



**UNICA**

UNIVERSITÀ  
DEGLI STUDI  
DI CAGLIARI

**IV LIGHT**

**RETREAT**

**DiSVA**

---

*6 February 2026*



**Programme**

08:20-09:00	Welcome Coffee
<b>Welcome and opening remarks</b>	
09:00-09:20	Greetings from the Authority and Director's Introductory Talk
<b>Presentation of newly approved projects</b>	
09:20-09:50	Section of Animal Biology and Ecology - Laura Carugati
	Biomedical Section - Angela Corona
	Section of Botanical Sciences - Andrea Maxia
	Section of Neuroscience and Anthropology - Enrico Sanna
	Section of Drug Sciences - Michele Schlich
Section of Pharmaceutical, Pharmacological and Nutraceutical Sciences - Francesco Corrias	
<b>Department research activities presented by selected speakers</b>	
<b>Session I - Section of Animal Biology and Ecology</b>	
09:50-10:00	Cristina Porcu – EASY Reproductive HEALTH, biosensors and computer vision to conserve and protect the marine ecoSYstems
10:00-10:10	Francesco Palmas – An island under siege: origin, fate and potential impacts of non-indigenous aquatic fauna in coastal wetlands of Sardinia (Western Mediterranean Sea)
10:10-10:20	Chiara Barbieri – People, plants, and cultures in the Neotropics: reconstructing Venezuelan history across deep and recent time
<b>Session II - Biomedical Section</b>	
10:20-10:30	Sonia Floris – Multifunctional compounds for the prevention of skin diseases: antioxidant activity and inhibition of skin aging-related enzymes
10:30-10:40	Elisa Fanunza – Restoring the host innate immunity by targeting the SARS-CoV-2 endoribonuclease Nsp15
10:40-10:50	Paolo Malune – $\gamma$ -Phosphonate monoalkyl nucleotide analogues inhibit SARS-CoV-2 replication in vitro by inducing dissociation of the minimal replication-transcription complex
<b>Session III - Section of Botanical Sciences</b>	
10:50-11:00	Antonio De Agostini – Perspectives on the cultivation in vertical farming of the Sardinian endemics <i>Hypericum scruglii</i> Bacch., Brullo & Salmeri
11:00-11:10	Mauro Fois – Floristic surveys (and not only) on Sardinia's wetlands: exchange of experiences, data and an invitation to collaborate
11:10-11:20	Emma Cocco – Biomonitoring and urban greening strategies: a practical application of the TERSICORE Project
11:20-12:00	Coffee Break and Poster Session
<b>Session IV - Section of Neuroscience and Anthropology</b>	
12:00-12:10	Eduardo Pizzo Junior – Body composition in patients with epilepsy
12:10-12:20	Enrico Sanna – D-serine treatment and striatal synaptic plasticity in an alpha-synuclein over-expression rat model of Parkinson's disease
<b>Session V - Section of Drug Sciences</b>	
12:20-12:30	Erica Sanna – The coronavirus helicase as a drug target: new chemical approaches against a conserved viral engine
12:30-12:40	Luca Casula – Electrospinning-based nanofibers as versatile drug delivery platforms
12:40-12:50	Sergio Murgia – Development of photoactivatable liquid-crystalline nanoparticles for the therapy of non-small cell lung cancer
<b>Session VI - Section of Pharmaceutical, Pharmacological and Nutraceutical Sciences</b>	
12:50-13:00	Davide Moi – Activation of carbonic anhydrases encoded by the human probiotics to enhance gut microbiota performance
13:00-13:10	Mattia Casula – Mass spectrometry-based omics approaches: studying <i>Chlorella vulgaris</i> in extreme environments
13:10-13:20	Andrea Deserra – Mass spectrometry applications in food chemistry: egg yolk from different hen rearing systems
13:20-15:10	Light Brunch and Poster Session
<b>Conclusions and closing remarks</b>	
15:10-15:30	Enzo Tramontano – Conclusions & Remarks



## Poster Session - Book of Abstracts

N	PhD Student	Section	PhD Course	Poster Title	Supervisors
P1	Eleonora Metta	Animal Biology and Ecology	Life, Environmental and Drugs sciences	Genome-resolved insights reveal extensive taxonomic novelty in Sardinian hypersaline ecosystems	A. Pusceddu; N. Grandi
P2	Claudia Cabiddu	Biomedical	Life, Environmental and Drugs sciences	Evaluation of the effect of Human Endogenous Retrovirus (HERV) envelope proteins in a <i>Drosophila melanogaster</i> model	N. Grandi; E. Tramontano
P3	Marianna Camasta	Biomedical	Life, Environmental and Drugs sciences	Investigation of Ebola virus protein VP35 wild-type and dsRNA-binding deficient mutant inclusion bodies formation	E. Tramontano; A. Corona
P4	Laura Dettori	Biomedical	One health approaches to infectious diseases and life science research (DIN)	Effect of catechol derivatives on SARS-CoV-2 exoribonuclease nsp14/10 activity	F. Esposito; A. Corona
P5	Roberta Emmolo	Biomedical	Life, Environmental and Drugs sciences	Identification and characterization of a new broad-spectrum helicase inhibitor against human coronaviruses	A. Corona; E. Tramontano
P6	Salvatore Nieddu	Biomedical	Life, Environmental and Drugs sciences	Identification of new SARS-CoV-2 Mpro inhibitors with a pyrimidine scaffold	F. Esposito; A. Corona
P7	Sara Piras	Biomedical	Life,	Metabolic pathway	A. Corona; N.



