

Cognitive Deficits in an Experimental Model of Alzheimer's Disease in Female Rats: Association with Depressive-like Behaviors and Inflammatory Cytokines

Mechelk Lucía[1], Urbanavicius Jessika[2], Daghero Hellen[3], Bollati-Fogolin Mariela[3], Galeano Pablo[4], Lagos Patricia[1]

[1]Unidad Académica de Fisiología, Laboratorio de neurotransmisión peptídica, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay; [2]Departamento de Neurofarmacología Experimental, Instituto de Investigaciones Biológicas Clemente Estable. Montevideo, Uruguay; [3]Unidad de Biología Celular, Institut Pasteur de Montevideo; [4]Laboratory of Brain Aging and Neurodegeneration, Fundación Instituto Leloir (IIBBA-CONICET), Buenos Aires, Argentina.

Abstract: Alzheimer's Disease (AD) is a progressive neurodegenerative disorder characterized by memory loss that occurs more frequently in women. AD is highly comorbid with depressive symptoms, which are more prevalent and severe in women. When searching for shared underlying mechanisms, altered levels of inflammatory cytokines may be involved. However, studies in females are limited. We hypothesize that cognitive impairments emerge earlier in female rats than in males and co-occur with depressive-like behaviors, and that increased levels of inflammatory cytokines at systemic and central levels underlie these behavioral outcomes. We used a sporadic AD model by the intracerebroventricular administration of Streptozotocin (STZ) and assessed both the early and late stages (30 and 120 days post-STZ). Adult female Sprague-Dawley rats received either STZ or Artificial Cerebrospinal Fluid (aCSF), and their behavioral performance was evaluated using the Novel Object Recognition Test (NOR) and the Forced Swimming Test (FST). We measured cytokine levels in plasma, CSF, and hippocampus using Multiplex Cytokine Assay and flow cytometry. A significant reduction in time spent exploring the novel object was observed in STZ-treated rats at both the early and late stages, indicating cognitive impairment. In contrast, increased immobility time in the FST, indicative of a depressive-like phenotype, was only evident in the late stage. Notably, pro-inflammatory cytokine levels were significantly elevated in the CSF of STZ-treated rats at the late stage, with no changes observed in plasma or hippocampal samples. These results suggest that increased central inflammation may underlie the high comorbidity between AD and depression in female rats.

Keywords: Alzheimer's disease, inflammatory cytokines, depression.

Search for Endogenous Promoter Sequences in a Bacterial Strain of Antarctic Origin Using Function-Driven Metagenomics

Ordoqui Valentín[1], Platero Raúl[1] and Amarelle Vanesa[1]

[1]*Department of Biochemistry and Microbial Genomics, Instituto de Investigaciones Biológicas Clemente Estable*

Abstract: In our department, we are making new contributions to the field of synthetic biology. In this context, we have advanced in the characterization of the Antarctic strain *Pseudomonas sp.* UYIF39 as a potential biological chassis. We currently have a functional "molecular toolbox" for this microorganism. We also have the sequenced and closed genome of the strain, and we have made progress in elucidating the functions of the annotated genes, identifying essential genes and genes required under specific conditions by means of TnSeq. In this work, we used a "promoter trap" approach and a synthetic circuit harboring GFP as a reporter to search for promoter sequences functional in strain UYIF39. Using genomic DNA as input (fragments of 1-10 Kbp), we generated a library of approximately 800 clones. These clones will be assayed in different conditions to identify inducible and/or constitutive promoter sequences. We will evaluate the effect of different temperatures (5°C, 15°C, 25°C, 30°C), presence of metals (cobalt, manganese, iron, nickel, copper, zinc, magnesium, cadmium), carbon sources (glucose, mannitol, arabinose, galactose, xylose), and other molecules of interest (salicylic acid, 3-methylbenzoate, IPTG, microcystins) on the expression of the reporter gene. In this way, we will not only advance our knowledge of this Antarctic chassis, but we will also generate transcriptional biosensors in response to some of the compounds or conditions evaluated.

Keywords: Synthetic biology, functional metagenomics, promoter, biosensor.

Light-induced *Arc* Expression as a Tool to Study Ocular Dominance Plasticity in the Visual Cortex

Calero Eugenia[1], Acuña Alejo[1] and Rossi Francesco Mattia[1]

[1]*Laboratorio de Neurociencias "Unidad de Neuroplasticidad", Facultad de Ciencias, Universidad de la República*

Abstract: The Visual Cortex (VC) is a classical model for studying experience-dependent plasticity. During the critical period of plasticity, Monocular Deprivation (MD) induces dramatic changes in the VC, while in adults, it has little or no effect. This adaptive capacity to the environment is known as Ocular Dominance Plasticity (ODP), and it is traditionally studied using electrophysiology or *in vivo* imaging.

In our laboratory, we are optimizing an alternative methodology that involves analyzing light-induced mRNA expression of the Arc gene via *in situ* hybridization. It has been shown that the medio-lateral extension of Arc expression in the VC ipsilateral to the stimulated eye is an indicator of plasticity.

We generated a probe for the Arc gene through *in vitro* transcription using digoxigenin-labeled UTP and detected it with an anti-DIG antibody by fluorescence or luminometry.

Initially, we observed a clear signal in layers 2–4 and 6 of the ipsilateral VC in light-stimulated juvenile animals, but not in unstimulated control animals. We then assessed the utility of this technique to detect ODP. In juvenile animals subjected to 3 days of MD, we observed a greater medio-lateral extension of the Arc signal compared to control animals (no MD).

We plan to apply this methodology in projects evaluating whether treatments such as ibogaine or cofilin-1 modulators can restore ODP in the VC of adult animals.

Keywords: Visual cortex, monocular deprivation, ocular dominance plasticity.

Characterization of Porcine Circovirus Type 4 Viral Pseudoparticles

Paradeda Gabriela[1], Fadel Florencia[1], Olivero-Deibe Natalia[2], Pantano Sergio[3] and Ortega Claudia[1]

[1]Programa de Tecnología Molecular, Celular y Animal, Institut Pasteur de Montevideo; [2]Laboratorio de Inmunovirología, Institut Pasteur de Montevideo; [3]Laboratorio de Simulaciones Biomoleculares, Institut Pasteur de Montevideo

Abstract: ***Introduction*:** Members of the Circoviridae family are the smallest viruses capable of infecting mammalian cells. The capsid protein is responsible for the immune response. Within the Circovirus genus, PCV2 is the causative agent of several diseases in pigs. Recently, a new viral genotype, PCV4, has been identified. It is more closely related to circoviruses that infect other species. Its role in disease development is unclear, but it raises great concern due to its ability to infect livestock. Viral-Like Particles (VLPs) present a promising alternative to traditional vaccines.

***Hypothesis*:** Development of a serological diagnostic test for PCV4 through the production of PCV4 VLPs and study of these as potential vaccine candidates.

***Materials and Methods*:** The Cap4 protein was cloned and expressed in the EXPI293F suspension cell line. VLPs were subsequently purified using discontinuous CsCl gradient ultracentrifugation and biophysical and biochemical characterization.

***Main Results*:** PCV4 VLPs were successfully expressed and purified, exhibiting the expected size and morphology, and their structure was confirmed by DLS.

***Discussion and Conclusions*:** Different VLPs are expected to be obtained and characterized in terms of composition, purity, size, yield, and stability. The production of antibodies specific to PCV4 VLPs will subsequently be evaluated by Western blot, ELISA, and cytometry.

Keywords: Circoviridae family, Viral-Like Particlesm, PCV4.

Modulation of CpG Frequency in the Mayaro Virus Genome Through Genetic Engineering for Potential Use as a Live Attenuated Vaccine

Ferreiro Irene[1,2], Fajardo Álvaro[1,2,3], Paz Mercedes[1,2,4], Simón Diego[1,2], Moreno Pilar[1,2,4] and Moratorio Gonzalo[1,2,4]

[1]Laboratorio de Virología Molecular, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [2]Laboratorio de Evolución Experimental de Virus, Institut Pasteur de Montevideo, Montevideo, Uruguay; [3]Department of Microbiology, NYU Langone Health, New York, NY, USA; [4]Centro de Innovación en Vigilancia Epidemiológica, Institut Pasteur de Montevideo, Montevideo, Uruguay

Abstract: Mayaro Virus (MAYV) is an *Alphavirus* responsible for dengue-like symptoms and prolonged joint pain, transmitted in urban areas by the widespread Aedes aegypti mosquito in South America. Since MAYV has been detected in multiple Latin American countries, the PAHO issued an epidemiological alert in 2019, which received limited attention due to the onset of the COVID-19 pandemic. Developing effective strategies for future outbreak preparedness is therefore essential.

Unlike arboviruses, mosquito-specific viruses exhibit high frequencies of CpG dinucleotides in their genomes. Studies suggest that boosting CpG frequencies can enhance immune activation in vertebrates, potentially explaining the low CpG presence in RNA viruses that infect vertebrates exclusively.

In this study, we used synthetic biology to increase CpG dinucleotide frequency in the MAYV genome through synonymous recoding. We generated three MAYV mutants with incremental CpG frequencies, each modified in different genome regions: (1) the entire coding sequence, (2) exclusively the non-structural region, and (3) only the structural region.

Our findings revealed that synonymous mutations led to an attenuated MAYV phenotype in immunocompetent mammalian cells, while no such effect was observed in mosquito cells. In addition, the mutants showed similar ratios of viable particles to viral genomes (specific infectivity) to the wild-type virus, proving that the added mutations do not cause replication

artifacts. Genetic stability tests through whole-genome sequencing after 10 serial passages in both mammalian and mosquito cells confirmed the persistence of the introduced modifications.

Importantly, there was significant attenuation of the MAYV mutants in several target organs in Balb/cJ mice, whereas blood-feeding infection in Aedes aegypti mosquitoes showed no differences between WT and our mutants. Further *in vivo* studies, including neutralizing antibody generation and challenges with pre-immunised and susceptible mice, are underway.

Our results suggest that the CpG-enriched MAYV mutants generated in this study are promising candidates for live attenuated vaccines. Above all, this CpG modulation strategy could be adapted to other regionally relevant arboviruses, providing a novel approach to vaccine development against emerging viral threats.

Keywords: Arbovirus, attenuation, Mayaro virus, genetic engineering.

Characterization of the Melanin-Concentrating Hormone (MCH) System and *Akt* Pathway Mediated by Insulin Receptor Substrate-1 (IRS-1) in a Rat Model of Sporadic Alzheimer's Disease (sAD)

Niño-Rivero Sofia[1], de Ceglia Marialuisa[2], Gavito Ana[2], Rodríguez de Fonseca Fernando[2], Urbanavicius Jessika[3], and Lagos Patricia[1]

[1]Unidad Académica de Fisiología, Facultad de Medicina. Universidad de la República; [2]UGC Salud Mental, Instituto de Investigación Biomédica de Málaga, Hospital Regional Universitario de Málaga, Universidad de Málaga, Málaga, España; [3]Departamento de Neurofarmacología Experimental, Instituto de Investigaciones Biológicas Clemente Estable, Ministerio de Educación y Cultura, Montevideo, Uruguay

Abstract: Brain insulin resistance causes cellular and cognitive alterations in patients with sAD. The MCH peptidergic system is implicated in memory processes, but its role in sAD remains unexplored. We characterize the modifications in the MCHergic system and its potential interaction with the Akt–IRS-1 signaling pathway in a sAD model induced by intracerebroventricular (i.c.v.) administration of streptozotocin (STZ; an insulin signaling disruptor). RT-qPCR, Western blot, and immunohistochemistry analyses were performed on hypothalamic and hippocampal samples at 15, 30, 60, 90, and 120 days post-STZ or Artificial Cerebrospinal Fluid (aCSF) administration. We assessed preproMCH and receptor MCHR-1 mRNA levels, as well as MCHR-1 protein levels, MCHergic neurons and fibers, and components of the Akt–IRS-1 pathway. We found that preproMCH mRNA levels increased in both the hypothalamus and the hippocampus in STZ15 versus aCSF15, while MCHR-1 mRNA and protein levels increased in STZ30 versus aCSF30. The number of MCHergic neurons increased in STZ90 and STZ120 versus STZ60, and MCHR-1(+) signals increased in STZ90 versus STZ30 and STZ60. Fiber density decreased in STZ30 versus aCSF30 in both the *stratum oriens* and *radiatum* from the hippocampus. Phospho-IRS-1 (Ser612) levels were elevated in STZ60 versus aCSF60, STZ30, and STZ120. Total Akt levels increased in STZ15 versus STZ90, while phospho-Akt (Ser473) levels increased in STZ60 versus STZ30. GSK3β levels were higher in STZ15 versus STZ90, and phospho-Tau (Ser202/Thr205) levels decreased in STZ120 versus STZ15 and STZ90.

These findings suggest that various components of the MCHergic system and the Akt–IRS-1 pathway undergo transient alterations in this sAD model.

Keywords: Alzheimer's, STZ, MCH, MCHR-1, Akt–IRS-1 pathway.

Synthesis and Characterization of Ga(III) Complexes with Antitumor Activity

Fernández Carlos Y. [1], Rosas Matías[1], Álvarez Belén[1], Collazo Victoria[1] and Facchin Gianella[1]

[1]*Área de Química Inorgánica, Departamento Estrella Campos, Facultad de Química, Universidad de la República*

Abstract: Ga(III)-containing coordination compounds show potential for the development of antitumor agents. $GaNO_3$ has been approved for the treatment of cancer-related hypercalcemia. The coordination of Ga with organic ligands is a promising strategy for developing new agents with higher bioavailability, improved cellular membrane penetration, and fewer side effects compared to simple Ga salts.

In this context, work has focused on the design and characterization of Ga(III) coordination complexes with potential antitumor applications, aiming to include a variety of donor atoms and ligands, both with and without intrinsic biological activity. Several families of complexes have been studied to date. These include homoleptic complexes with diimines such as 1,10-phenanthroline, neocuproine, 4-methyl-phenanthroline, and tetramethyl-phenanthroline, with the general formula $[Ga(diimine)(NO_3)_2]PF_6$.

Homoleptic complexes of the type $[Ga(dipeptide)_3]$ were also obtained, using dipeptides such as Ala-Gly, Ala-Phe, Gly-Val, and Gly-Phe. In addition, complexes with Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) of the general formula $[Ga(NSAID)_3]$ were prepared, using mefenamic acid and flufenamic acid as ligands.

Moreover, heteroleptic complexes of the type $[Ga(diimine)(cbdc)]PF_6$ were developed, incorporating cyclobutane-1,1-dicarboxylic acid (cbdc) as an additional ligand, aiming to improve the compounds' solution stability.

Structural characterization was carried out by IR spectroscopy, ^1H NMR, and elemental analysis. Cytotoxic activity evaluation in MCF-7 cells (breast adenocarcinoma) showed that several of these compounds exhibit greater activity than cisplatin, which was used as a reference drug.

Keywords: Gallium, coordination compounds, cytotoxic activity.

Modulation of Host Cell Membrane Biophysics Dynamics by Neospora Caninum: A Study Using Laurdan Fluorescence with Hyperspectral Imaging and Phasor Analysis

Díaz Marcela[1], Cabrera Andrés[2,3], Robello Carlos[2,4] and Malacrida Leonel[1,5]

[1]*Unidad Bioimagenología Avanzada, Institut Pasteur de Montevideo y Universidad de la República. Montevideo / Uruguay;* [2]*Laboratorio de Interacciones Hospedero-Patógeno, Institut Pasteur de Montevideo. Montevideo/ Uruguay;* [3]*Unidad Académica de Parasitología y Micología, Facultad de Medicina, Universidad de la República. Montevideo / Uruguay;* [4]*Unidad Académica de Bioquímica, Facultad de Medicina, Universidad de la República. Montevideo / Uruguay;* [5]*Unidad Académica de Fisiopatología, Hospital de Clínicas, Facultad de Medicina, Universidad de la República. Montevideo/Uruguay*

Abstract: *Neospora caninum* is the causative agent of bovine neosporosis, a disease leading to significant economic losses in livestock production. As an obligatory intracellular parasite, *N. caninum* relies on the host cell for survival and replication. A crucial step in its life cycle is the formation of the Parasitophorous Vacuole (PV), where tachyzoites proliferate while evading the host immune system. The PV facilitates host cell manipulation and lipid recruitment, though the impact of this lipid redistribution on host membranes remains unclear. Cholesterol plays a key role in membrane structure, making its metabolism a potential target for the treatment of neosporosis. *N. caninum* hijacks fatty acids and cholesterol into the PV, but the broader effects on membrane composition and dynamics are not well understood. LAURDAN, a polarity-sensitive fluorescent probe, is widely used to assess membrane fluidity based on cholesterol content. Using hyperspectral imaging and spectral phasor analysis, we examined membrane dynamics in *N. caninum*-infected Vero cells. The results revealed a significant decrease in plasma and internal membrane order upon infection, indicating a redistribution of cholesterol from

the plasma membrane to PVs. Uninfected cells treated with Methyl-β-Cyclodextrin (MBCD) increased membrane fluidity, mimicking cholesterol depletion upon NC infection. Conversely, replenishment of cholesterol-loaded MBCD in infected cells was observed to partially restore membrane order, thereby indicating an enrichment of cholesterol. These findings provide novel insights into how *N. caninum* manipulates host cell membrane dynamics through lipid redistribution, potentially supporting its intracellular survival.