			Environmental and Drugs sciences	alteration in flavivirus infection: exploitation to find potential therapeutic targets	Grandi
<b>P8</b>	<b>Alessandra Schirru</b>	Biomedical	Life, Environmental and Drugs sciences	Proteomic characterization of human saliva in patients with atopic dermatitis	T. Cabras; B. Manconi
<b>P9</b>	<b>Stefano Francesco Farci</b>	Botanical Sciences	Earth and Environmental Sciences and Technology	Preparative isolation and preliminary characterization of LHCI trimers and PSII monomers from <i>Posidonia oceanica L.</i>	D. Piano
<b>P10</b>	<b>Giulia Atzeni</b>	Drug Sciences	One health approaches to infectious diseases and life science research (DIN)	Synthesis of dual NS3 protease-helicase inhibitors as broad-spectrum antivirals against WNV and ZIKV	E. Maccioni; E. Tramontano
<b>P11</b>	<b>Laura Demuru</b>	Drug Sciences	Life, Environmental and Drugs sciences	Identification and optimization of novel allosteric inhibitors of ZIKV NS2B–NS3pro	R. Meleddu; S. Distinto
<b>P12</b>	<b>Eleonora Lai</b>	Drug Sciences	Life, Environmental and Drugs sciences	Development and characterization of a Cannabidiol nanosuspension for pulmonary administration	M. Schlich; F. Lai
<b>P13</b>	<b>Alessio Pittiu</b>	Drug Sciences	Life, Environmental and Drugs sciences	Microfluidic production of Ru(II) polypyridyl complex-loaded cubosomes for photodynamic therapy of non-small cell lung cancer	M. Schlich; F. Lai



<b>P14</b>	<b>Roberta Anedda</b>	Neuroscience and Anthropology	Life, Environmental and Drugs sciences	The bioarcheology of Nuragic children and infants: demography and society of bronze age Sardinia	E. Marini; V. Sparacello
<b>P15</b>	<b>Laura Flore</b>	Neuroscience and Anthropology	Life, Environmental and Drugs sciences	Maternal lineages and population dynamics in the Western Mediterranean: a mtDNA study of Sardinia, Sicily, and Corsica	C.M. Calò; P. Francalacci
<b>P16</b>	<b>Federica Frau</b>	Neuroscience and Anthropology	Life, Environmental and Drugs sciences	BIA International Database (BIAID): results on device technical performance survey	E. Marini; M. Massidda
<b>P17</b>	<b>Carla Maserati</b>	Neuroscience and Anthropology	Life, Environmental and Drugs sciences	Violence and conflict at the end of prehistory: from bones to behaviour	V. Sparacello
<b>P18</b>	<b>Alberto Deplano</b>	Pharmaceutical, Pharmacological and Nutraceutical Sciences	Life, Environmental and Drugs sciences	Tuning the selective activation of probiotic bacterial carbonic anhydrases to enhance microbiota performance	V. Onnis; D. Moi
<b>P19</b>	<b>Roberta Puliga</b>	Pharmaceutical, Pharmacological and Nutraceutical Sciences	Life, Environmental and Drugs sciences	Caffeine and Red Bull® differentially modulate alcohol-induced mesocorticolimbic activation: a behavioral, immunohistochemical and neurochemical study	E. Acquas; V. Bassareo; L. Dazzi



## **P1 - Genome-resolved insights reveal extensive taxonomic novelty in Sardinian hypersaline ecosystems**

<sup>1</sup>\*E., Metta; <sup>1</sup>A., Caredda; <sup>1</sup>C., Cabiddu; <sup>1</sup>C., Mastio; <sup>1</sup>E., Tramontano; <sup>1</sup>A., Pusceddu; <sup>1</sup>N., Grandi.

[eleonora.metta@unica.it](mailto:eleonora.metta@unica.it)

<sup>1</sup> University of Cagliari, Department of Life and Environmental Sciences, Cittadella Universitaria, 09042, Monserrato (CA), Italy

Multi-pond salterns are valuable natural hypersaline ecosystems for investigating microbial diversity along salinity gradients, yet underexplored despite their ecological and biotechnological relevance.