Keywords: *Neospora caninum*, hyperspectral imaging, phasor plots.

Determination of the Region of the Nuclear Receptor Eg2DBDα.1 Required for Homodimerization

Mozzo Bruno[1], Blanco Valentina[1,2] and Alvite Gabriela[1]

[1]Laboratorio de Bioquímica, Facultad de Ciencias, Universidad de la República, Uruguay; [2]Laboratorio de Genómica Funcional, Institut Pasteur de Montevideo, Uruguay

Abstract: The larval form of the multispecies complex *Echinococcus granulosus sensu lato* (parasitic platyhelminths, Cestoda) causes cystic echinococcosis, a cosmopolitan zoonosis that constitutes a public health and economic problem. We have cloned the cDNA of the nuclear receptor (NR) Eg2DBDα.1 from protoscolices of *E. granulosus s.l.* This NR belongs to the 2DBD subfamily, whose members possess two DNA-binding domains and have been identified only in a few invertebrates. Since 2DBD-NRs are not present in parasites' hosts and NRs from parasitic helminths are considered potential targets for new anthelmintic drugs, we aimed to elucidate the function of Eg2DBDα.1. We have previously determined that this NR is capable of forming homodimers through its ligand-binding and C-terminal domains (EF domains). In this work, our objective was to analyze the dimerization capacity of C-terminally truncated forms of Eg2DBDα.1-EF, using yeast two-hybrid assays. We cloned the cDNAs for Eg2DBDα.1-EF (400 AA) and for the truncated forms Eg2DBDα.1-HKW (250 AA) and Eg2DBDα.1-QQL (191 AA) to perform these assays. Our results indicate that Eg2DBDα.1-EF is able to interact with the truncated forms Eg2DBDα.1-HKW and Eg2DBDα.1-QQL. Furthermore, we determined that Eg2DBDα.1-QQL homodimerizes, whereas Eg2DBDα.1-HKW does not, a striking result given that the latter contains the Eg2DBDα.1-QQL region. We are now evaluating whether putative changes in the secondary and/or tertiary structure of Eg2DBDα.1-HKW could be responsible for the loss of homodimerization capacity. In addition, we are performing co-immunoprecipitation assays with the *in vitro* translated proteins to confirm these results.

Keywords: 2DBD nuclear receptors, *Echinococcus granulosus*, dimerization.

Study of the Early Cellular Response Activated by a Mechanical Injury in the Spinal Cord of *A. Charrua*

Silva Jaureguiberry Stephanie[1], Berrosteguieta Inés[1,2], Herrera-Astorga Laura[1,3], Rosillo Juan Carlos[1,4] and Fernández Anabel[1,5]

[1]Laboratorio de Neurobiología Comparada, Departamento de Neurociencias Integrativas y Computacionales, Instituto de Investigaciones Biológicas Clemente Estable, Ministerio de Educación y Cultura. Montevideo, Uruguay; [2]Unidad Académica ESFUNO, Facultad de Enfermería, Universidad de la República. Montevideo, Uruguay; [3]Sección Fisiología y Nutrición, Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay; [4]Departamento de Histología y Embriología Facultad de Medicina, Universidad de la República. Montevideo, Uruguay; [5]Laboratorio de Neurociencias Facultad de Ciencias, Universidad de la República. Montevideo, Uruguay

Abstract: Unlike mammals, fish can respond to spinal cord injury by restoring function. This process is described in *Danio rerio*, with three initial phases: an inflammatory phase 3 days post-injury (dpi), where glia is activated, a regenerative phase

at 7 dpi with peak proliferation, and a final repair phase. *Austrolebias charrua* are annual fish, recognized for their great capacity to adapt to extreme environmental variations, employing unique strategies. Their nervous system expresses significant proliferative potential compared to other fish, but their response to injury is unknown. Considering their short life cycle and the importance of their motor function for reproduction, efficient and rapid reparative mechanisms are expected to be observed in the event of spinal cord injury. The objective was to study the early cellular response to spinal cord injury in A. charrua, evaluating cell proliferation, glial activation, and Pax6+ progenitors as indicators of early events. A control group was compared with two others at 3 dpl and 7 dpl, all injected 24 h earlier with the cell proliferation marker 2'-Deoxy-5-Ethynyluridine (EdU). EdU was combined with the markers Iba1 (microglia) and Pax6 (progenitors). Preliminary results showed increased cell proliferation in injured fish compared to controls at 7 dpl and changes in the expression patterns of the cell markers used. This would indicate a conservation of the initial repair mechanisms in D. rerio. This study offers a first approach to understanding early repair in this species.

Keywords: Cell proliferation, regeneration, spinal cord, fish.

Uterine Response to the Administration of Oncologic Drugs Combined with a Mitochondrial Modulator

Vidal Santiago, Toledo Agustina, Anesetti Gabriel, Hernández Karina and Chávez Rebeca

Reproductive Biology Laboratory, Academic Unit of Histology and Embryology, Faculty of Medicine, Universidad de la República, Montevideo, Uruguay

Abstract: The administration of chemotherapeutic agents, used as clinical tools for the treatment of oncological diseases, can lead to alterations in the gonadal reserve and possibly in other components of the reproductive system. This has prompted the study of protocols aimed at minimizing their effects, as well as the search for new drugs.

In this study, we evaluated the effects of two widely used chemotherapeutic drugs—vincristine (V) and cyclophosphamide (C)—administered with or without a mitochondrial modulator, Dichloroacetate (DCA), on various morphometric parameters of the uterus in 7–8-week-old female C57BL/6 mice.

Administration of any of the drugs (V, C, or DCA) resulted in a significant increase in uterine wall thickness, particularly in the epithelium and in the area occupied by collagen fibers, compared to vehicle-treated animals ($p < 0.05$). DCA administration did not reverse the effects observed with the chemotherapeutic agents.

These changes indicate that chemotherapeutic agents affect uterine tissue and are likely associated with long-term fertility issues, underscoring the need for further research into these effects.

Keywords: Chemotherapeutic agents, oncological diseases, reproductive system.

ISCOM-matrices Based on *Quillaja Brasiliensis* Saponins Improve Immune Response and Survival in Aged and Immunosuppressed Mice Following Viral Challenge

Deutsch Natalia[1], García Florencia[1], Puentes Santiago[2], Grezzi Leticia[3], Casaravilla Cecilia[3], Chabalgoity José A.[1], Baz Mariana[4] and Silveira Fernando[1]

[1]Unidad Académica de Desarrollo Biotecnológico, Instituto de Higiene, Facultad de Medicina, Universidad de la República. Montevideo, Uruguay; [2]Instituto Tecnológico Superior Buceo, DGETP- UTU. Montevideo, Uruguay; [3]Área Inmunología, Departamento de Biociencias (Facultad de Química) y Cátedra de Inmunología, Instituto de Química Biológica (Facultad de Ciencias), Universidad de la República, Montevideo, Uruguay; [4]Department of Microbiology, Infectious Disease and Immunology, Faculty of Medicine, Université Laval, Quebec, Canada

Abstract: Viral respiratory infections, particularly influenza, continue to pose a major global public health challenge, contributing to significant morbidity and mortality annually. These impacts are disproportionately borne by high-risk groups, such as older adults and immunodeficient individuals. Although vaccination is the most effective preventive strategy, current vaccines still demonstrate suboptimal efficacy against many infectious diseases. In this study, we investigated the use of *Quillaja brasiliensis* saponin-based ISCOM matrices (IMXQB) as an adjuvant to enhance the Trivalent Influenza Vaccine (TIV) against seasonal influenza virus in an aged and immunosuppressed mouse model. Female Balb/c mice were divided into three groups and immunized intranasally with two doses (on days 0 and 14) of either TIV, TIV-IMXQB, or saline. TIV-IMXQB elicited significantly higher levels of serum IgM, IgG (including isotypes), IgA, and hemagglutination inhibition antibody titers compared to TIV alone. Moreover, mice receiving TIV-IMXQB exhibited increased IL-2 and IFN-γ cytokine responses. Thirty days after the first dose, the mice were immunosuppressed with cyclophosphamide and challenged with the A/Uruguay/897/2018 (H1N1)pdm09 virus. Mice in the TIV-IMXQB group showed significantly reduced viral loads in both the lungs and nasal turbinates, with no mortality observed. In contrast, mortality rates reached 80% and 100% in the TIV and saline groups, respectively. These findings demonstrate that TIV- IMXQB provides enhanced immunogenicity, protection, and recovery against the (H1N1)pdm09 virus, highlighting ISCOM-matrices technology based on *Quillaja brasiliensis* saponins as a promising platform for seasonal influenza vaccine development.

Keywords: Saponins, adjuvant, ISCOM-matrices, *Quillaja brasiliensis*, immunosuppressed, aged mice.

Optimization of Genomic Selection Strategies in *Eucalyptus Grandis*

Rodríguez Virginia[1], Duarte Damián[2], Cappa Eduardo P.[3,4] and Quezada Marianella[1]

[1]Laboratory of Biotechnology, Department of Plant Biology, Faculty of Agronomy, Universidad de la República; [2]Research and Development, Forestal Oriental, UPM; [3]Research Center on Natural Resources, Institute of Biological Resources, National Institute of Agricultural Technology (INTA); [4]National Scientific and Technical Research Council (CONICET)

Abstract: Forest tree breeding programs are complex, long-term, and costly. Genomic Selection (GS) develops a predictive model using a Training Population (TP) that integrates genotypic, phenotypic, and pedigree information to predict the genetic values of Selection Candidates (SP) based on genomic data. This approach improves the accuracy of breeding value estimation and reduces breeding cycles through early selection. However, the predictability decreases as the generational distance between TP and SP increases through generations. The objective of this study was to optimize the TP in a *Eucalyptus grandis* population spanning four consecutive generations (G1, G2, G3, and G4). Growth data (Volume) were available for 18,097 trees, and 4,016 had measurements for Basic Density (BD) and Pulp Yield (PY). A total of 1,787 individuals were genotyped using the EUCHIP60K or Euc72K Axiom SNP chips. We compared ssGBLUP models using TPs composed of all previous generations; only the immediate previous generation; and only the base generation (G1), considering also the pedigree relationships between TP and SP. The highest predictive abilities for PY (0.35) and BD (0.25) were obtained

when using G3 to predict G4. In contrast, for Volume, the best result was achieved using G1 to predict G4 (0.27). When using only the parents of G4 in the TP, predictive abilities were higher than when using all individuals from the generation. These results provide insights for optimizing TPs and promoting the implementation of GS in forest breeding programs.

Keywords: Forest tree breeding, genomic selection, breeding cycles.

The Atypical Psychedelic Ibogaine Increases Plasticity in the Visual Cortex of Mice

Acuña, Alejo[1], Hayek Emilia[1], Calero Eugenia[1], Billieri Federico[2], Totaro Valentino[2], Pizzorusso Tommaso[2], Mesa Juan Manuel[3], Carrera Ignacio[3], Urbanavicius Jessika[4] and Rossi Francesco M[1]

[1]Laboratorio de Neurociencias "Unidad de Neuroplasticidad", Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [2]BIO@SNS laboratory, Scuola Normale Superiore, Pisa, Italia; [3]Laboratorio de Síntesis Orgánica, Departamento de Química Orgánica, Facultad de Química, Universidad de la República, Montevideo, Uruguay; [4]Departamento de Neurofarmacología Experimental, Instituto de Investigaciones Biológicas Clemente Estable, Ministerio de Educación y Cultura, Montevideo, Uruguay

Abstract: The atypical psychedelic ibogaine has potential for treating psychiatric disorders. It is proposed that this effect is mediated by an increase in neuroplasticity that happens after its consumption. However, evidence in support of this hypothesis is limited.

We investigated Ibogaine's effect on neuroplasticity, using the ocular dominance paradigm, as well as its impact on Perineuronal Nets (PNNs)—extracellular matrix structures that inhibit plasticity.

We quantified visual acuity (VA, cycles/degree) and dendritic spine density (DSD, spines/μm) in the Visual Cortex (VC) of adult (P60) C57BL/6J mice divided into four groups: mice deprived of vision for four days and treated intraperitoneally with ibogaine (40 mg/kg) or saline (+MD / IBO and -MD / SAL), and mice not deprived of vision, treated with ibogaine or saline (-MD / IBO and - MD / SAL). PNNs were quantified in the VC of two other groups of mice treated with Ibogaine or saline (without MD), using immunohistochemistry with *Wisteria floribunda* agglutinin.

In the +MD / IBO group—but not in the other groups—VA was lower in the deprived eye (n = 7; deprived: 0.28 ± 0.03 *vs*. non-deprived: 0.36 ± 0.02; $p < 0.01$), and there was a reduction in DSD in the VC contralateral to the deprived eye (+MD / IBO, n = 19 neurons: 0.62 ± 0.06 *vs*. +MD / SAL, n = 29: 0.92 ± 0.04; $p < 0.001$). Additionally, IBO mice showed lower PNN density (IBO, n = 6; 74 ± 16 PNNs/mm² *vs*. SAL, n = 6: 102 ± 12 PNNs/mm²; $p < 0.05$).

Our results show that ibogaine facilitates experience-dependent plasticity induced by visual deprivation, and that this facilitation may be mediated by a reduction in PNN density.

Keywords: Ibogaine, psychedelics, neuroplasticity.

Risk Analysis of Livestock Intoxication by Toxic Cyanobacteria and Pathogenic Bacteria in Watering Sites: Preliminary Findings based on AmpliSeq Panel

Gonzalez-Izaguirre Andrea[1,2], Martinez de la Escalera Gabriela[1,2], Kruk Carla[3,4], Segura Angel[4], Tiscornia Fabrizio[2,4], Piñeiro Gervasio[5,6], Gallego Federico[3], Piñeiro-Guerra Juan Manuel[4], Balado Irene[7], González Revello Álvaro[1,2,8] and Piccini Claudia[1,2]

[1]Departamento de Microbiología, Instituto de Investigaciones Biológicas Clemente Estable (IIBCE), Montevideo, Uruguay; [2]Centro de Investigación en Ciencias Ambientales (IIBCE), Montevideo, Uruguay; [3]Instituto de Ecología y Ciencias Ambientales, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [4]Departamento de Modelación Estadística de Datos e Inteligencia Artificial, CURE, Universidad de la República, Rocha, Uruguay [5]Laboratorio de Análisis Regional y Teledetección - Instituto de Investigaciones Fisiológicas y Ecológicas Vinculadas a la Agricultura, Facultad de Agronomía, Universidad de Buenos Aires (UBA) - CONICET, Buenos Aires, Argentina; [6]Departamento de Sistemas Ambientales, Facultad de Agronomía, Universidad de la República, Montevideo, Uruguay; [7]Departamento de Geomática, Facultad de Ingeniería, Universidad de la República, Montevideo, Uruguay; [8]Departamento de Ciencia y Tecnología de Alimentos, Facultad de Veterinaria, Universidad de la República, Montevideo, Uruguay

Abstract: Water contamination in artificial ponds represents a threat to animal health, contributing to the spread of zoonotic diseases and the eventual contamination of meat and milk with cyanotoxins. In Uruguay, cyanobacterial blooms are observed year-around and raise concern due to toxic-related events that lead to serious health problems and, in some cases, animal mortality. The objective of this work is to determine the co-occurrence of toxic cyanobacteria and pathogenic waterborne bacteria in artificial farm ponds in order to assess the risk to livestock health. For this purpose, AmpliSeq technology was applied to water samples obtained from different ecosystems (estuaries, farm ponds, rivers), using a panel designed by our research group, which is composed of 548 primer sets targeting 71 virulence genes. Environmental information (temperature, turbidity, conductivity, nutrient concentrations, dissolved oxygen, etc.) and fecal contamination data are also available for each sample. Preliminary results indicate that farm ponds have a greater number of reads for virulence factors related to fecal contamination, whereas rivers and estuaries exhibit a higher proportion of reads associated with genes responsible for microcystin production. Finally, in all water reservoirs, the presence and origin of genes vary according to the site. These differences may be associated with the location of each water body within the watershed, land use, hydrological connectivity, and seasonality affecting the presence, persistence, and abundance of these organisms.