We present the first genome-resolved metagenomic analysis of two Mediterranean salterns in South Sardinia: Conti Vecchi (still active) and Molentargius (inactive). Water and sediment samples were collected from ponds with a varying salinity during winter and summer 2024. DNA extracted from triplicates was sequenced, quality-controlled, assembled, and binned. Genome bin quality was assessed with CheckM2, and taxonomy was assigned using GTDB-Tk.

We recovered 1537 genome bins from Conti Vecchi and 1249 from Molentargius, including 534 and 423 high-quality MAGs, respectively. Overall, 372 genome-resolved species were identified in Conti Vecchi (334 Bacteria, 38 Archaea) and 316 in Molentargius (247 Bacteria, 69 Archaea). Notably, over 70% of these could not be confidently assigned to known species, and many MAGs remained unclassified at higher taxonomic ranks (genus, family, and order), revealing extensive taxonomic novelty in hypersaline microbial communities.

Functional potential was annotated using DRAM, providing a foundation for future analyses of metabolic capabilities and adaptive strategies across salinity gradients.

Overall, Cagliari salterns emerge as major reservoirs of previously uncharacterized microbial diversity, contributing to the expansion of genome-resolved reference databases. We are currently extending analyses to eukaryotic communities, and integrating them with metatranscriptomic data to link taxonomic features with metabolic activity.



## **P2 - Evaluation of the effect of Human Endogenous Retrovirus (HERV) envelope proteins in a *Drosophila melanogaster* model**

<sup>1</sup>C., Cabiddu; <sup>2</sup>M., Simbula; <sup>3</sup>F., Feiguin; <sup>1</sup>E., Tramontano; <sup>1</sup>N., Grandi.

[claudia.cabiddu@unica.it](mailto:claudia.cabiddu@unica.it)

<sup>1</sup>University of Cagliari, Department of Life and Environmental Sciences, Cittadella Universitaria, Building E, 09042 Monserrato (CA), Italy

<sup>2</sup>Institute of Genetic and Biomedical Research (IRGB), National Research Council (CNR), 09042 Monserrato (CA), Italy

<sup>3</sup>University of Cagliari, Department of Life and Environmental Sciences, Cittadella Universitaria, Building D, 09042 Monserrato (CA), Italy

Human Endogenous Retroviruses (HERVs) account for approximately 8% of the human genome and derive from ancient viral infections that affected primate germline cells. Once integrated, they became fixed in the genome and were subsequently transmitted through generations.

Among HERV-derived products, the envelope proteins (Env) are currently the most investigated due to their involvement in diseases with complex etiology - such as autoimmunity and cancer - as well as in physiological processes, including placenta formation and cellular senescence.

In this study, five Env proteins were selected: Syncytin-1, used as a physiological control due to its well-characterized role in placental development; MSRV, for its ability to induce multiple sclerosis-like hallmarks in mouse models; HERVKcon, for its modulation of senescence; ERV3-1 and ERVV2, for their putative involvement in tumorigenesis.

For these reasons, the aim of this project is to evaluate the physio-pathological impact of HERV Env proteins through the generation of transgenic lines of *Drosophila melanogaster*.

The observation of altered phenotypes or abnormal behaviours, compared to controls, will be further validated by molecular analyses.

After transgenic flies' generation, genetic crosses were performed using the GAL4-UAS system. From these crosses, progeny of interest was selected for phenotypic and behavioural analyses and one of these lines showed promising results, which will need to be confirmed through further experiments.



## **P3 - Investigation of Ebola virus protein VP35 wild-type and dsRNA-binding deficient mutant inclusion bodies formation**

<sup>1</sup>M., Camasta; <sup>2</sup>Y., Wang; <sup>3</sup>M., Schauflinger; <sup>2</sup>L., Zinzula; <sup>3</sup>S., Becker; <sup>1</sup>E., Tramontano.

[marianna.camasta@unica.it](mailto:marianna.camasta@unica.it)

<sup>1</sup> Department of Life and Environmental Sciences, University of Cagliari, Cagliari, Italy

<sup>2</sup> iHuman Institute, ShanghaiTech University, 201210 Shanghai, China

<sup>3</sup> Institut für Virologie, Philipps-Universität Marburg, Marburg, Germany

Filoviruses have a linear non-segmented ssRNA(-) genome and a typical filamentous shape, hence their name. Some of them such as Marburg virus (MARV) and Ebola virus (EBOV) are highly lethal for humans. Among the seven proteins encoded by EBOV genome, virion protein 35 (VP35) is well-known to suppress the innate immune system response through both dsRNA binding-dependent and -independent mechanisms. Specifically, VP35 prevents the recognition of viral dsRNA by retinoic acid inducible gene type I (RIG-I) and to interact with other cellular proteins of the pathway, thus blocking the cascade and, consequently, type I interferon (IFN-I) production. Though VP35 IFN-I antagonism has been widely studied, the specific level of interaction between VP35 and cellular factors within RIG-I pathway is still unclear. Moreover, it has been shown that EBOV infected cells produce inclusion bodies containing VP35 together with other viral replicative proteins. Here we show by immunofluorescence that transiently expressed VP35 alone results in unusual architectures reminiscent of inclusion bodies formation, suggesting its interaction with cellular proteins. Furthermore, we demonstrate through biophysical techniques a stable complex of VP35 and the RIG-I pathway component inhibitor of the nuclear factor kappa-B kinase subunit epsilon (IKK $\epsilon$ ). In addition, we show that transiently expressed dsRNA-binding deficient mutant VP35-R322A retains the ability to form inclusion bodies, however with better-structured cytoplasmic organization that appear completely different with respect to wild-type. These findings are indicative of a VP35 inclusion bodies role in EBOV innate immune evasion that goes beyond dsRNA-binding mediated suppression.



## P4 - Effect of catechol derivatives on SARS-CoV-2 exoribonuclease nsp14/10 activity

<sup>1,2\*</sup>L., Dettori; <sup>3</sup>B., Biersack; <sup>3</sup>R., Schobert; <sup>2</sup>A., Corona; <sup>2</sup>F., Esposito; <sup>2</sup>E., Tramontano.

[laura.dettori@unica.it](mailto:laura.dettori@unica.it)

<sup>1</sup>National PhD Programme in One Health approaches to infectious diseases and life science research, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, 27100, Italy

<sup>2</sup>Department of Life and Environmental Sciences, University of Cagliari, 09042, Monserrato, Italy

<sup>3</sup>Organic Chemistry 1, University of Bayreuth, Universitätsstrasse 30, 95440 Bayreuth, German

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the etiological agent responsible for the Coronavirus Disease 2019 (COVID-19) pandemic, which has caused substantial global morbidity and mortality. Viral replication and transcription depend on a coordinated set of non-structural proteins forming a replication–transcription complex. The exoribonuclease function of nsp14 is significantly stimulated by its interaction with the cofactor nsp10, forming the nsp14/nsp10 complex, which ensures high-fidelity genome replication and viral fitness by ensuring proofreading activity.

Targeting this enzymatic activity represents an attractive antiviral strategy, as inhibition of nsp14/10 ExoN activity can compromise viral genome stability and replication, leading to an accumulation of mutations and, consequently, attenuation of viral propagation.

In this study, a panel of nine compounds was evaluated for their ability to inhibit the nsp14/10 exoribonuclease activity *in vitro*. Several compounds exhibited potent inhibitory effects, with half-maximal inhibitory concentration (IC<sub>50</sub>) values in the low micromolar range, indicating strong interference with the enzymatic function.

To further assess their antiviral potential, these compounds were tested in a cell-based system using HCoV229E-infected human bronchial epithelial (BEAS-2B) cells.

Our preliminary results, highlight the nsp14/nsp10 exoribonuclease complex as a promising target for the identification of new chemical scaffolds for the potential development of therapeutics against SARS-CoV-2 and related coronaviruses.



## **P5 - Identification and characterization of a new broad-spectrum helicase inhibitor against human coronaviruses**

<sup>1</sup>R., Emmolo; <sup>1</sup>G., Atzeni; <sup>1</sup>A., Lupia; <sup>1</sup>E., Sanna; <sup>1</sup>S., Distinto; <sup>1</sup>E., Maccioni; <sup>2</sup>J., Neyts; <sup>2</sup>D., Jochmans;  
<sup>1</sup>E., Tramontano; <sup>1</sup>A., Corona.

[roberta.emmolo@unica.it](mailto:roberta.emmolo@unica.it)

<sup>1</sup>Dipartimento di Scienze della Vita e dell'Ambiente, Università degli Studi di Cagliari, Cittadella Universitaria di Monserrato, SS-554, Monserrato, Cagliari, Italy

<sup>2</sup>KU Leuven, Department of Microbiology, Immunology and Transplantation, Rega Institute, Laboratory of Virology and Chemotherapy, 3000, Leuven, Belgium

Human coronaviruses are significant pathogens of the respiratory tract, with their global impact underscored by the recent SARS-CoV-2 pandemic. This crisis has emphasized the urgent need for broad-spectrum antiviral agents targeting coronaviruses, enabling combination therapies that enhance the genetic barrier to resistance. Coronaviruses helicase (NSP13) has emerged as a particularly attractive target due to its indispensable role in the viral life cycle. Its sequence conservation across coronaviruses suggests that inhibitors targeting this protein could offer broad-spectrum antiviral activity.