Keywords: Water contamination, cyanobacterial, pathogenic bacteria, artificial ponds, livestock.

Incidence and Characterization of *Fusarium* Species Causing Infection in Barley Grains

Álvarez Angie[1], Garmendia Gabriela[1], Pereyra Silvia[2] and Vero Silvana[1]

[1]Laboratory of Biotechnology, Microbiology Area, Faculty of Chemistry, Universidad de la República (Universidad de la República), Montevideo, Uruguay; [2]National Institute of Agricultural Research (INIA), La Estanzuela, Colonia, Uruguay

Abstract: Barley (*Hordeum vulgare L.*) is the second most important winter crop in Uruguay after wheat, with a production of 889 thousand tons during the 2020/2021 season. This production can be affected by the emergence of fungal diseases, among which Fusarium head blight (FHB) stands out. This disease, caused by various species of the *Fusarium* genus, not only reduces grain quality but is also associated with a loss of safety in the harvested grain.

In recent years, changes have been observed in the species composition responsible for the disease in different regions. Therefore, this study aimed to update the information on the incidence of *Fusarium* species causing infection in barley grains from different varieties and regions of the country. Based on 50 grains per sample, the infection rate by *Fusarium* spp. was determined through culturing. The isolated strains were identified using molecular techniques. Subsequently, the

samples with the highest contamination levels were selected for species identification by high-throughput sequencing of the TEF-1α gene from cultured mycelium.

As a result, infection rates ranged from 2% to 36%. Most isolates were identified as *F. graminearum*, followed by *F. poae* in lower proportions. High-throughput sequencing confirmed the presence of these species and enabled the detection of other minor species.

Keywords: *Fusarium* spp., barley, Fusarium head blight.

Bioreduction of Tannins in Sorghum by Filamentous Fungi to Improve Bioethanol Production

Arbildi Ferreira Erika[1,2], Ovsejevi Karen[2] and Vero Silvana[1]

[1]Microbiology Area, Department of Biosciences, Faculty of Chemistry, Universidad de la República, Uruguay; [2]Biochemistry Area, Department of Biosciences, Faculty of Chemistry, Universidad de la República, Uruguay

Abstract: Bioethanol is a renewable alternative to fossil fuels. In Uruguay, it is mainly produced from sugarcane (ALUR Bella Unión) and cereals (ALUR Paysandú). Among the raw materials used is sorghum, a starch-rich cereal that can be cultivated under diverse conditions.

Sorghum cultivars are classified by their tannin content as low (0.0–0.4%), medium (0.4–1.0%), and high (1.0–10%). High-tannin sorghum offers production advantages, such as resistance to fungi and predators. However, its use in ethanol production is limited, as tannins interfere with enzymatic saccharification and fermentation processes, reducing yield.

This project aims to develop fungal enzymatic supernatants capable of degrading sorghum tannins, thus improving ethanol and by-product yields.

Twenty-four fungal strains capable of growing with tannins as the sole carbon source were isolated from soil, fermented tea, compost, and sorghum grains. Among them, Aspergillus strains with tannase activity were identified. The highest tannase activity—8.8 (± 0.06) µmol of gallic acid/min—was observed in strain HT4, identified as Aspergillus uvarum. Genome analysis revealed a high-quality assembly with 98.8% completeness and the presence of 15 tannase-coding genes.

For condensed tannins, an enzymatic supernatant from Alternaria alternata achieved a 67.9% (± 6.6) degradation under the tested conditions. In addition, yeast cell walls were shown to reduce tannins in solution by 42.9% (± 0.5).

Keywords: Sorghum, tannins, tannase, filamentous fungi, bioethanol.

Light Intensity Modulates Anxiety-like Behavior in the Light-Dark Box in Rats: Impact of Benzodiazepine Sensitivity

Bai Florencia[1], Perini Valentina[1], Scorza Cecilia[1] and Urbanavicius Jessika[1]

[1]*Departamento de Neurofarmacología Experimental, Instituto de Investigaciones Biológicas Clemente Estable*

Abstract: The Light-Dark Box (L-D box) is a widely used behavioral paradigm to assess anxiety-like responses in rodents. It consists of two compartments: a brightly lit, aversive open area and a dark, safe, enclosed area. Light intensity in the lit compartment is a critical variable that could influence baseline anxiety as well as the efficacy of anxiolytic or anxiogenic compounds. We hypothesized that high light intensities enhance anxiety in the L-D box, which could be attenuated by anxiolytic drugs. Adult male Wistar rats (300–350 g) were previously handled (5 min/day for 3 days) before testing. On the test day, animals were placed in the open field (OF; 10 min) to assess locomotor activity, and were immediately moved to the L-D box test (10 min) under different illumination conditions: 65, 330, and 1000 lux. The effect of acute i.p. administration of benzodiazepines (Bz), alprazolam (0.2 and 0.4 mg/kg), and diazepam (1 mg/kg) was also tested. Total distance travelled in the OF and time spent in the light compartment, number of transitions between compartments and rearings (exploratory behavior) in the L-D box, were recorded. Data showed that the highest illumination level (1000 lux) resulted in a significant reduction of the time spent in the light compartment, transitions, and rearings, suggesting an anxiogenic response. Diazepam, but not alprazolam, decreased the locomotor activity in the OF. Neither alprazolam nor diazepam exerted anxiolytic effects under any lighting condition. Future experiments will be performed to clarify the lack of effect of Bz in the L-D box.

Keywords: Anxiety, handling, light-dark box, open field, locomotion.

Cardiovascular Response to *Trypanosoma Cruzi* Infection: Role of Mitochondrial Fission Process 1 Protein

Barreiro Nicolás[1], Tomasina Ramiro[2,3], Cabrera Andrés[2,3], Greif Gonzalo[2], Wai Timothy[4], Robello Carlos[2,5] and Contreras Paola[1]

[1]*Laboratorio de Fisiología Cardiovascular, Unidad Académica de Fisiología, Facultad de Medicina, Universidad de la República;* [2]*Laboratorio de Interacciones Hospedero-Patógeno, Institut Pasteur de Montevideo, Uruguay;* [3]*Unidad Académica de Parasitología y Micología, Instituto de Higiene, Facultad de Medicina, Universidad de la República;* [4]*Mitochondrial Biology Group, Institut Pasteur, CNRS UMR 3691, Université Paris Cité, Paris, France;* [5]*Unidad Académica de Bioquímica, Facultad de Medicina, Universidad de la República.*

Abstract: ***Introduction*:** Deletion of the Mitochondrial Fission Process 1 Protein (MTFP-1) in mice leads to progressive dilated cardiomyopathy. Chronic infection with *Trypanosoma cruzi* produces pathological cardiac remodeling in humans. Hypothesis: The loss of MTFP-1 in the Myocardium (MTFP-1KO) aggravates the cardiovascular pathology caused by chronic *T. cruzi* infection.

***Materials and Methods*:** Electrocardiograms (ECGs) were recorded weekly in conscious, freely moving male mice with the non-invasive ECGenie system. Rhythm alterations, Heart Rate (HR), and Heart Rate Variability (HRV) indices were analyzed in four groups: Wild-Type (WT), MTFP-1KO, infected WT, and infected MTFP-1KO (total number of mice = 11). All procedures followed protocol 003-24, annex 1, (Institut Pasteur Montevideo).

***Results*:** In the acute phase (8-15 days post-infection [dpi]), the infected groups showed a tendency toward reduced HR after an increased HR at 1 dpi. Both changes were less marked in the infected MTFP-1KO mice. From 29 dpi onward, all infected mice showed a rise in HRV relative to the WT group mean. One MTFP-1KO mouse died at 55 dpi after developing severe dyspnea.

***Conclusions*:** To draw significant conclusions, we plan to increase the sample size and extend monitoring into the late chronic phase of the infection, as well as to examine the response in female mice, to better characterize the long-term interaction between MTFP-1 deficiency and the *T. cruzi* infection.

Keywords: *T. cruzi*, heart rate variability, conditional MTFP-1KO mice.

Epidemiological Survey of Human Pegivirus (HPgV-1) in Uruguay

Bentancor Dana[1], Álvarez Hérnan[1], Bauzada Alejandra[1], Nin Diego[1], Rodríguez Santiago[1], Mirazo Santiago[1] and Cancela Florencia[1]

[1]*Laboratorio de Ecología Viral y Virus Zoonóticos, Unidad Académica de Bacteriología y Virología, Instituto de Higiene-Facultad de Medicina, Universidad de la República*

Abstract: Human Pegivirus Type 1 (HPgV-1), classified within the family *Flaviviridae*, species Pegivirus C (humans and non-human primates), comprises seven genotypes with distinct geographic distributions. Its genome is a single-stranded, positive-sense RNA with a size of approximately 9.4 kb and is transmitted through blood, sexual contact, and vertical routes. Even though HPgV-1 was initially identified in patients with acute or chronic non-A–E hepatitis, its pathogenicity remains unclear, with no direct association to clinical disease. HPgV-1 is currently estimated to have a global seroprevalence of 1/6. In South America, reports remain scarce and are mainly limited to Brazil (5.9%–12.42% viremia in blood donors and 23.3% viremia in pediatric oncology patients). As part of ongoing research on emerging viruses conducted by our laboratory, we carried out the first epidemiological survey of HPgV-1 in Uruguay, focusing on patients with hepatitis of unknown etiology (non-A–E) and HIV-1 infection, given their shared transmission routes. A total of 69 serum samples, corresponding to 37 adults and 32 children, were analyzed using molecular methods (RT-qPCR and RT-PCR). HPgV-1 RNA was detected exclusively in pediatric samples, accounting for 7.2% of all cases (5/69) and 15.6% (5/32) of the pediatric group. Genetic characterization and phylogenetic analyses revealed that these strains belonged to genotype 2, showing a high nucleotide homology towards isolates from Brazil.

Keywords: Human pegivirus, HPgV-1, pediatric patients, RNA prevalence, uruguay.

Prototyping Space: Open-Source Creation of Scientific Equipment for Bioscience Research

Bentancor Marcel[1], Casaretto Esteban[2], Pereyra Gustavo[2], Gastón Quero[2] and Borsani Omar[2]

[1]*Laboratorio de Biología Molecular Vegetal, Instituto de Química Biológica, Facultad de Ciencias, Universidad de la República;* [2]*Laboratorio de Bioquímica, Departamento de Biología Vegetal. Facultad de Agronomía, Universidad de la República*

Abstract: Access to specialized scientific instrumentation represents a challenge for research in Latin American countries. The Prototyping Space was created by researchers from the Plant Molecular Biology laboratories (Faculty of Sciences) and Biochemistry (Faculty of Agronomy) at the Universidad de la República to address this limitation.

The collaborative development of scientific instrumentation in open-source mode allows overcoming economic and technological barriers, democratizing access to specialized tools in the biosciences.

The space features traditional tools and a digital fabrication laboratory that includes 3D printers (filament deposition and resin polymerization), CNC milling machines and drills with sub-millimetric precision, and chambers for 3D scanning. Machine learning tools were also implemented for analyzing data obtained with this equipment and with commercial instruments, such as a drone equipped with a multispectral camera. Various prototypes for plant biology research have been developed, and collaborations have been established with national and international university groups, expanding their application to areas such as molecular biology, microscopy, and physical chemistry. The collaborative and open science model has enabled maximizing resources, reducing technological gaps through interinstitutional synergies, and establishing an interdisciplinary scientific cooperation network. The systems and accessories generated demonstrate that open-source equipment development constitutes a viable alternative for strengthening local scientific research with potential regional impact. The Prototyping Space is open to new collaborations with research groups interested in developing technological solutions adapted to their specific needs.

Keywords: Open hardware, phenomics, digital fabrication.

Modafinil, A Cognitive Enhancer that Increases Gamma Activity (~40 Hz) of the EEG

Costa Alicia[1], Mateo Diego[2,3,4], Pascovich Claudia[1,5], Castro-Zaballa Santiago[1], Bisagno Verónica[4,6], Urbano Francisco J[4,7] and Torterolo Pablo[1]

[1]Laboratorio de Neurobiología del Sueño, Unidad Académica de Fisiología, Facultad de Medicina. Universidad de la República. Montevideo, Uruguay; [2]Faculty of Science and Technology. Universidad Autónoma de Entre Ríos (UADER, Entre Ríos, Argentina ;[3]Instituto de Matemática Aplicada del Litoral (IMAL-CONICET-UNL), CCT CONICET, Santa Fe, Argentina; [4]Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina; [5]Consciousness and Cognition Laboratory, Department of Psychology, University of Cambridge, Cambridge, United Kingdom; [6]Instituto de Investigaciones Farmacológicas, Instituto Universidad de Buenos Aires. Buenos Aires, Argentina; [7]Instituto de Fisiología, Biología Molecular y Neurociencias, Facultad Ciencias Exactas. Universidad de Buenos Aires. Buenos Aires, Argentina

Abstract: Cognitive processes that occur during wakefulness, such as attention and perception, have been associated with an increase in the gamma band activity (~40 Hz) of the EEG. Modafinil is a pro-wakefulness drug that has gained popularity as a cognitive enhancer due to its ability to improve attention, executive function, and learning. We hypothesize that, to produce this effect, modafinil must enhance the gamma activity of the EEG. To assess this possibility, we analyzed EEG activity during the wakefulness produced by modafinil, using the cat as an experimental model. Animals with chronic intracranial electrodes in the prefrontal, posterior parietal, and visual cortices were used. The experimental protocol consisted of the oral administration of modafinil (5 mg/kg) or its control (empty capsule), followed by polysomnographic recording for 4 hours under semi-restricted conditions. The treatments were counterbalanced, leaving a minimum interval of two days between them. Our results show that the modafinil-induced wakefulness is characterized by: a) an increase in local activity (power) in the gamma band (30 – 45 Hz); b) an increase in the ratio between the gamma and theta frequency bands (5 – 8 Hz), suggesting a higher alert level; c) an increase in the complexity of the signal in the band gamma, measured by Lempel-Ziv complexity. These findings suggest possible neurophysiological mechanisms by which modafinil could act as a cognitive enhancer.

Keywords: Wakefulness, modafinil, gamma band, cognitive enhancer.

Genomic, Population, and Phenotypic Characterization of the *Catenibacterium* Genus

Costa Daniela[1,2], Giménez Matías[1,2], Peñalba Florencia[1,2], Vera Josefina[1,2], Perdomo Valentina[1,2], Salazar Cecilia[1] and Riera Nadia[1,2]

[1]Microbial Genomics Laboratory, Institut Pasteur Montevideo, Uruguay; [2]Faculty of Engineering, Universidad ORT, Montevideo, Uruguay

Abstract: The gut microbiome harbors a vast diversity of microorganisms, many of which play a fundamental role in its physiology, with their composition varying according to numerous factors. The genus *Catenibacterium*, belonging to the phylum *Bacillota*, was first described in 2000 and comprises three species: *Catenibacterium mitsuokai*, *C. tridentinum*, and *C. faecis*. Information on this microorganism is scarce and comes mainly from human and animal gut microbiome studies, where it has been associated with both healthy and diseased states, as well as with different lifestyles and dietary patterns, making its physiological role uncertain. The variability observed in its associations with different health states across populations may be explained by the presence of distinct *Catenibacterium* species or lineages that differ in their pro-inflammatory potential.

Unpublished studies suggest the presence of antimicrobial and anti-inflammatory activity in the supernatants of strains isolated in our laboratory. To determine whether a population structure exists in which strains with different ecological traits are differentially distributed, genomes from the previously isolated strains will be combined with publicly available genomes, and comparative genomics analyses will be performed. Using this genome set, we will evaluate, among other aspects, the presence and distribution of biosynthetic gene clusters potentially responsible for the observed antimicrobial and anti-inflammatory activities. The results are expected to help explain the variability of responses attributed to the presence of *Catenibacterium* in the gut microbiome.

Keywords: Population genomics, microbiome, genomic characterization.