In this study, we present preliminary results of in-house molecules, selected with an in-silico screening as potential pan-helicases inhibitors and subsequently optimized. The most promising compound showed an EC<sub>50</sub> value of 6.5 μM in VeroE6-GFP and 14.5 μM in A549 dual cells against SARS-CoV-2 and no toxicity up to 100 μM. Also, it was tested on both the SARS-CoV-2 NSP13 unwinding and ATPase associated biochemical functions, proving an inhibition of the enzyme activity in the low micromolar range. Broad-spectrum activity was evaluated against human betacoronavirus OC43 (HCoV-OC43) and alphacoronavirus 229E (HCoV-229E). Given that HCoV-OC43 serves as a suitable surrogate for SARS-CoV-2, we used it for mode-of-action studies in HeLa cells. Time-of-drug-addition assays proved an inhibition in a timeframe that is in accordance with the NSP13 target, while no entry neither inactivation effect was detected. Finally, the compound showed an inhibition of HCoV-OC43 replication and no toxicity in primary upper airway epithelial cells. These encouraging results pave the way for further lead optimization.



## **P6 - Identification of new SARS-CoV-2 Mpro inhibitors with a pyrimidine scaffold**

<sup>1</sup>\*S., Nieddu; <sup>1</sup> P., Malune; <sup>1</sup> S., Giunta; <sup>2</sup> M., Arpacioğlu; <sup>2,3</sup> G., Ruggieri; <sup>2</sup> E., Cara; <sup>2</sup> L., Zarbo; <sup>2</sup> V. N., Mada; <sup>2</sup> D., Ialongo; <sup>2</sup> A., Albano; <sup>2</sup> E., Patacchini; <sup>2</sup> F., Saccoliti; <sup>2,3</sup> A., Messori; <sup>2</sup> R., Costi; <sup>2</sup> R., Di Santo; <sup>1</sup> A., Corona; <sup>1</sup> E., Tramontano; <sup>1</sup> F., Esposito.

[salvatore.nieddu@unica.it](mailto:salvatore.nieddu@unica.it)

<sup>1</sup> Dipartimento di Scienze della vita e dell'ambiente, Università degli Studi di Cagliari, Cittadella Universitaria di Monserrato, SS-554, Monserrato, Cagliari, Italy

<sup>2</sup> Dipartimento di Chimica e Tecnologie del Farmaco, Istituto Pasteur-Fondazione Cenci Bolognetti, "Sapienza" Università di Roma, p.le Aldo Moro 5, I-00185, Rome, Italy

<sup>3</sup> Department of Public Health, Experimental Medicine and Forensic, University of Pavia, 27100 Pavia, Italy.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is still a major public health issue even today. SARS-CoV-2 possesses a positive-sense ssRNA genome encoding for 16 non-structural proteins (nsp), 4 structural proteins and several accessory ones. Among the viral functional proteins, the main protease (Mpro, also known as 3Clpro), is a cysteine protease composed by a homodimer, one of the crucial enzymes in the proteolytic cleavage of the viral polyprotein during the first steps of infection, therefore necessary for the viral replication and considered as one of the best drug targets for the treatment of SARS-CoV-2 infections.

At the moment, only two antiviral agents have received an emergency approval for the COVID-19 treatment, namely the disease caused by SARS-CoV-2 infection. A third drug, molnupiravir, has been withdrawn from the market. For these reasons, we need to develop new safe and effective anti-SARS-CoV-2 drugs.

In the present work, we designed and synthesized new SARS-CoV-2 Mpro small molecule inhibitors endowed with a pyrimidine scaffold. A series of derivatives was evaluated in both biochemical and cell-based assays to assess their antiviral efficacy.

Some of them were able to inhibit the SARS-CoV-2 Mpro with an IC<sub>50</sub> in the low micromolar range and one of them suppressed viral replication in cell culture. The characterization of the mechanism of action of the most active compounds is ongoing.



## **P7 - Metabolic pathway alteration in flavivirus infection: exploitation to find potential therapeutic targets**

<sup>1</sup>S., Piras; <sup>1</sup>S., Scognamiglio; <sup>1</sup>N., Grandi; <sup>1</sup>E., Tramontano; <sup>1</sup>A., Corona.

[sara.piras9@unica.it](mailto:sara.piras9@unica.it)

<sup>1</sup>University of Cagliari, Department of Life and Environmental Sciences, Cittadella Universitaria, 09042, Monserrato (CA), Italy

West Nile Virus (WNV) is a (+)ssRNA zoonotic flavivirus emerging as a pathological threat in the mediterranean area. WNV can reprogram host metabolism to enhance its replication, even if the underlying mechanism remains poorly understood. Previous multi-omics analysis of BEAS-2B cells 24 hours after WNV infection revealed a profound rewiring of the cellular metabolism. Starting from the metabolomic data, we identified the Lysine pathways and its associated genes as deeply affected by WNV infection, being particularly interesting given its potential antiviral role.

Two lysine-pathway enzymes - aminoadipate semialdehyde synthase (AASS) and aldehyde dehydrogenase 7 family member A1 (ALDH7A1) - were also reported to interact with WNV non-structural proteins 4B (NS4B), suggesting a direct viral modulation of this metabolic pathway not yet described. Aiming at characterizing these interactions, we cloned WNV NS4B, AASS, and ALDH7A1 into eukaryotic expression vectors to analyse protein expression and interaction in BEAS-2B and human foreskin fibroblast (HFF-1) cells. We are checking NS4B expression and its effect on AASS and ALDH7A1 protein amount and intracellular Lysine levels. The results will be then validated in the context of WNV infection. Additionally, as Lysine metabolism occurs in mitochondria organelle, essential for cellular homeostasis and antiviral signalling, we will also investigate WNV-induced mitochondrial morphological and bioenergetic alterations. This approach aims to clarify the interplay between viral infection and host metabolic machinery, contributing to novel antiviral targets identification.



## **P8 - Proteomic characterization of human saliva in patients with atopic dermatitis**

<sup>1</sup>A., Schirru; <sup>1</sup>G., Lai; <sup>1</sup>C.Contini; <sup>1</sup>B., Manconi; <sup>1</sup>A., Olianas; <sup>2</sup>A., Perra; <sup>3</sup>I., Cara; <sup>3</sup>D., Firinu; <sup>1</sup>T., Cabras.

[alessandra.schirru@unica.it](mailto:alessandra.schirru@unica.it)

<sup>1</sup> Department of Life and Environmental Sciences, University of Cagliari, 09042, Monserrato CA, Italy

<sup>2</sup> Department of Biomedical Sciences, Unit of Oncology and Molecular Pathology, University of Cagliari, CA, Italy

<sup>3</sup> Department of Medical Sciences and Public Health, 09124 Cagliari, Italy

Atopic Dermatitis (AtD) is a chronic inflammatory skin disease characterized by epidermal barrier dysfunction and immune dysregulation. Beyond skin manifestations, AtD is associated with systemic molecular alterations detectable in peripheral biofluids. Saliva, a non-invasive and proteome-rich fluid, reflects immune activation and oxidative imbalance. In this study, the salivary proteome of 35 AtD patients and 35 healthy controls (HC, 18-69 years) was analyzed by LC-MS (HPLC–LTQ–XL) using a targeted top-down proteomic approach. About 50 salivary proteoforms were identified, of which 16 showed significant quantitative differences by label-free analysis and Mann–Whitney U test. AtD subjects showed a significant downregulation of proteoforms secreted by salivary glands, as acidic proline-rich proteins (PRP-1 mono-, di-, tri- and non-phosphorylated forms, and PRP-3 di-phosphorylated), together with reduced levels of specific statherin proteoforms (di-phosphorylated and N-terminal truncated forms) and a significant decrease of histatins according with a possible impaired secretory activity of major salivary glands. Conversely, cystatin A (native and N-acetylated forms), cystatin B and its S-glutathionylated proteoform (CysB-SSG), as well as S100 proteoforms (S100A7 and phosphorylated S100A9), were significantly upregulated in AtD saliva, according with the enhanced epithelial inflammation and oxidative stress typical of the disease. Overall, these findings reveal a distinctive salivary proteomic signature in AtD, reflecting salivary gland functional alterations and redox imbalance, and support saliva as a promising tool for non-invasive biomarker discovery in atopic dermatitis.



## **P9 - Preparative isolation and preliminary characterization of LHCII trimers and PSII monomers from *Posidonia oceanica* L.**

<sup>1</sup>S.F., Farci; <sup>2</sup> L., Iesu; <sup>3</sup> C., Slavov; <sup>4</sup> H.M., Kalaji; <sup>1</sup> D., Farci; <sup>1</sup> D., Piano.

[s.farci5@studenti.unica.it](mailto:s.farci5@studenti.unica.it)

<sup>1</sup>Laboratory of Plant Physiology and Photobiology, Department of Life and Environmental Sciences, University of Cagliari, Cagliari, Italy

<sup>2</sup>Université Paris-Saclay, Univ Evry, CY Cergy Paris Université, CNRS, LAMBE, 95000, Cergy, France

<sup>3</sup>Ultrafast spectroscopy, Photochemistry and Biophysics Laboratory, Department of Chemistry, University of South Florida, Tampa, USA

<sup>4</sup>Laboratory of Photosynthesis, Department of Plant Physiology, Warsaw University of Life Sciences SGGW, Warsaw, Poland

*Posidonia oceanica* L. is a vascular marine plant representing a valuable model for plant physiology, particularly for studying the evolutionary and ecological adaptations of the photosynthetic apparatus. This work describes a direct and effective method for fractional thylakoid solubilization specifically designed for plants with coriaceous leaves rich in polyphenolic compounds.

A crude leaf extract, obtained by blending, is first depleted of polyphenols and then subjected to direct solubilization. The resulting thylakoid preparations are processed through a chromatographic workflow that allows the preparative isolation of trimeric Light-Harvesting Complex II and the monomeric Photosystem II core complex.

Protein identification is achieved through mass spectrometry and peptide homology analysis, compensating for the lack of a curated *P. oceanica* proteome. The isolated fractions are suitable for downstream functional and structural analyses, providing the first preparative approach for investigating the photosynthetic machinery of this ecologically distinctive marine plant.