Inter-Species Cooperation: Elucidating the Role of the Microbiome in the Success of *Microcystis*

Croci Carolina[1], Martínez de la Escalera Gabriela[1], Kruk Carla[2,3], Segura Angel[3] and Piccini Claudia[1]

[1]Laboratorio de Ecología Microbiana Acuática, Departamento de Microbiología, Instituto de Investigaciones Biológicas Clemente Estable (IIBCE), Montevideo, Uruguay; [2]Instituto de Ecología y Ciencias Ambientales, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [3]Departamento MEDIA (Modelización Estadística de Datos e Inteligencia Artificial), CURE, Universidad de la República, Rocha, Uruguay

Abstract: Intensive agricultural production practices, a consequence of the extractive model and the indiscriminate use of inputs, cause contamination of water bodies with nitrogen and phosphorus. This has led to the increasingly common occurrence of large cyanobacterial blooms, not only in our country but throughout the world. In particular, large blooms of organisms of the genus *Microcystis* develop in freshwater systems and estuaries such as the Río Negro, the Río Uruguay, and the Río de la Plata. In natural ecosystems, this cyanobacterium forms colonies associated with a diversity of microorganisms. In previous work, we linked the different stages of colonial growth to various microbial groups that are part of the *Microcystis* microbiome and hypothesized that the colonies constitute a multispecific biofilm, where interspecific cooperation is a mechanism that contributes to the success of the *Microcystis* holobiont (cyanobacteria and its microbiome). In this study, based on the microbial taxa identified as relevant to colonial growth, we evaluated which functional genes are necessary for colonies to develop and form a bloom. To this end, *Microcystis* colonies of different sizes were obtained and analyzed using shotgun metagenomics. The results obtained so far show that, although 50% of the total reads encode hypothetical proteins, which poses a major challenge for annotation, the presence of various genes previously described as relevant for the survival of *Microcystis* was identified in the microbiome. These preliminary results suggest that there are mechanisms of cooperation between cyanobacteria and their microbiome that ensure the success of these organisms.

Keywords: *Microcystis* blooms, microbiome, metagenomic shotgun.

Characterization of Natural Biomaterials by Non-destructive Methods

Pereyra Mariana[1,2], Bentancur-Viglione Gabriela[3], Martinez Juan Pedro[4], Fagúndez Pablo[1], Valente Paulo[4], Pereyra Javier[4], Morelli Enrique[3], Marotti Ricardo[4], Dalchiele Enrique[4]

[1]Unidad de Bioquímica Analítica, Centro de Investigaciones Nucleares, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [2]Espacio Interdisciplinario, Universidad de la República, Montevideo, Uruguay; [3]Sección Entomología, Instituto de Biología, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [4]Instituto de Física, Facultad de Ingeniería, Universidad de la República, Montevideo, Uruguay

Abstract: The study of natural biomaterials has enabled us to identify unique physicochemical and optical properties, including superhydrophobicity, structural color, and transparency. A process called biomimicry seeks to "imitate" nature to apply sustainable solutions to human challenges or problems. Therefore, the development of characterization techniques is of utmost importance to understand the processes that lead a material to have specific properties and then emulate the patterns and strategies used by nature in a laboratory or for industrial development. This work describes the characterization of a natural biomaterial, such as the butterfly wing, using non-destructive sampling techniques. The techniques employed in this work were SEM, AFM, FTIR, RAMAN, reflectance, and transmittance. The specimens used were *Episcada hymenaea* and *Heliconisa pagenstecheri* from the entomology collection of the Faculty of Sciences at Universidad de la República. The uniqueness of these species lies in their wings, which lack scales and are transparent. The techniques allowed us to determine the morphological characteristics, chemical composition, and optical properties of the specimens. The analyses also allowed us to identify properties of these materials that could be associated with the behavior of these species. Due to the characteristics of these analyses, the techniques can be applied to study other specimens as well.

Keywords: Biomaterials, transparency, characterization.

PBCA Nanoparticles: Effectiveness in Biofilm Inhibition on Medical Surfaces

Cruz Jorge, Erlen[1], Navarro Martínez Nicolás[1], González María José[1], Ramos Carriles Yaquelín[2,3], Méndez Eduardo[4], Robino Luciana[5], Álvarez Brito Rubén[2,3] and Scavone Paola[1]

[1]Department of Microbiology, Microbial Biofilms Laboratory, Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay; [2]Faculty of Chemistry, University of Havana, Havana, Cuba; [3]Center for Genetic Engineering and Biotechnology @ University of Havana, Joint Nano-Biomedicine Laboratory, Havana, Cuba; [4]Biomaterials Laboratory, Faculty of Science, Universidad de la República, Montevideo, Uruguay; [5]Department of Bacteriology and Virology, Faculty of Medicine, Universidad de la República, Montevideo, Uruguay

Abstract: Biofilm-associated infections represent a significant challenge in the clinical setting, as these bacterial communities can colonize medical surfaces and exhibit high resistance to antibiotics, making them difficult to eliminate. Therefore, developing strategies to prevent their formation is crucial.

In this study, the ability of poly(n-butyl cyanoacrylate) nanoparticles (PBCA-NPs) to inhibit biofilm formation by *E. coli*, *P. mirabilis*, *S. aureus*, *S. epidermidis*, *A. baumannii*, and *P. aeruginosa* was evaluated. To this end, 96-well plates and glass coverslips were coated with PBCA NPs (0.210 mg/mL) and incubated with bacterial cultures. Biofilm formation on the plates was assessed using the crystal violet method, while on coverslips, it was analyzed by fluorescent staining and confocal microscopy.

The results showed that PBCA-NPs significantly reduced biofilm formation of *E. coli*, *P. mirabilis*, *S. aureus*, *S. epidermidis*, and *A. baumannii* in 96-well plates, whereas *P. aeruginosa* showed no inhibition. On the coverslips, *E. coli*, *P. mirabilis*, and *S. aureus* did not grow in the coated areas, whereas *S. epidermidis* was able to develop on the coating. These findings suggest that PBCA-NPs can interfere with bacterial adhesion and prevent biofilm formation in certain species. Given their biodegradable nature and potential to reduce bacterial colonization on surfaces, they may be a valuable tool in the design of coatings for medical devices, contributing to the prevention of biofilm-associated infections.

Keywords: Biofilms, nanoparticles, poly(n-butyl cyanoacrylate), medical surfaces.

Eliminating Dbc1 in the Hippocampus: Age-dependent Effects on Neurogenesis and Memory

Cuccillo-Martínez Michelle[1], Benítez-Rosendo Andrés[1,2], Santos Leonardo[1], Escande Carlos[1] and Calliari Aldo[1,2]

[1]Laboratory of Metabolic Diseases and Aging, Institut Pasteur de Montevideo, Uruguay [2]Department of Biosciences, Faculty of Veterinary Medicine, Universidad de la República (Universidad de la República), Montevideo, Uruguay

Abstract: Dbc1, also known as CCAR2, is involved in multiple cellular processes, such as transcriptional regulation, DNA damage repair, metabolic modulation, and cell cycle regulation. It exerts its function by physically interacting with enzymes, transcription factors, and epigenetic modulators, thereby regulating their biological activity. Classical Dbc1 KO mice, in which gene expression is eliminated in all cells of the organism, show a reduction in the number of neuroblasts in the Dentate Gyrus (DG) of the hippocampus and display specific behavioral changes, likely due to a decrease in neuroblast generation or impaired differentiation, affecting hippocampal function. Thus, it is unclear whether this effect is due to the specific control of Dbc1 over adult neurogenesis in the dentate gyrus or an indirect consequence of its absence in other areas of the nervous system. In this study, we investigated the specific role of Dbc1 in the regulation of the cell cycle of neuronal precursors in the DG and its possible impact on cognitive functions such as memory and learning. To this end, we used a

conditional mouse model, Dbc1$^{fl/fl}$; Nestin-Cre/ERT2, in which, after tamoxifen administration, Dbc1 expression is specifically eliminated in DG neuronal precursors. Two months after tamoxifen administration, we evaluated cognitive performance using the novel object recognition test, the Barnes maze, the elevated plus maze, and the open field test. Our results show that the effects of Dbc1 deletion vary with age: in young mice, Dbc1 elimination significantly improved short-term memory and novelty response; in contrast, in adult animals, a reduction in the number of neuroblasts was observed, with no detectable cognitive changes. These findings suggest that Dbc1 regulates adult neurogenesis in an age-dependent manner.

Keywords: Dbc1 protein, neurogenesis, neuroblasts, hippocampus, memory.

Longitudinal *In Vivo* Analysis of the 3xTg-AD Mouse Model to Study the Role of Glia in Neuroinflammation

Dapueto Rosina[1], Reyes Laura[1], Bentura Manuela[1], Paolino Andrea[1], Isaurralde Fabiana[1], Zirbesegger Kevin[1], Kreimerman Ingrid[1], Damián Andrés[1], Ferrando Rodolfo[1], Falasco Germán[1], Urrutia Leandro[1], Gambini Juan Pablo[1], Duarte Pablo Savio Eduardo[1] and Arredondo Florencia[1]

[1]Área de I+D Biomédico, Departamento de Radiofarmacia, Centro Uruguayo de Imagenología Molecular, Montevideo, Uruguay

Abstract: Alzheimer's Disease (AD) is the most common form of dementia, affecting 5–10% of individuals over 65 years of age. Unfortunately, current therapeutic approaches are exclusively palliative and focus on disease symptoms. An early histopathological feature of AD is a strong glial reactivity, which precedes axonal and synaptic dysfunction and underpins the neuroinflammatory microenvironment alongside the neurodegenerative process. In our effort to understand the role of glia in neurodegeneration and to find novel diagnostic and therapeutic strategies to address AD, we conducted a longitudinal *in vivo* study to analyze its progression in the 3xTg-AD mouse model. This transgenic model combines the mutant transgenes hAPP (Swedish), PSEN1 (MM146V), and tau (P301L), recapitulating Aβ and tau pathologies in brain regions associated with AD. We performed PET/MRI neuroimaging studies in transgenic and control female mice using [18F]-FDG to evaluate cerebral glucose metabolism during disease progression, [11C]-DED to detect changes in astroglial reactivity, and [11C]-PIB to visualize Aβ plaque formation, as well as MRI images to analyze structural modifications. Our preliminary results showed significant changes in brain images obtained at the cortical level between non-Tg and 3xTg animals in aged mice, evidencing functional changes throughout disease progression, which correlates with immunohistochemical observation of Aβ plaques and markers of interest for AD.

Keywords: Alzheimer´s disease, neuroinflammation, transgenic mice model, PET/MRI.

Detection and Characterization of *Turnip Yellow Virus* in Rapeseed Crops from Uruguay

Delfino Jimena[1], Silva Horacio[2], Ponce de León Inés[1], Hoffman Esteban[3], Cibils Ximena[4], Stewart Silvina[4] and Agorio Astrid[1]

[1]Departamento de Biología Molecular, Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay; [2]Facultad de Agronomía, Estación experimental Mario A. Cassinoni, Paysandú, Uruguay; [3]Unicampo Uruguay, Paysandú, Uruguay; [4]Instituto Nacional de Investigación Agropecuaria, La Estanzuela, Colonia, Uruguay

Abstract: Rapeseed (*Brassica napus*) is primarily cultivated for the production of vegetable oil, biodiesel, and animal feed. It ranks second only to soybeans in global oilseed production and is one of the main winter crops in Uruguay. However, rapeseed does not reach its full yield potential worldwide, and the infection by *Turnip Yellows Virus* (TuYV) is believed to

be a major contributor to this yield reduction. The symptoms of this infection (yellowing, leaf reddening, interveinal chlorosis, and stunted growth) are easily mistaken for those caused by abiotic stress, making molecular techniques essential for accurate detection.

In 2023, our group reported the presence of TuYV in Uruguay for the first time. Here, we present the results obtained to date from the study of plants in ten fields along the western littoral of Uruguay, in the departments of Paysandú, Río Negro, and Colonia, during the 2023 and 2024 growing seasons. Virus detection was carried out using RT-PCR with three sets of primers, yielding reproducible results with two of them, which were further confirmed by DAS-ELISA. Additionally, phylogenetic analysis of TuYV genomic fragments identified in Uruguay and TuYV sequences from other parts of the world revealed high genetic variability of TuYV in Uruguay.

Having a reliable virus detection system is key to establishing effective agronomic strategies and minimizing economic losses. The findings reported here have contributed to the agricultural sector in that regard.

Keywords: *Turnip Yellows Virus*, *Brassica napus*, RT-PCR, DAS-ELISA, phylogeny.

Genomic Surveillance of Canine Distemper Virus in Latin America

Escardó Josefina[1], Condon Emma[1], Grecco Sofía[1], Enciso Javier[2], Aldaz Jaime[3], Bucafusco Danilo[4], Pérez Ruben[1] and Panzera Yanina[1]

[1]Sección Genética Evolutiva, Facultad de Ciencias, Universidad de la República; [2]Universidad Científica del Sur, Lima, Perú and Clínica Veterinaria Enciso, Perú; [3]Escuela de Medicina Veterinaria y Zootecnia, Facultad de Ciencias Agropecuarias, Universidad Estatal de Bolívar, Guaranda, Ecuador; [4]Cátedra de Virología, Facultad de Ciencias Veterinarias, Universidad de Buenos Aires, Argentina

Abstract: Canine Distemper Virus (CDV), a member of the genus *Morbillivirus* within the family *Paramyxoviridae*, causes a severe multisystemic disease in domestic dogs and affects various carnivore species, often leading to high mortality rates. Its single-stranded RNA genome encodes six structural and two non-structural proteins. Classification, primarily based on the hemagglutinin (H) glycoprotein, identifies 17 global lineages.

Our Evolutionary Genetics Laboratory developed an innovative multiplex-PCR-NGS system for recovering complete CDV genomes directly from biological samples. We employed this method to obtain 34 complete genomes from strains across various Latin American countries, primarily from domestic dogs and one wild carnivore. These genomes, representing three distinct lineages, include the first fully sequenced genomes from several countries, significantly expanding regional genomic data.

Since the first CDV genome was deposited in a public database in 1997, only 259 complete genomes have been reported worldwide. Our NGS system represents a transformative advancement in CDV genomic characterization, enabling high-throughput sequencing and real-time surveillance. These findings enhance the understanding of CDV epidemiology and molecular evolution, offering critical insights for improved prevention and control strategies. By safeguarding animal health, supporting biodiversity conservation, and aligning with the One Health framework, this study underscores the importance of genomic surveillance in managing zoonotic and wildlife diseases.

Keywords: Canine distemper virus, NGS, genomic surveillance.

In Vitro Studies on the Role of Copper Complexation in the Antitumor Activity of Phenanthroline and Derivatives

Collazo Victoria[1], Brooks Lirka[1], Palmeira-Mello Marcos V.[2], Arandia Inés[1], Fernández Carlos Y.[1], Alvarez Natalia[1], Ellena Javier[3], Costa-Filho Antonio J.[4], Batista Alzir A.[2], Facchin Gianella[1]

[1]Á. Química Inorgánica, Departamento Estrella Campos, Facultad de Química, Universidad de la República; [2]Departamento de Química, Federal University of São Carlos, São Carlos, Brazil; [3]São Carlos Institute of Physics, University of São Paulo, São Carlos, Brazil; [4]Ribeirão Preto School of Philosophy, Science and Literature, University of São Paulo, Ribeirão Preto, Brazil

Abstract: Diimines, such as phenanthroline (phen) and its derivatives, are widely used in inorganic medicinal chemistry in the search for antitumor compounds, often as ligands in metal complexes. There is ongoing debate over whether the cytotoxic activity of copper coordination compounds with diimines is due to the intact complex, the ligand itself, whether the metal delivers the ligand into the cell or vice versa, or whether the coordination is lost before the copper or the ligand reaches the cell. Our research group, as part of the development of new compounds with antitumor activity, aims to understand the role of Cu-diimine-coligand systems in biological activity. In this study, we present results obtained for the Cu-diimine-dipeptide system (diimines: phen, methylphen, neocuproine, and tetramethylphen; and various dipeptides), which showed potent cytotoxic activity in tumor cell cultures. We investigated the cytotoxicity in human ovarian cancer A2780 cell cultures of the free diimines and their complexes under different medium compositions and incubation times. Additionally, we explored the relationship between *in vitro* DNA binding (determining binding constants and viscosity changes) and cytotoxicity. Our findings confirmed the central role of the Cu-diimine complex in the cytotoxic activity of both the free diimines and their complexes. The complexes bind to DNA *in vitro*, and the interaction is mediated by the Cu-diimine complex; however, no clear correlation was found between DNA binding parameters and cytotoxicity.

Keywords: Copper complexes, phenanthroline, cytotoxic activity.

Effect of Light Intensity and Salinity on a Toxic Cyanobacterium

Fernandez Sofía and Bonilla Sylvia

Limnology Section, IECA, Faculty of Sciences, Universidad de la República

Abstract: Toxic cyanobacterial blooms are an increasing environmental problem, affecting water quality and human health. Large coastal ecosystems, such as the Río de la Plata estuary (Uruguay), are frequently impacted by these blooms. The use of *in vivo* pigments is an essential tool for monitoring in these highly dynamic environments. Chlorophyll *a* and phycocyanin are commonly used as proxies for cyanobacterial biomass. However, the cellular content of these pigments may vary depending on the organisms' responses to environmental changes, such as light intensity and salinity. This study evaluated the effect of light intensity and salinity on the performance of a toxic cyanobacterium (Microcystis cf. aeruginosa, MVCC42). A factorial experiment was conducted under different combinations of light intensity (15 and 45 μmol m^{-2} s^{-1}) and salinity (0, 2, 4, and 8 g/L NaCl). Response variables included growth rate, cellular pigment content (phycocyanin and chlorophyll a), colony morphology, and total microcystin concentration. Results indicate that light is the main modulator of growth, serving as an essential resource for these organisms, with significantly higher rates under high light intensity conditions. Salinity had a secondary effect, interacting with light intensity by reducing growth, altering colony morphology, and modifying cellular pigment content. Under higher salinity conditions, combined with both high and low light levels, a decrease of up to 40% in chlorophyll *a* content and 50% in phycocyanin was observed. No differences in total microcystin concentrations were found that could be attributed to the treatments. These findings may have implications for pigment-based environmental monitoring, as variations in these compounds could lead to incorrect inferences about biomass, underestimating the potential risk of toxin exposure. Understanding these effects is essential for enhancing the management and control of cyanobacterial blooms.

Keywords: Microcystis, phycocyanin, salinity.

Epigenetic Regulation of Astrocytic Homeostasis in Epileptogenesis: A Focus on DNA Methylation

Gomez DD[1,2], Rossi A[1], Villarreal A[1], D´Alessio L[1], Ramos, AJ[1]

[1]IBCN UBA-CONICET, Facultad de Medicina, Universidad de Buenos Aires; [2]LIN - UAC, Universidad Andina del Cusco

Abstract: Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures, resulting from an imbalance between excitatory and inhibitory neuronal activity. Despite the availability of Antiepileptic Drugs (AEDs), approximately 30% of patients remain pharmacoresistant, with no effect on disease progression. Temporal Lobe Epilepsy (TLE), the most prevalent focal epilepsy, is commonly preceded by an Initial Precipitating Event (IPE) in early life, followed by a silent period during which epileptogenesis occurs. This latent phase involves progressive glial and neuronal remodeling that contributes to long-term seizure susceptibility.

Here, we investigated the role of DNA methylation in astroglial dysfunction during epileptogenesis. Human cortical tissue from drug-resistant TLE patients showed astrocyte-specific DNA hypermethylation. Using the lithium-pilocarpine model in rats, we observed astroglial DNA hypermethylation at 7, 21, and 35 days post-IPE. Immunohistochemistry revealed reduced expression of key homeostatic proteins (Kir4.1, AQP4), together with reactive gliosis and neurodegeneration.

In vitro, primary astrocyte cultures exposed to HMGB1—a DAMP released from injured neurons—exhibited persistent DNA hypermethylation, elevated IL-1β and IL-6 levels, and increased Dnmt1, Dnmt3a, and MAFG expression. These changes persisted for at least 7 days and were associated with transcriptional silencing of key astrocytic genes (LDHA, GS, Kcnj10, Slc16a1, Aqp4), confirmed by promoter-specific methylation analysis. Treatment with decitabine (100 μM) restored gene expression, suggesting a causal role of DNA methylation in astrocytic dysfunction.

Our findings demonstrate that astrocytes undergo sustained epigenetic alterations during epileptogenesis, compromising their homeostatic roles. Targeting DNA methylation may represent a promising therapeutic approach to mitigate glial dysfunction in epilepsy.

Keywords: Astrocytes, DNA methylation, epilepsy, homeostasis, epigenetics.

Isolation and Characterization of Virulent Phages Against Multidrug-resistant and Biofilm-producing Uropathogenic Bacteria

Gutiérrez María Victoria[1,2], Olivera Álvaro[3], Perbolianachis Paula[1,2], Rey Sebastián[1,2], Megrián Daniela[4] and Echeverría Natalia[1,2]

[1]Laboratorio de Virología Molecular, Centro de Investigaciones Nucleares, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [2]Laboratorio de Evolución Experimental de Virus, Institut Pasteur de Montevideo, Montevideo, Uruguay; [3]Laboratorio de Alta Resolución, Centro Universitario Regional Este, Universidad de la República, Rocha, Uruguay; [4]Unidad de Bioinformática, Institut Pasteur de Montevideo, Montevideo, Uruguay.

Abstract: Urinary tract infections are among the most common in humans, and in recent years, antimicrobial resistance has increased drastically, sometimes complicating treatment. In this context, phage therapy has emerged as a promising alternative. The aim of this study was to isolate and characterize virulent (strictly lytic) bacteriophages with activity against *Klebsiella pneumoniae* and *Escherichia coli*, as an initial approach to identifying potential biotherapeutic agents. Water samples from two wastewater treatment plants in Uruguay were used, leading to the isolation of 13 phages active against *Klebsiella pneumoniae* and 4 against *Escherichia coli*. Host range assays revealed that one-third of the clinical isolates tested were susceptible to at least one phage from the collection, including uropathogenic strains. All phages were evaluated for their ability to eradicate biofilms, and some of them achieved a reduction of approximately 50% in biofilm biomass. Four phages were selected for further characterization. Transmission electron microscopy showed that all exhibited myovirus morphology (icosahedral head and contractile tail). Thermal and pH stability assays indicated that some phages

remained stable across a wide range of conditions. Finally, genome sequencing using Oxford Nanopore Technologies enabled the determination of genome sizes and lifestyles. All phages were found to be strictly lytic, lacking virulence and resistance genes, with genome sizes ranging from 45 to 180 kb. This study represents one of the first in our country to characterize local phages with bactericidal activity against human pathogens, identifying phages with promising traits for use as biocontrol agents.

Keywords: Bacteriophages, phage therapy, uropathogens, biofilm, antibiotic resistance.

TgGSK, an Essential Regulator of Centrosome Segregation and Cell Division in *Toxoplasma Gondii*

Horjales Sofía[1], Krueger Amanda[2], Arrizabalaga Gustavo[3] and Francia María E.[1,4]

[1]Laboratorio de Biología de Apicomplejos. Institut Pasteur de Montevideo. Montevideo, Uruguay; [2]Department of Pharmacology and Toxicology, Indiana University School of Medicine. Indiana, USA; [3]Department of Microbiology and Immunology, Jacobs School of Medicine and Biomedical Sciences, University of Buffalo, New York, USA; [4]Unidad Académica de Parasitología y Micología. Facultad de Medicina. Universidad de la República, Montevideo, Uruguay

Abstract: *Toxoplasma gondii* is an obligate intracellular parasite and the causative agent of toxoplasmosis, a disease with serious consequences in immunocompromised individuals and in congenital infections. Current treatments only control the acute phase, while the chronic phase is refractory to them. The asexual multiplication of the parasite within cells, its main mechanism of pathogenesis, occurs by endodyogeny, a type of semi-closed mitosis with internal formation of daughter cells. This process is regulated by local physical anchors and, globally, by kinases and transcription factors, with the centrosome as the physical 'master' regulator of division.

TgGSK is a promising therapeutic target, being more similar to plant kinases than to its mammalian counterparts. In this study, we characterized TgGSK and demonstrated its essentiality for *T. gondii* endodyogeny. Its localization varies during the cell cycle: in interphase, it is nuclear, while during division, it is redistributed to the cytoplasm, concentrating in centrosomes and the basal pole. Conditional depletion of TgGSK alters the synchrony of division, centrosome duplication, and organelle segregation, leading to the death of the parasite.

TgGSK-dependent phosphorylation was identified in key proteins for RNA processing, centrosome function, and the basal pole. Transcriptomic studies reinforce its possible role as a splicing regulator. TgGSK interacts with the acetyltransferase GCN5b, whose inhibition causes TgGSK degradation, suggesting regulation by acetylation. We are currently exploring the link between TgGSK and differentiation into bradyzoites, the latent stage of the disease.

Reference: Krueger, A*., Horjales, S*., Yang, C., Blakely, W. J., Francia, M. E., & Arrizabalaga, G. (2025). The essential kinase TgGSK regulates centrosome segregation and endodyogeny in Toxoplasma gondii. mSphere, 10(4), e0011125. https://doi.org/10.1128/msphere.00111-25

Keywords: *Toxoplasma gondii*, endodyogeny, centrosome, kinases, cell cycle.

Impact of Ivermectin on Standard Metabolic Rate (SMR) in the Dung Beetle *Onthophagus Hircus*

Jabs Mathias[1], González-Vainer Patricia[1], Suárez Gonzalo[2] and Clavijo-Baquet Sabrina[3]

[1]Entomology Section, Faculty of Sciences, Universidad de la República, Iguá 4225, 11400 Montevideo, Uruguay; [2]Pharmacology and Therapeutics Unit, Faculty of Veterinary Medicine, Universidad de la República, Ruta 8 km 18, 13000 Montevideo, Uruguay; [3]Ethology Section, Faculty of Sciences, Universidad de la República, Iguá 4225, 11400 Montevideo, Uruguay

Abstract: Exposure of organisms to toxic contaminants, such as veterinary antiparasitic drugs (e.g., Macrocyclic Lactones), leads to an increase in the production of antioxidants and stress proteins, thereby increasing their metabolism. Dung beetles of the Scarabaeidae family play a key role in agricultural ecosystems by incorporating nutrients into the soil through the breakdown of ruminant feces. Previous studies have shown that exposure to Ivermectin (IVM) in a dung beetle increases the standard metabolic rate (SMR), which reduces the energy available for other functions and could lead to trade-offs with reproduction. This study evaluated the effect of acute IVM exposure in *Onthophagus hircus*. Twenty-six individuals of *O. hircus* were exposed to cattle dung without lactone (control) and with IVM (0.05 ppm). CO_2 production was recorded to estimate SMR (mL/h.g) weekly for 4 weeks in a crossover design: 2 treatments (Control *vs*. IVM), 2 sequences, 4 periods (weeks). SMR in *O. hircus* was negatively affected by the treatment (0.773 ± 0.425 control *vs*. 0.592 ± 0.304 IVM; p = 0.007), with a sequence effect (0.828 ± 0.443 CICI *vs*. 0.526 ± 0.202 ICIC; $p = 0.0001$) and no period effect ($p = 0.19$). This reduction indicates negative metabolic consequences that could potentially affect the biological status and, consequently, the long-term ecological sustainability of agricultural systems.

Keywords: Metabolism, ivermectin, dung beetles, standard metabolic rate, agricultural ecosystems.

Antidepressant Effect of Ibogaine in Female Rats According to the Estrous Cycle Phase

Lacurcia Clara[1,2], Mesa Juan Manuel[3], Carrera Ignacio[3], Agrati Daniella[2], Prieto José[1]

[1]Neuroscience Laboratory, School of Science, Universidad de la República, Montevideo, Uruguay; [2]Physiology and Nutrition Section, School of Science, Universidad de la República, Montevideo, Uruguay; [3]Department of Organic Chemistry, School of Chemistry, Universidad de la República, Montevideo, Uruguay

Abstract: Currently, the therapeutic potential of psychedelics is being increasingly explored. Among substances of growing interest is ibogaine, an atypical psychedelic obtained from the root of the *Tabernanthe iboga* shrub. While acute administration of ibogaine has been reported to induce an antidepressant-like effect in male rats, there is a gap in the preclinical literature regarding its antidepressant potential in female rats. This is highly relevant, since ovarian steroids modulate the activity of numerous neurotransmission systems involved in the action of psychedelic drugs. The present study evaluated the hypothesis that ibogaine exerts an antidepressant-like effect in female rats and that its intensity varies according to the estrous cycle phase. Adult female cycling rats (Wistar) received a single administration of ibogaine (40 mg/kg, intraperitoneal) or its vehicle during the proestrus or metestrus phases, characterized by high and low plasma estrogen levels, respectively. Animals were evaluated four hours post-injection in the forced swimming test. Ibogaine induced a decrease in immobility time in both estrous cycle phases, associated with an increase in swimming behaviour only in metestrus females. These findings suggest that ibogaine possesses an antidepressant-like effect in female rats, with differential behavioural manifestations according to the estrous cycle phase. This indicates that the endocrine profile of female rats may modulate the effects of this psychedelic.

Keywords: Psychedelic, ibogaine, estrous cycle, depression.

Computational Analysis of Cell-Cell Interactions from scRNA-seq Data

Moreno Laura[1,2,3], Russo Sofía[1,2], Naya Hugo[3,4,5], Segovia Mercedes[1,2], Hill Marcelo[1,2] and Rego Natalia[3,4]

[1]Unidad Académica de Inmunobiología, Facultad de Medicina, Universidad de la República, Uruguay; [2]Laboratorio de Inmunorregulación e Inflamación, Institut Pasteur de Montevideo, Uruguay; [3]Unidad de Bioinformática, Institut Pasteur de Montevideo, Uruguay; [4]Laboratorio de Genómica Evolutiva, Facultad de Ciencias, Universidad de la República, Uruguay; [5]Departamento de Producción Animal y Pasturas, Facultad de Agronomía, Universidad de la República, Uruguay

Abstract: Cell-Cell Communication (CCC) is an essential component of biological systems, regulating key processes such as immunity, homeostasis, and development. Single-cell transcriptomics (scRNA-seq) has revolutionized the study of CCC by enabling the inference of ligand-receptor interactions at an unprecedented resolution. This study proposes the development of a flexible and modular bioinformatics pipeline for the systematic analysis of CCC in scRNA-seq data, integrating multiple complementary tools, such as CellPhoneDB, CellChat, Scriabin, NicheNet, MEBOCOST, and MultiNicheNet. Additionally, methods will be incorporated to generate consensus across tools and interactive visualizations to facilitate biological interpretation. The pipeline will be applied to data generated by our group, including *in vitro* differentiated Th17 cells from WT and Tmem176b$^{-/-}$ mice, in order to study how the deletion of the TMEM176B ion channel affects communication between these cells and other immune populations. Public datasets of murine immune cells will also be integrated using robust methods such as STACAS, CCA, and Harmony. This computational strategy aims to generate biologically relevant hypotheses that can be experimentally validated in the future. We will present the progress on integrating and annotating our own data with public datasets, as well as the implementation of the CCC analysis pipeline.

Keywords: ScRNA-seq, cell-cell interactions, TMEM176B.

Adaptation of scRNA-Seq Protocols for the Study of Axonal Transcriptomes

Ortiz Natalia[1], Garat Joaquín[1], Sotelo Silveira[1], José Roberto[1]

[1]Department of Genomics, Instituto de Investigaciones Biológicas Clemente Estable, MEC, Montevideo, Uruguay

Abstract: The study of axonal RNA is key to understanding neuronal function. By adapting single-cell transcriptomics protocols and microdissection of axoplasm bundles, we aim to obtain high-quality axonal transcriptomes at single-axon resolution. The Smart-seq2 protocol, designed for single-cell RNA-seq, is ideal due to its high RNA capture efficiency. Initially, we amplified RNA from axoplasm bundles (~30 axons) down to individual axons. After obtaining cDNA, we analyzed it using capillary electrophoresis and qPCR with neuronal (Nefh, Sb2b) and glial (Mag, Skap) markers, confirming sample purity and absence of glial contamination. Electrophoresis profiles suggest variations in transcriptome composition depending on the amount of starting material. Most samples displayed peaks around 900 bp, consistent with expected profiles. We then built libraries and sequenced them at low depth to evaluate which transcripts are captured and potential biases affecting the protocol. Results indicate that the protocol enables the detection of transcripts from single axons and improves the quality of the obtained transcriptomes. This approach opens new avenues for studying heterogeneity in axonal gene expression. The ability to analyze transcriptomes from such low RNA amounts (< 1 pg) represents a significant advancement for molecular neuroscience, enabling studies on RNA regulation and localization in individual axons.