### **References**

Farci SF, Iesu L, Farci D, Piano D. (2026). Preparative isolation and preliminary characterization of LHCII trimers and PSII monomers from *Posidonia oceanica* L. *Photosynthesis research*.

DOI:10.1007/s11120-026-01196-3



## **P10 - Synthesis of dual NS3 protease-helicase inhibitors as broad-spectrum antivirals against WNV and ZIKV**

<sup>1,2\*</sup>G., Atzeni; <sup>1</sup>A., Lupia; <sup>1</sup>R., Emmolo; <sup>1</sup>A., Corona; <sup>1</sup>S., Nieddu; <sup>1</sup>F., Esposito; <sup>1</sup>E., Sanna; <sup>1</sup>A., Onali; <sup>1</sup>L., Demuru; <sup>1</sup>F., Cottiglia; <sup>1</sup>S., Distinto; <sup>1</sup>R., Meleddu; <sup>1</sup>E., Tramontano; <sup>1</sup>E. Maccioni.

[giulia.atzeni@unica.it](mailto:giulia.atzeni@unica.it)

<sup>1</sup>Department of Life and Environmental Sciences, University of Cagliari, Cittadella Universitaria, Monserrato, Italy

<sup>2</sup>National PhD Programme in One Health approaches to infectious diseases and life science research, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Pavia, 27100, Italy

NS3 is a multifunctional, highly conserved flavivirus protein that integrates protease and helicase functions and is indispensable for viral maturation, replication, and infectivity. While most antiviral efforts focus on single-target inhibitors, dual inhibitors targeting both protease and helicase activities offer the potential for enhanced efficacy and reduced resistance. Using Computer-Aided Drug Design (CADD), we identified a series of compounds capable of inhibiting both NS3 helicase and protease activities of West Nile virus (WNV) and Zika virus (ZIKV) at low micromolar concentrations. Scaffold optimization through multiple structural modifications is ongoing to improve antiviral potency and reduce cytotoxicity. Pure enantiomers of the most active compound were isolated and evaluated, showing no significant difference in biological activity. These findings underscore the promise of broad-spectrum dual NS3 inhibitors as an effective antiviral strategy against flaviviruses.

**P11 - Identification and optimization of novel allosteric inhibitors of ZIKV NS2B-NS3<sup>pro</sup>**

<sup>1</sup>\*L., Demuru; <sup>1</sup>A., Lupia; <sup>1</sup>S., Nieddu; <sup>1</sup>R., Emmolo; <sup>1</sup>A., Paulis; <sup>1</sup>F., Esposito; <sup>2</sup>S. D., Bryant; <sup>1</sup>A. Onali; <sup>1</sup>E. Sanna; <sup>1</sup>G. Atzeni; <sup>1</sup>F. Cottiglia; <sup>1</sup>N., Grandi; <sup>1</sup>A., Corona; <sup>1</sup>E., Tramontano; <sup>1</sup>E., Maccioni; <sup>1</sup>R., Meleddu; <sup>1</sup>S., Distinto.

[laura.demuru2@unica.it](mailto:laura.demuru2@unica.it)

<sup>1</sup> Department of Life and Environmental Sciences, University of Cagliari, Cittadella Universitaria, Monserrato, Italy

<sup>2</sup> Inte:Ligand GmbH, Mariahilfer Straße 74B/11, 1070 Vienna, Austria

Zika Virus (ZIKV), a member of the Flavivirus genus, is transmitted by Aedes mosquitoes and represents a persistent public health threat. The viral NS2B-NS3 protease (NS2B-NS3<sup>pro</sup>) is essential for replication, as it cleaves the viral polyprotein into structural and non-structural proteins. The structural homology between the active site of NS3<sup>pro</sup> and various host serine proteases, and the inefficacy of covalent peptide derivative inhibitors highlight the development of allosteric inhibitors a more promising therapeutic strategy. Currently, no approved antivirals or vaccines are available. In this study, an integrated approach combining various in silico techniques with biochemical assays was employed to identify potential hits targeting NS3<sup>pro</sup> from commercial and FDA-approved databases. Owing to the high conservation of flavivirus proteases, the compounds were evaluated not only against ZIKV<sup>pro</sup>, but also against WNV<sup>pro</sup>. Out of the selection, three compounds exhibited IC<sub>50</sub> values in the low micromolar range in both ZIKV<sup>pro</sup> and WNV<sup>pro</sup>. Based on these results, the scaffold of the active compound 43P was selected for further optimization, leading to the synthesis of a library of 42 analogues. Among the fourteen compounds tested to date, three demonstrated improved inhibitory activity against ZIKV NS3<sup>pro</sup>, and four showed enhanced activity against WNV NS3<sup>pro</sup>. In addition, the known allosteric inhibitor NSC135618 was synthesized as reference. Furthermore, enzyme kinetics studies are ongoing to confirm the allosteric inhibition mechanism of the newly identified compounds and biochemical studies are underway to complete the screening panel of the entire library of synthesized analogues. These efforts will guide further synthetic optimization.