Keywords: Axonal RNA, Smart-seq2, axonal heterogeneity, single-axon transcriptome.

A New AI-based Method for Tracking Changes in Nuclear Orientation in CAL27 Cells

Parietti, Felipe[1], Silva Alejandro[2], Llaguno Juan[2], Demczylo Roman[2], Gaál Belén[2], Fernández Ariel[2], Alonso Julia[2], Hochmann Jimena[3] and Arocena Miguel[1]

[1]Departamento de Biología Odontológica, Facultad de Odontología, Universidad de la República, Uruguay; [2]Instituto de Física, Facultad de Ingeniería, Universidad de la República, Uruguay; [3]Departamento de Patología Molecular Estomatológica, Facultad de Odontología, Universidad de la República, Uruguay

Abstract: The orientation and dynamics of the cell nucleus are intimately linked to cellular physiology and disease states, including cancer. In this study, we developed an artificial intelligence framework to quantitatively analyze nuclear rotation in oral squamous carcinoma cells (CAL27) under various stress conditions. CAL27 cells were cultured in low-glucose DMEM at 37 °C, 5% CO_2, and seeded at high confluence. Using a label-free quantitative holotomographic microscope, nuclei were tracked over 48 hours with one-minute temporal resolution. A deep learning model was trained for segmentation and tracking of nuclei, and the moment of inertia tensor was computed to infer orientation changes over time. This enabled the calculation of the Mean Squared Angular Displacement (MSAD), a rotational analogue to the mean squared displacement. All treatments tested (hypoxia, cisplatin, and rotenone) led to increased MSAD compared to untreated cells, with rotenone showing the most pronounced effect. These results suggest a disruption in cytoskeletal components responsible for nuclear anchoring, potentially reflecting mechanical responses to cellular stress. This method offers a robust approach for characterizing nuclear dynamics and may reveal novel biophysical markers relevant to carcinogenesis.

Keywords: Nuclear rotation, holotomographic microscopy, artificial intelligence.

Association Between the Circadian System and Depression

Paz Valentina[1,2], Garfield Victoria[3], Tassino Bettina[2,4] and Silva Ana[2,5]

[1]Instituto de Psicología Clínica, Facultad de Psicología, Universidad de la República, Montevideo, Uruguay; [2]Grupo Cronobiología, Comisión Sectorial de Investigación Científica, Universidad de la República, Montevideo, Uruguay; [3]Department of Pharmacology and Therapeutics, University of Liverpool, Liverpool, UK; [4]Sección Etología, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [5]Laboratorio de Neurociencias, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay

Abstract: The circadian system regulates the endogenous rhythms of various bodily functions. Disruption of this system has been associated with depression. However, it remains unclear which circadian alterations are most strongly associated with depression, and whether they are causally related. This study investigates the association between circadian rhythms and depressive symptoms in Uruguayan youth and explores the bidirectional causal association between circadian rhythms and depression in adults from the United Kingdom. Uruguayan youth were studied as a special model due to their extreme eveningness, using psychological interviews, subjective methods (self-report instruments), and objective methods (actigraphy, hormonal samples, and body temperature measurements). Additionally, data from 408,480 adults in the UK Biobank were analyzed using Mendelian randomization. First, an association between circadian rhythms and depressive symptoms was observed in Uruguayan youth, highlighting their eveningness, poor sleep quality and duration, and the presence of insomnia symptoms. Second, a bidirectional causal association between depression and insomnia symptoms was found in the UK Biobank cohort. This work contributes to the understanding of the association between circadian rhythms and depression, addressing this link comprehensively by applying diverse methodological approaches. Furthermore, it enhances our knowledge of the pathogenic processes underlying depression, identifying potential markers of this disorder that could aid in developing more effective strategies for its prevention, diagnosis, and treatment.

Keywords: Depression, circadian rhythms, sleep.

CD8$^+$ T Cells as Key Mediators of *Salmonella*-induced Antimetastatic Protection in a Murine Melanoma Model

Plata María Clara[1], Mónaco Amy[1], Chabalgoity José Alejandro[1] and Moreno María[1]

[1]*Unidad Académica de Desarrollo Biotecnológico, Instituto de Higiene, Facultad de Medicina, Universidad de la República, Montevideo, Uruguay*

Abstract: *Salmonella* has been studied as an immunotherapy for various types of cancer. In our group, we demonstrated that an attenuated strain of *S.* Typhimurium (*aroC* mutant strain, LVR01) may be an interesting alternative, especially against melanoma. We observed delayed tumor growth and prolonged survival in animals with melanoma, although its effect is transient and limited, and does not achieve complete remission. However, when the primary tumor is surgically removed, neoadjuvant treatment with LVR01 reduces the development of metastases, allowing complete recovery.

To study the mechanism of protection against tumor spread, we used B16F1 and B16F10, melanoma models. Once the tumor became palpable, an intratumoral dose of LVR01 ($1x10^6$ CFU) was administered. The primary tumor was subsequently removed, and disease progression was evaluated.

The treatment provided protection against the development of B16F10 lung metastases and conferred partial specific protection against a challenge with a homologous tumor in the B16F1 model. Furthermore, the generated immunity was transferable through splenocytes from previously treated mice. Although the immune response was independent of IFN-γ and CD8$^+$ T cells during primary tumor treatment, both effectors were essential for developing effective protection against metastatic disease, as their absence increased metastasis incidence and reduced animal survival. These results highlight the potential of *Salmonella* LVR01 to induce antitumor responses at different stages of the disease, where multiple cellular and molecular effectors play key roles. Understanding these mechanisms may facilitate their application in clinical therapies.

Keywords: Salmonella, immunotherapy, melanoma, metastases.

Evaluation of the Lytic Capacity of *Klebsiella Pneumoniae* Phages on Local Multidrug-resistant and Biofilm-forming Clinical Strains

Rey Sebastián[1,2], Gutiérrez María Victoria[1,2], Perbolianachis Paula[1,2], Megrián Daniela[3] and Echeverría Natalia[1,2]

[1]*Laboratorio de Virología Molecular, Centro de Investigaciones Nucleares, Facultad de Ciencias, Universidad de la República;* [2]*Laboratorio de Evolución Experimental de Virus, Institut Pasteur de Montevideo;* [3]*Unidad de Bioinformática, Institut Pasteur de Montevideo*

Abstract: The introduction of antibiotics was crucial for controlling infections, but the resistance of *Klebsiella pneumoniae* to all current antimicrobials has prompted the use of bacteriophages as a therapeutic alternative. In this study, the lytic capacity of six *K. pneumoniae* phages isolated in the United Kingdom was evaluated on 25 local multidrug-resistant and biofilm-forming clinical strains. Roth 8 and Roth 23 phages showed the widest host ranges, productively infecting eight strains, and were selected to further evaluate their stability at different pH values and temperatures. Both demonstrated stability at pH 5, 7, 9, and 11, and at temperatures of 4°, 25°, 37°, and 42°C, but were inactivated at pH 3 and showed decreased viability at 60°C. The ability of the 8 susceptible strains to form biofilms was evaluated, and carbapenemase-producer strain M1443 was found to be a strong biofilm former. Roth 23 showed the highest plating efficiency in this strain, so its ability to eradicate preformed biofilms at different concentrations was evaluated. The results showed a significant decrease in biomass at the highest phage concentration used. Likewise, infection curve assays showed early control of bacterial growth, with complete inhibition at high MOIs. However, resistant strains emerged after 4-5 hours of infection in all cases. Finally, Roth 23 was sequenced to verify the absence of changes in its sequence compared to the original (GenBank

accession number: PQ657796). This study suggests that Roth 23 is a promising candidate for the biocontrol of *K. pneumoniae* strain M1443 and other similar strains.

Keywords: Biofilms, phages, biocontrol, multiresistant.

β-lactamase-mediated Hydrolysis of Cefiderocol: Insights from Nuclear Magnetic Resonance Spectroscopy

Rodríguez, Magdalena[1], Warecki Brenda[2], Ruggiero Melina[3], Mahler Graciela[1], Hernandez Gonzalo[4], Vila Alejandro J.[2], Power Pablo[3] and Bonomo Robert A.[5]

[1]Laboratorio de Química Farmacéutica, Departamento de Química Orgánica, Facultad de Química, Universidad de la República, Montevideo, Uruguay; [2]Instituto de Biología Molecular y Celular de Rosario, CONICET - Universidad Nacional de Rosario, Rosario, Argentina; [3]Instituto de Investigaciones en Bacteriología y Virología Molecular, Universidad de Buenos Aires, Buenos Aires, Argentina; [4]Laboratorio de Resonancia Magnética Nuclear, Departamento de Química Orgánica, Facultad de Química, Universidad de la República, Montevideo, Uruguay; [5]Department of Medicine, Case Western Reserve University, Cleveland, United States

Abstract: Cefiderocol (CFD) is a novel cephalosporin antibiotic, approved by the FDA in 2019 and indicated for the treatment of infections caused by carbapenem-resistant Gram-negative bacteria. It was designed as a siderophore analogue, allowing its uptake in the periplasm through iron transporters. Despite its recent approval, the emergence of resistance has been reported, driven by mutations in iron transporters and, more recently, by expression of metallo-β-lactamases such as NDM and serine-β-lactamases like PER.

This work focuses on the study of the hydrolysis mechanism of Cefiderocol mediated by class A (PER-2) and class B (NDM-1, VIM-2, IMP-1) β-lactamases, using Nuclear Magnetic Resonance (NMR) spectroscopy.

PER-2, NDM-1, IMP-1, and VIM-2 enzymes were expressed in E. coli BL21 (DE3) cells and purified by affinity chromatography. NMR experiments were performed on Bruker Avance NEO 400 MHz or Avance III 700 MHz spectrometers. Spectra were acquired in buffer and 10% D_2O using standard pulse sequences and water suppression conditions, with 20 mM CFD and 25 μM enzyme.

NMR experiments show that all tested β-lactamases are capable of hydrolyzing CFD into a single product, which was fully characterized. This product, common to both enzymatic and alkaline hydrolysis of CFD, presents a highly reactive site, prone to forming adducts with the enzyme.

This work aims to contribute to the understanding of β-lactamase-mediated resistance mechanisms to Cefiderocol, which is critical to preserve the clinical efficacy of this novel agent.

Keywords: Antibiotic resistance, carbapenemases, cefiderocol.

Pharmacogenetic Variants in the Uruguayan Population

Rodríguez de Ávila Lucas Ignacio[1], Colistro Valentina[2], Burgueño-Rodríguez Gabriela[1], Luna-Andrade Lorena[3], Solé-Sanjurjo Horacio[3], Sans Mónica[4], Abayubá da Luz Julio[1] and Soler Ana María[1]

[1]Laboratorio de Genética Molecular Humana, Departamento de Ciencias Biológicas, CENUR Litoral Norte, Universidad de la República (Universidad de la República), Salto, Uruguay; [2]Departamento de Medicina preventiva y Social, Facultad de Medicina, Universidad de la República (Universidad de la República), Montevideo, Uruguay; [3]PDU de Diversidad Genética Humana, CENUR Noreste, Universidad de la República (Universidad de la República), Tacuarembó, Uruguay; [4]Departamento de Antropología Biológica, Facultad de Humanidades y Ciencias de la Educación, Universidad de la República (Universidad de la República), Montevideo, Uruguay

Abstract: Pharmacogenetics studies how genetic variants influence drug response, emphasizing those related to absorption, distribution, metabolism, and excretion. The frequency of many of these variants differs among various global populations, making it difficult to extrapolate data from one population to another. Particularly, Uruguay is a tri-hybrid population with a majority component of European origin, followed by Amerindian and African components. This structure suggests that, in our population, diverse variants may coexist with frequencies different from those reported for other populations. This study aims to analyse the presence of variants in 21 pharmacogenes categorized at Level A by the Clinical Pharmacogenetics Implementation Consortium (CPIC) in 201 Uruguayans from different regions of the country. These individuals were genotyped using an Axiom array (Axiom Spain Biobank Array), which includes approximately 800,000 polymorphisms (SNPs) distributed throughout the genome. Of the 914 SNPs present in these pharmacogenes, 662 were found in the 1000 Genomes database, and 16 of them, located in 8 of the 21 pharmacogenes (CYP2C9, CYP2D6, CYP2B6, CYP2C19, CYP3A5, DPYD, TPMT, and SLCO1B1), were associated with actionable pharmacogenetic variants according to CPIC. 85% of individuals (171) presented at least one actionable pharmacogenetic variant, while 51% were carriers of at least two variants. These results highlight the importance of understanding the pharmacogenetic variants that segregate in different populations to adapt therapy according to genotype and advance towards personalized medicine.

Keywords: Pharmacogenetics, Uruguayan population, ancestry, genetic variants.

Functional Assessment of BAG Genes in *Physcomitrium Patens via CRISPR/Cas9*

Rondán Santiago[1], Saavedra Laura[2,3], Castro Alexandra[1]

[1]Laboratorio de Biología Molecular Vegetal, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay; [2]Unidad de Estudios Agropecuarios (UDEA), Unidad Ejecutora de Doble Dependencia INTA-CONICET, Córdoba, Argentina; [3] Cátedra de Fisiología Vegetal, Facultad de Ciencias Exactas, Físicas y Naturales, Universidad Nacional de Córdoba, Córdoba, Argentina

Abstract: Climate change represents one of the greatest environmental challenges with significant consequences for ecosystems and human society. Plants have developed defense mechanisms that allow them to adapt to adverse environmental conditions, which have been crucial for their survival in the terrestrial habitat. Understanding how plants tolerate these adverse conditions is key to developing strategies to mitigate the effects of climate change.

In *Physcomitrium patens*, we identified ten *PpBAG* genes, a family of highly conserved anti-apoptotic proteins known to interact with HSP70 and modulate processes such as Programmed Cell Death (PCD). Transcriptomic analysis revealed that four of these genes (*PpBAG1-3* and *PpBAG8*) are significantly upregulated under heat stress and during recovery. To further investigate, we used CRISPR/Cas9 technology to generate knockout mutants for *PpBAG1, 2, 3,* and *8* in wild-type *P. patens* and in the Atg8:GFP line. This will allow us to monitor autophagy and phenotypically characterize the mutants to elucidate the role of *PpBAG* in stress adaptation and PCD regulation.

This research aims to enhance our understanding of the genetic basis of stress tolerance in plants, contributing to the development of crops with improved resilience to climate change.

Keywords: BAG genes, heat stress, *Physcomitrium patens*, climate change, CRISPR/Cas.

Evaluation of Cell Proliferation in the Olfactory Bulb of *Austrolebias Charrua* Exposed to Glyphosate

Rosillo, Juan Carlos[1,2], Hayek, Emilia[3], Berrosteguieta Inés[4,5], Silva Stephanie[4], Herrera-Astorga Laura[4,6], Leites Ana Paula[2], Hernández Karina[2], Montero Lucía[2], Casanova Gabriela[7], Olivera-Bravo Silvia[8] and Fernández Anabel[3,4]

[1]Confocal and Epifluorescence Microscopy Platform, Instituto de Investigaciones Biológicas Clemente Estable (IIBCE), Montevideo, Uruguay; [2]Academic Unit of Histology and Embryology, School of Medicine, Universidad de la República (Universidad de la República); [3]Neuroscience Laboratory, Faculty of Sciences, Universidad de la República, Montevideo, Uruguay; [4]Comparative Neurobiology Laboratory, Department of Integrative and Computational Neurosciences, IIBCE and Faculty of Sciences, Universidad de la República, Montevideo, Uruguay; [5]ESFUNO Curricular Unit, School of Nursing, Faculty of Sciences, Montevideo, Uruguay; [6]Physiology and Nutrition Section, Faculty of Sciences, Universidad de la República, Montevideo, Uruguay; [7]Electron Microscopy Unit, Faculty of Sciences, Universidad de la República, Montevideo, Uruguay; [8]Department of Neurobiology and Neuropathology, IIBCE, Montevideo, Uruguay

Abstract: Glyphosate is the most widely used herbicide in agriculture, and in Uruguay, it is applied in soybean and rice crops without studies on its accumulation or effects. Native fish living near these crops could serve as environmental biomonitors for glyphosate and other agrochemicals. *Austrolebias charrua* is our model for studying brain neurogenic activity, particularly in the Olfactory Bulb (OB). The OB of fish is directly exposed to substances present in the water. Field studies have shown impairments in various functions in exposed fish. Here, we evaluate whether neuronal turnover in the OB is affected by glyphosate exposure. Two groups were analyzed: 1) fish exposed to glyphosate at a concentration of 1 mg/liter, and 2) control condition fish. Cell proliferation and glial expression in the OB were assessed. Two cell proliferation markers were applied after one week of glyphosate exposure. EdU (7 days) and BrdU (1 day) were used along with glial markers. Both groups of fish were fixed by intracardiac perfusion, OBs were sectioned with a vibratome, immunohistochemistry was performed to reveal the different markers, and EdU+ nuclei were quantified using FIJI software. Our preliminary results showed reduced cell proliferation in the glyphosate-treated group and increased expression of glial markers (n=4 per group). Liver and gill fractions were processed to analyze histological alterations.

Keywords: Cell proliferation, olfactory bulbs, EdU, glyphosate.

Prenatal Care Specified in Flowcharts for the SEPEPE App

Ruiz Evangelina[1], Mañosa Javier[1], Rey Grazzia[1] and Simini Franco[1]

[1]Núcleo de Ingeniería Biomédica de las Facultades de Medicina e Ingeniería, Universidad de la República, Montevideo, Uruguay

Abstract: Prenatal care has helped reduce perinatal morbidity and mortality. However, there is still room to improve the timely detection of high-risk pregnancies and adherence to treatment. Telematics offers new opportunities for patient empowerment, close monitoring, and support.

We present a method to translate prenatal care guidelines into digital specifications in the form of flowcharts. This specification is intended for the implementation of an innovative medical informatics system called *Personalized Perinatal Monitoring* (SEPEPE), designed to meet the same criteria as the *Perinatal Information System* (SIP).

As a diagnostic aid during medical consultations, SEPEPE suggests a profile to every patient, from 12 pathological profiles and one low-risk profile. Associated with each of the 12 profiles, SEPEPE has a *RecetApp*® mobile App, which consists of logical sequences of counseling, referrals, counter-referrals, and reminders that become active during the patient's everyday life.

Based on perinatal care guidelines, we developed 12 flowcharts to be programmed into their respective *RecetApp*®.

RecetApp® extends as a timely and interactive doctor-patient relationship, fulfilling prenatal care standards, since it is installed on the patient's phone during the medical visit. SEPEPE records data in the form of texts or answers triggered by *RecetApp®* at key points during pregnancy. This information is later available to the physician in subsequent consultations, for inclusion in the electronic medical record.

Using SEPEPE, pregnancy documentation is enriched with first-hand information collected by the patient in daily life, and adherence to care is expected to improve.

Keywords: Pregnancy follow-up, antenatal care, treatment adherence, flowchart, computer specifications.

Harmful Blooms in Uruguay: An Approach based on Functional Traits

Santillán Ignacio[1], Sampognaro Lía[2], Terra Rocha Valentina[1], Cabral Agustina[1,3], Ferrari Graciela[3], Segura Angel[1,4], Piccini Claudia[2,4] and Kruk Carla[1,2,4]

[1]Centro Universitario Regional Este (CURE), Universidad de la República, Rocha, Uruguay; [2]Instituto de Ciencias Ambientales, Facultad de Ciencias, Montevideo, Uruguay; [3]Laboratorio Tecnológico de Uruguay (LATU), Montevideo, Uruguay; [4]Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay

Abstract: Harmful Blooms (HB) constitute a long-standing ecological challenge that has intensified in recent decades across aquatic ecosystems worldwide, including Uruguay. HB in freshwater, estuarine, and coastal ecosystems causes adverse effects on human and animal health, as well as significant socioeconomic impacts. The functional trait-based approach provides a robust framework to understand phytoplankton responses to environmental gradients. Functional ecology principles enable the identification of the mechanisms driving HB formation and persistence, as well as the prediction of their occurrence and impacts. Machine Learning (ML) provides a powerful methodological framework for identifying and quantifying non-linear relationships between environmental drivers and HB dynamics while delivering scalable solutions for operational risk assessment in bloom forecasting. This presentation will showcase progress from a doctoral thesis in biological sciences investigating HB and their main drivers across three interconnected systems: the Uruguay River (UR), Río de la Plata estuary (RdlP), and Atlantic coast (AC). An integrated watershed-to-coast assessment of the UR-RdlP-AC continuum will be conducted to address system complexity. Phytoplankton communities will be characterized through functional trait-based classification to develop ML-based predictive algorithms. Outputs will include probabilistic forecasts and management-ready risk maps for bloom mitigation. These models will make it possible to estimate the HB occurrence probabilities and generate spatially explicit risk maps applicable to the design of early-warning systems. These results will support evidence-based strategies to manage and mitigate HB impacts.

Keywords: Harmful blooms, functional traits, machine learning, watershed-to-coast.

Slit1a as a Contributing Factor in Zebrafish Retinal Development

Siciliano Agustín[1], Zolessi Flavio R.[1,2] and Davison Camila[1,2]

[1]Cell Biology of Neural Development Laboratory, Cell Biology Section, Facultad de Ciencias, Universidad de la República.; [2]Institut Pasteur de Montevideo, Uruguay

Abstract: The vertebrate retina presents three cellular layers arranged along the apico-basal axis. The Retinal Ganglion Cell (RGC) layer is the first to differentiate and is located in the basal region of the tissue. The axons of these cells fasciculate and exit the retina, forming the optic nerves, which cross at the midline to create the optic chiasm. The organisation of axons in the optic nerve and chiasm are highly regulated process involving several signalling pathways, with the Slit/Robo pathway standing out. Slit factors are extracellular proteins that interact with transmembrane receptors of the Robo family. These proteins mainly act as repulsive cues for axonal growth. Previous studies from our laboratory have demonstrated the importance of Slit2 and Slit3 in the correct organisation of axons in the optic nerve and chiasm. Based on this, we decided to

analyse the function of a third Slit factor, Slit1a, in optic-pathway organisation during development, using mutants generated by the CRISPR/Cas9 gene editing system. In these mutants, we observed a reduction in the diameter of the optic nerve, associated with a decreased volume of the RGC layer. This seems to indicate that Slit1a has a mechanism of action different from that of Slit2 and Slit3, possibly related to neurogenesis, a hypothesis we are currently investigating. Our studies provide further information on the functioning of the different components of the Slit/Robo pathway in the development of the zebrafish optic pathway.

Keywords: Retina, neurogenesis, axon guidance, Slit/Robo, slit1a.

Water Monitoring and Action Plan for Eutrophication Mitigation in Agricultural Reservoirs

Simon, Claudia[1], Vallejos María[2], Gallego Federico[3], Marioetta Julieta[1], Schusselin Marcelo[1] and Ciganda Verónica[1]

[1]Área de Recursos Naturales, Producción y Ambiente, INIA La Estanzuela, Semillero, Uruguay; [2]Departamento de Métodos Cuantitativos y Sistemas de Información; Laboratorio de Análisis Regional y Teledetección, Facultad de Agronomía, Universidad de Buenos Aires, Buenos Aires, Argentina; [3]Instituto de Ciencias Ambientales, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay.

Abstract: The recent expansion of agricultural activities in Uruguay has led to an increase in the construction of water reservoirs for irrigation and livestock supply. However, these water bodies face a growing risk of eutrophication and the proliferation of toxic cyanobacteria, posing challenges to the sustainability of agricultural systems. In this context, implementing effective management strategies to preserve water quality is essential. Since 2019, two reservoirs used for agricultural purposes at the INIA La Estanzuela experimental station have been monitored monthly. These systems exhibit critical eutrophication conditions, with maximum recorded values of 5.8 mg/L of phosphorus, 25.97 mg/L of nitrogen, chlorophyll concentrations up to 844 µg/L, and cyanobacterial densities exceeding 7 million cells/mL. This study aimed to design and implement a management plan focused on reducing nutrient inputs and availability. The actions included the exclusion of livestock from sensitive areas, controlled fertilizer application, regulation of the spillway to stabilize water levels, and the promotion of macrophyte development. The stakeholders involved have progressively adopted the plan. Preliminary results indicate improvements in water quality in one of the reservoirs. Cyanobacteria concentrations dropped to undetectable levels (0 cells/mL) in December 2024, and nutrient concentrations have decreased, although phosphorus levels still exceed 0.025 mg/L. Long-term effects are expected, given the system's resilience.

Keywords: Harmful algal blooms, water quality, irrigation, nutrients.

Ultrastructure and Sperm Mitochondrial Morphometry as an Approach to Understanding the Role of the Mitochondrion in the Sperm Cell

Skowronek María Fernanda[1], Pietroroia Santiago[1], Cassina Adriana[2,3] and Sapiro Rossana[1]

[1]Unidad Académica de Histología y Embriología, Facultad de Medicina, Universidad de la República, Montevideo Uruguay; [2]Unidad Académica de Bioquímica, Facultad de Medicina, Universidad de la República, Montevideo Uruguay; [3]Centro de Investigaciones Biomédicas, Facultad de Medicina, Universidad de la República, Montevideo Uruguay

Abstract: Mitochondrial morphology varies across tissues and cell types and often determines the function of these highly dynamic and multifunctional organelles. The dynamic nature of mitochondria is evident from descriptions of their diverse shapes and cristae remodeling. However, sperm mitochondria exhibit a highly organized arrangement, which raises questions about their ability to undergo morphological changes or exhibit dynamism. The application of image acquisition and processing methodologies enables the detection and quantification of subtle morphological changes under physiological

conditions, such as sperm capacitation, and provides insight into the role of mitochondria during this process. To investigate potential mitochondrial morphological changes during capacitation, mouse spermatozoa were processed for Transmission Electron Microscopy (TEM) under both capacitating and non-capacitating conditions. The resulting images were analyzed using Fiji/ImageJ. Regions of Interest (ROIs) were defined, and both ultrastructural and morphometric features of the mitochondria were examined. In most analyzed sections, mitochondria and their membranes showed a regular arrangement around the axoneme. In capacitated spermatozoa, mitochondria appeared closer to the axoneme. Morphometric analysis revealed a significant decrease in the area and perimeter of the Midpiece (MP) in capacitated spermatozoa. Mitochondria with irregular shapes and electron-lucent areas between cristae membranes were more frequently observed in capacitated cells. These findings suggest that mitochondrial morphological changes occur during capacitation, possibly associated with mitochondrial reorganization and functional modulation. Morphometric analysis contributes to the morpho-functional characterization of sperm mitochondria.

Keywords: Sperm mitochondrial ultrastructure, morphometry, sperm capacitation.

Antimicrobial Peptides Extracted from Native South American Plants: A Potential Treatment Against Microbial Biofilms

Strauch Paul[1], Castro Roberto[1], Raffaelli Sofía[1,2] and Barraco Vega Mariana[1]

[1]Área Microbiología, Departamento de Biociencias, Facultad de Química, Universidad de la República; [2]Laboratorio de Farmacognosia y Productos Naturales, Departamento de Química Orgánica, Facultad de Química, Universidad de la República

Abstract: The rise of antimicrobial resistance is a threat to global health. The widespread overuse of antimicrobials has diminished their effectiveness, and few alternatives are currently under investigation. Antimicrobial Peptides (AMPs) have garnered increasing attention due to their favorable physicochemical properties and their ability to limit the development of resistance through multitargeted mechanisms of action. Moreover, recent studies have indicated that AMPs possess antibiofilm potential, a property of particular interest given the critical role of biofilms in antimicrobial resistance. In this study, the antimicrobial and antibiofilm activities of seven AMPs derived from native South American plants were evaluated. A rapid screening method was employed using soluble fractions of recombinant proteins expressed in *E. coli* (HisTag:Trx:defensin) tested against five clinically relevant pathogens, including bacteria and yeast. The three most active AMPs -E1 (from ceibo), M4 (from congorosa), and P4 (from ibirapitá)-were selected and purified via His-tag affinity chromatography. Their ability to inhibit biofilm formation by *Pseudomonas aeruginosa* and *Candida tropicalis* was assessed, with inhibition levels reaching up to 100% at concentrations of 15–36 µM and 7.5–36 µM, respectively. These findings highlight the potential of native plant-derived AMPs as innovative alternatives for combating infections associated with microbial biofilms.

Keywords: Antimicrobial peptides, biofilm inhibition, native South American plants, recombinant defensins, drug resistance.

Reevaluating the Risk of Vincristine on the Ovary

Toledo Agustina[1], Suárez Belén[1], Hernández Mir Karina[1], Chávez-Genaro Rebeca[1] and Anesetti Gabriel[1]

[1]Laboratorio de Biología de la Reproducción, UA Histología y Embriología, Facultad de Medicina, Universidad de la República

Abstract: Ovarian follicles are sensitive to the gonadotoxic effects of certain chemotherapeutic drugs. Vincristine, widely used for the treatment of oncological diseases, has been classified as a low gonadotoxic risk agent. It acts by inhibiting tubulin polymerization, thereby arresting mitosis at metaphase and inducing cell death. Although it does not cause direct DNA damage, negative effects were observed on growing follicles and oocytes lately.

In this study, we analyzed the effects of vincristine on cyclicity, the population of primordial and growing follicles, and some parameters associated with mature oocytes.

In young adult females, vincristine treatment altered ovarian cyclicity during and up to 4 weeks after administration. There was also a significant increase in primordial follicle activation (via Foxo3a) and enhanced atresia of growing follicles. Ovulated oocytes were affected as well, showing an increase in size and in the meiotic spindle, along with a decrease in fertilization rates.

This study reveals previously unrecognized effects of vincristine on the ovary and oocytes, which could have important long-term implications for fertility in females exposed to this drug.

Keywords: Gonadotoxic, vincristine, fertility.

Limnological Characterization, Main Biological Communities and Trophic State of a Freshwater, Turbid Coastal Lagoon (Laguna Negra, Rocha, Uruguay)

Latchinian Maceo[1], Rodríguez Lorena [2] and Conde Daniel[3]

[1]Limnology Section, Institute of Ecology and Environmental Sciences (School of Sciences, Universidad de la República) (undergraduate student); [2]Interdisciplinary Department of Coastal and Marine Systems (Eastern Regional University Center (CURE, Universidad de la República); [3]Limnology Section, Institute of Ecology and Environmental Sciences (School of Sciences, Universidad de la República)

Abstract: This study presents a limnological characterization of Laguna Negra, located in the department of Rocha (Uruguay), a shallow, freshwater coastal lagoon with consistently high turbidity. The objective was to assess the trophic status and describe the main biological communities, considering both environmental and anthropogenic factors affecting water quality. The analysis was based on data from summer monitoring campaigns conducted between 2015 and 2023. Physicochemical variables (temperature, pH, turbidity, nutrients, others) in water and sediments, biological variables (phytoplankton, zooplankton, benthos), and sediment characteristics were assessed using standard methods and further described and evaluated by principal component analysis. The lagoon was found to range from mesotrophic to eutrophic according to various indices. Phytoplankton was dominated by diatoms, while benthic organism abundance was extremely low. Persistent turbidity appears to be partially due to organic matter input from ancient littoral peats and the wind-driven resuspension of fine sediments. However, additional factors and processes must be investigated to fully understand this phenomenon, which reduces water transparency and may limit the system's productivity and biodiversity. These features, combined with the potential effects of water management and land use in the watershed, emphasize the ecosystem's vulnerability. The results are discussed in relation to the limited historical limnological records available for this system. This work provides a baseline for future research and offers valuable input for the environmental management of Laguna Negra, particularly in support of present efforts to develop a management plan, following its recent inclusion in the National System of Protected Areas of Uruguay.

Keywords: Laguna negra, eutrophication, turbidity.

Toxoplasma Gondii Seroprevalence, Seroconversion Rates, and Genetic Variability in Humans from Uruguay

Valentín-Decuadro Alejandra[1,2,3], Tana-Hernández Leandro[2], Faral-Tello Paula[2], Fresia Pablo[4,5], Guirado Mariana[6], Rodríguez Rey Marianella[7], Díaz Gonzalo[8], Giménez Valentina[8], Greising Gabriela[8], Fernández, Nora[1,9], Gesuele Juan[8] and Francia María E.[1,2]

[1]Academic Unit of Parasitology and Mycology, Hygiene Institute, School of Medicine, Universidad de la República, Montevideo, Uruguay; [2]Laboratory of Apicomplexa Biology, Institut Pasteur Montevideo, Montevideo, Uruguay; [3]Academic Unit of Clinical Pathology Laboratory, Bioanalysis Subunit – Parasitology Section, School of Medical Technology (EUTM), School of Medicine, Universidad de la República, Montevideo, Uruguay; [4]Joint Unit Pasteur + INIA (UMPI), Institut Pasteur Montevideo, Montevideo, Uruguay; [5]Bioinformatics Unit. Institut Pasteur de Montevideo, Uruguay; [6]Academic Unit of Infectious Diseases, School of Medicine, Universidad de la República, Montevideo, Uruguay; [7]Academic Unit of Neonatology, "Dr. Manuel Quintela" Hospital de Clínicas, School of Medicine, Universidad de la República, Montevideo, Uruguay; [8]High-Risk Obstetric Clinic, Centro Hospitalario Pereira Rossell, School of Medicine, Universidad de la República, Montevideo, Uruguay; [9]Neonatology Department, Centro Hospitalario Pereira Rossell, Montevideo, Uruguay

Abstract: Toxoplasmosis is one of the most prevalent zoonotic parasitoses worldwide, caused by the obligate intracellular Apicomplexan parasite *Toxoplasma gondii*. When acquired during pregnancy, *T. gondii* can be transmitted vertically, infecting the fetus. Congenitally acquired toxoplasmosis can result in severe complications, including miscarriage, stillbirth, and long-term neurological and ocular sequelae in the newborn. Prenatal screening can detect maternal seroconversion, providing a window of opportunity for timely intervention and prevention of vertical transmission. In Uruguay, mandatory serological screening for *T. gondii* infection during pregnancy is implemented. However, the general prevalence of *T. gondii* in the population and the rate of seroconversion have not been updated in the last 20 years. Furthermore, the genetic diversity of the parasite is still largely unknown. Herein, we update the toxoplasmosis seroprevalence and seroconversion rates of a cohort of patients based on serological surveys. Seroprevalence was found to have slightly declined from 50% in 1998 to 45.5%, with a current 0.58% congenital transmission rate. Additionally, we pursued molecular detection of *T. gondii* in various samples, followed by genotyping by *in silico* RFLP. This uncovered ample genetic diversity of *T. gondii* strains circulating in the human population, identifying for the first time unique allele combinations present in the Uruguayan population. The high prevalence, together with the presence of genetically non-archetypal strains of *Toxoplasma gondii* in Uruguay, adds to the existing body of knowledge from other countries in the region, underscoring the importance of optimizing surveillance and prevention strategies in the context of congenital toxoplasmosis in South America.

Keywords: Congenital toxoplasmosis, toxoplasmosis seroprevalence, genotyping, seroconversion, non-clonal strains.

Sex or Sugar? A Model for Exploring the Interaction Between Competitive Motivations in Sexually Active Female Rats

Turnes Ainara[1] and Agrati Daniella[1]

[1]Department of Physiology and Nutrition, Faculty of Sciences, Universidad de la República, Montevideo, Uruguay.

Abstract: The sexual behavior of female rats is highly motivated. Although the mesolimbic dopaminergic system has been implicated in regulating this behavior, we found that blocking dopaminergic transmission in the nucleus accumbens, a node of this system, only slightly affects its execution. Since this system regulates decision-making related to the energy costs associated with different rewards, we hypothesize that manipulating dopaminergic neurotransmission reduces sexual interaction in females when a more sedentary, rewarding activity is available. To test this hypothesis, we are validating a time-investment preference model between two rewarding activities: sexual interaction, which is more active, and eating palatable food (Froot Loops®), which is more sedentary, in cycling rats tested in the late proestrus phase of the estrous cycle. We trained the females during three consecutive proestrus cycles, exposing them to a male (with a vaginal mask) and, separately,

to Froot Loops® within a three-chamber model. In the fourth proestrus, the females interacted with both stimuli simultaneously (control situation). In subsequent proestrus, they were tested with both stimuli 50 minutes after receiving the dopaminergic antagonist haloperidol (0.1 or 0.2 mg/kg, i.p.). Haloperidol doses were administered in a counterbalanced manner, interspersed with washout tests (drug absence). We observed that, when both stimuli competed, the females engaged in both activities, but spent more time on sexual interaction. Haloperidol administration reduced the display of proceptive behaviors but increased the time females spent with the male. This led to a decrease in Froot Loops® intake. These results highlight the high value of sexual interaction for females and suggest that reduced dopaminergic transmission under these conditions is associated with investing limited energy resources in the preferred, rewarding activity. To make the model more robust, we must pharmacologically challenge this choice in a situation where the physical effort required to access the male exceeds that required to access food.

Keywords: Female rat, dopamine, sexual behavior, reward competition.

Functional Symbiosis Between *Raphidiopsis Raciborskii* and the Microbiome: An Adaptive Mechanism for Survival in Nitrogen-depleted Environments

Vico Paula[1,2], Bonilla Sylvia[2], Iriarte Andrés[3] and Piccini Claudia[1]

[1]Departamento de Microbiología, Instituto de Investigaciones Biológicas Clemente Estable. Avenida Italia 3318. Montevideo 11600, Uruguay; [2]Departamento de Desarrollo Biotecnológico del Instituto de Higiene; [3]Sección Limnología, Facultad de Ciencias. Universidad de la República. Iguá 4225. Montevideo 11400, Uruguay

Abstract: The increasing frequency of *Raphidiopsis raciborskii* toxic blooms on a global scale has raised substantial concern. Such distribution has been associated with the diversification of ecotypes characterized by niche differentiation and heterogeneous environmental responsiveness. Emerging evidence suggests that the microbial consortium embedded in the mucilage—the cyanobacterial microbiome—may play a fundamental role in enhancing the ecological performance of the host. This microbiome provides essential metabolic functions and bioactive compounds, facilitating a mutual dependency between host and associated bacteria. Our previous work showed the structure of *R. raciborskii* microbiome as ecotype-dependent, dominated by genera related to nitrogen cycling (*e.g.*, *Rhizobium*).

In the present study, we applied a metatranscriptomic-based strategy to determine the functional role of both cyanobacteria and their microbiome. The obtained data revealed that photosynthesis and carbon capture were the main metabolic activities of *R. raciborskii*, while nitrogen-related processes, such as N_2 fixation, ammonification, and assimilation where the main functions exhibited by several bacterial taxa from its microbiome.

These findings support a model of metabolic cooperation where cyanobacteria supply photosynthetically derived substrates—such as mucilage-associated sugars—to sustain their microbiome. In exchange, they acquire nitrogen compounds from their microbial partners, potentially reducing the energetic demands associated with atmospheric nitrogen fixation. This metabolic interdependence may contribute to the establishment and maintenance of *R. raciborskii* blooms in nitrogen-limited aquatic environments.

Keywords: Microbiome, cyanobacteria, functional cooperation, nitrogen.

Effects of Maternal Supplementation During Gestation on Seminiferous Tubule Diameter and Sertoli Cell Count In 140-day-old Sheep

Viotti, Helen[1], Mernies Beatriz[2], Folgar Lilena[1], Cambruzzi Javier[1], Lombide Paula[1], Delmiro William[1], Martin Graeme B[3], Rodríguez Osorio Nélida[4] and Pedrana Graciela[1]

[1]Departamento de Biociencias Veterinarias, Facultad de Veterinaria, Universidad de la República, Montevideo, Uruguay; [2]Departamento de Producción Animal y Sistemas Productivos, Facultad de Veterinaria, Universidad de la República, Montevideo, Uruguay; [3]School of Agriculture and Environment and UWA Institute of Agriculture, University of Western Australia, Perth, Australia; [4]Unidad de Genómica y Bioinformática, Departamento de Ciencias Biológicas CENUR Litoral Noroeste, Universidad de la República, Salto, Uruguay

Abstract: Previous research in sheep has shown that maternal supplementation throughout gestation affects offspring testicular morphology. We investigated whether a shorter period of maternal supplementation has the same effects. Pregnant ewes (Corriedale × Hampshire Down) were randomly assigned to a control group (n = 20 on natural pasture) and a supplemented group (n = 20 on natural pasture + supplemented feed from day 70 of gestation until lambing). Male lambs (n = 24) were kept with their dams on natural pastures until 140 days of age, when their testes were processed for histology. Both seminiferous tubule diameter (158.3 ± 0.77 vs. 138.5 ± 0.75 µm, P = 0.0001) and Sertoli cell count (6 ± 0.09 vs. 4 ± 0.08, P = 0.0001) were significantly greater in the supplemented group. This outcome is consistent with the increased seminiferous tubule diameter and a tendency toward increased Sertoli cell count in previous studies with 99-day-old lambs. In conclusion, maternal supplementation under pasture conditions in the second half of gestation positively impacts the reproductive potential of rams.

Keywords: Programming, nutrition, DOhaD, testes, sertoli.

HSP90 and HSF-1 Immunopositive Leukocytes in Post-Insemination Endometritis in Mares

Camacho Ana[1], Vasconcellos Rossana[1], Lombide Paula[1], Viotti Helen[1], Cazales Nicolás[2], Martin Graeme. B [3] and Pedrana, Graciela [1]

[1]Departamento de Biociencias Veterinarias, Facultad de Veterinaria, Universidad de la República; [2]Departamento de Producción Animal y Salud de los Sistema Productivos, Facultad de Veterinaria, Universidad de la República; [3]School of Agriculture and Environment and UWA Institute of Agriculture, University of Western Australia, Perth, Australia

Abstract: The heat shock protein HSP90 is thought to play an important role in antigen presentation and cross-presentation by interacting with antigen-presenting cells through specific receptors and stimulating them to secrete inflammatory cytokines. We have recently shown that HSP90 and its transcription factor, HSF-1, are localized in the cytoplasm and nucleus of the epithelial cells of equine endometrium that have been affected by post-insemination endometritis. In the present study, we analyzed the immunoexpression of HSF-1 and HSP90 in leukocytes (neutrophils and lymphocytes) of endometrial connective tissue at 2 and 4 hours post-insemination in crossbred mares (n = 30). We used Abcam mouse monoclonal antibodies, both diluted 1/50: anti-Hsp90 antibody [AC88] (ab13492) and anti-HSF-1 (mouse polyclonal ab52813). For image analysis, we used a macro that analysed particles by shape descriptors: size and roundness. There were more leukocytes positive for HSP90 at 4 hours post-insemination than at 2 hours post-insemination (9 ± 1 v 6 ± 1; P = 0.002). There were also more HSF-1-positive leukocytes at 4 hours post-insemination than at 2 hours post-insemination (12 ± 2 v 9 ± 1; P = 0.05). We conclude that both HSP90 and HSF-1 regulate the presence of leukocytes in endometrial stromal connective tissue, and suggest that they play an important role in the inflammation process.

Keywords: Endometrium, mares, leucocytes, image-analysis.

PPAR Alpha Increases in FIGO 3 Grade in Endometrial Cancer in Women

Pedrana Graciela[1], Viotti Helen[1], Lombide Paula[1], Soria Silvana[1], Brady Mark F[2] and Spirtos Nicola[3]

[1]Departamento de Biociencias Veterinarias, Facultad de Veterinaria, Universidad de la República, Uruguay; [2]Department of Biostatistics and Bioinformatics, Roswell Park Cancer Institute, Buffalo, New York, United States of America; [3]Woman´s Cancer Center of Nevada, Nevada, United States of America

Abstract: Endometrial cancer is the second most prevalent cancer among women. We aimed to determine if the PPARα expression increases with endometrial cancer progression. Biopsies from 20 women were collected, fixed, and processed for immunohistochemistry against PPARα. Endometrial cancers were classified according to the Federation of Gynecological and Obstetrics (FIGO) classification. The samples were analysed in a batch process according to the date when immunohistochemistry was performed. The immunostaining area and integrated density were analyzed using Fiji (Just ImageJ). A Bayesian multilevel model was constructed using the R package brms to analyze the percent of staining, intensity, and FIGO grades I and III as independent variables. The results showed a significant difference in PPARα expression between FIGO grades. 50% of grade III specimens had medians above 7% staining, while only 7.6% of grade I specimens exceeded this value. The model estimated the median percent area stain to be 1.06 for grade I and 6.17 for grade III. The mean staining intensity for FIGO grade III was 5.81 times greater than for grade I. The study concluded that FIGO grade III uterine cancers are associated with a higher percent area stain for PPARα compared to grade I. This suggests that PPARα may be a potential biomarker for endometrial cancer progression and that PPARα agonists could be a potential anti-cancer therapy.

Keywords: Endocannabinoids, image-analysis, immunostaining, anti-cancer-therapy.

Optimizing *In Vitro* Conditions for the Study of Extracellular Vesicles Produced by a Human Trophoblast Cell Line (Swan 71)

Tosar Camila[1,2,3], Muniz Ana Clara[1,2,3,4], Núñez Victoria[1,2,3], Mourglia Gustavo[1,2,3] and Arbildi Paula[1,2,3]

[1]Área Inmunología, Departamento de Biociencias (DEPBIO), Facultad de Química, Universidad de la República, Montevideo, Uruguay; [2]Unidad Asociada de Inmunología, Instituto de Química Biológica (IQB), Facultad de Ciencias, Universidad de la República; [3]Departamento de Inmunología, Instituto de Higiene "Prof. Arnoldo Berta", Universidad de la República; [4]Posgrado en Biotecnología, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay

Abstract: Extracellular Vesicles (EVs) are lipid bilayer-defined nanoparticles secreted by various cell types as a form of intercellular communication. Placenta-derived EVs released into maternal circulation perform several functions, and their production and composition are influenced by the cellular environment. To study trophoblast-derived EVs *in vitro*, this work aimed to optimize experimental conditions for EV purification and characterization.

Basal EV release was assessed in Swan-71 cells (a first-trimester trophoblast cell line), cultured in the absence of fetal bovine serum. Culture requirements and metabolic activity were evaluated. Key variables analyzed included culture surface area, cell density, and incubation time. Quantitative and qualitative analyses of EVs were performed using Nanoparticle Tracking Analysis (NTA), while cell viability was measured via a resazurin reduction assay.

Under the conditions tested, metabolic activity significantly increased with incubation time. EV size distribution remained consistent across conditions (range: 91–190 nm), and EV production increased with incubation time (10^7 particles/mL at 24 h vs. 10^8 particles/mL at 48 hours).

In summary, optimal conditions for the *in vitro* study of EVs released by Swan-71 cells were successfully determined, and a generic EV enrichment protocol was validated. These findings establish a foundation for future evaluation of stimuli relevant to placental physio(patho)logy and their effects on EVs release.

Keywords: Trophoblast, extracellular vesicles, NTA.

Microglial/Macrophage Activation and Diffuse Inflammation in Multiple Sclerosis: Findings in Apparently Normal Tissue and Potential Pathophysiological Implications

Torres-Pérez Maximiliano[1,2], Gómez-Pinillos Daniel[2], M. Falcón Carolina[2], Marchena Miguel Prunell Giselle[1] and de Castro Fernando[2]

[1]Laboratory of Neurodegeneration and Neuroprotection Mechanisms, Department of Neurobiology and Neuropathology, Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay; [2] Developmental Neurobiology Group (GNDe), Instituto Cajal-CSIC, Madrid, Spain

Abstract: Multiple Sclerosis (MS) is a chronic neurodegenerative disease characterized by a heterogeneous immune response that generates focal demyelinating lesions, but also diffuses inflammatory processes that may contribute to disease progression. While microglial activation has been extensively studied in active demyelinating lesions, evidence remains limited regarding their activation in regions of apparently normal white and gray matter (NAWM and NAGM, respectively). To explore the distribution and organization of microglia/macrophages beyond visible lesions, we analyzed post-mortem samples from the cerebral cortex and cerebellum of MS patients. Immunofluorescence was performed using Iba1, HLA-DR, and MBP, and HLA-DR immunocytochemistry was combined with histochemical techniques to detect myelin loss (eriochrome cyanine) and nuclear staining (toluidine blue). Our analysis revealed partial colocalization patterns of HLA-DR and Iba1 in chronic-active and inactive demyelinating plaques, consistent with previous studies. However, we also consistently identified perivascular HLA-DR$^+$ cells in NAWM, HLA-DR$^+$ microglial nodules in NAGM, and diffuse HLA-DR$^+$ accumulations in NAGM. These findings suggest extralesional immune activation, potentially involved in early damage processes or in cumulative inflammatory mechanisms contributing to overall MS progression.

Keywords: Demyelination, primary demyelinating diseases, Iba1, HLA-DR, MBP.