## **P12 - Development and characterization of a Cannabidiol nanosuspension for pulmonary administration**

<sup>1</sup> L., Casula; <sup>1</sup> M., Schlich; <sup>1</sup> M.C., Cardia; <sup>1\*</sup> E., Lai; <sup>2</sup> S., Marceddu; <sup>1</sup> R., Pireddu; <sup>1</sup> D., Valenti; <sup>1</sup> C., Sinico;  
<sup>1</sup> F., Lai; <sup>3</sup> E., Pini.

[eleonora.lai4@unica.it](mailto:eleonora.lai4@unica.it)

<sup>1</sup> Department of Life and Environmental Sciences, University of Cagliari, Monserrato, CA, Italy

<sup>2</sup> Istituto di Scienze delle Produzioni Alimentari (ISPA)—CNR, Sez. di Sassari, Balduina, Italy

<sup>3</sup> Department of Pharmaceutical Sciences, (DISFARM), University of Milan, Milano, Italy

Cannabidiol (CBD) is a bioactive molecule extracted from *Cannabis sativa* with multiple therapeutic properties, including anti-inflammatory, antioxidant, and antibacterial effects. However, the therapeutic efficacy of CBD oral dosage forms is hampered by the low solubility in water and the extensive hepatic metabolism. For these reasons, in this study we developed an inhalable formulation of cannabidiol nanocrystals. In fact, the inhalation route allows to avoid first pass metabolism, while the nano-sizing of particles would increase the solubility of the drug, due to the enhancement of their specific surface area. Various compositions of CBD and surfactants were screened to identify the optimal parameters to obtain narrow-sized and stabile nanosuspensions employing the solvent/antisolvent nanoprecipitation technique. The optimized formulation was then characterized for dimensions, polydispersity index, Z potential, morphology and solid-state properties. Dissolution profiles were studied comparing the nanosuspension to the raw drug and a coarse suspension, demonstrating a significantly faster dissolution rate of CBD nanocrystals. Nebulization performance was evaluated using the Next Generation Impactor (NGI, Apparatus E, Ph. Eu), highlighting excellent aerodynamic properties. In fact, CBD nanosuspension presented a high fine particle fraction (FPF) and a mass median aerodynamic diameter (MMAD) of  $<5 \mu\text{m}$ , highlighting the potential to deposit in the deeper regions of the lungs. Finally, biocompatibility studies using human pulmonary cells provided a preliminary proof of the safety of the formulation.



## **P13 - Microfluidic production of Ru(II) polypyridyl complex-loaded cubosomes for photodynamic therapy of non-small cell lung cancer**

<sup>1</sup>A., Pittiu; <sup>2</sup>G. E., Giacomazzo; <sup>2</sup>L., Conti; <sup>1</sup>L., Casula; <sup>2</sup>C., Giorgi; <sup>3</sup>S. E., Moya; <sup>1</sup>C., Sinico; <sup>1</sup>S., Murgia; <sup>1</sup>M., Schlich.

[alessio.pittiu@unica.it](mailto:alessio.pittiu@unica.it)

<sup>1</sup> Department of Life and Environmental Sciences, University of Cagliari, Cittadella Universitaria Monserrato, Monserrato, CA, Italy

<sup>2</sup> Department of Chemistry "Ugo Schiff", University of Florence, 50019 Sesto Fiorentino, FI, Italy

<sup>3</sup> Centro de Investigación Cooperativa en Biomateriales (CIC BiomaGUNE), 20009 Donostia-San Sebastián, Guipúzcoa, Spain

Non-small cell lung cancer (NSCLC) remains one of the leading causes of cancer-related mortality worldwide. Chemotherapy and radiotherapy, often in combination with surgery, represent the primary therapeutic options, but their associated side effects present substantial clinical challenges. In recent years, photodynamic therapy (PDT) has emerged as a promising alternative or adjuvant modality in oncology. PDT is a minimally invasive treatment based on the administration of a photosensitizing agent that is pharmacologically inactive until it is activated by light of a specific wavelength in the presence of oxygen, thereby producing reactive oxygen species (ROS) that induce localized cytotoxicity and immune activation within the tumour microenvironment. Many potent photosensitizers are large, hydrophobic, organometallic molecules with poor water solubility and disadvantageous pharmacokinetics that hinder their clinical translation. To address these limitations, third-generation PDT agents are incorporated into nanocarrier systems enhancing aqueous dispersion and improving biodistribution, leading to tumour targeting at lower administered doses. Microfluidic micromixing represents a state-of-the-art method for producing uniform nanoparticles in a scalable and cost-efficient manner. In this work, a newly synthesized photosensitizer based on a Ru(II) polypyridyl complex was encapsulated within liquid crystalline lipid nanoparticles (cubosomes) produced by microfluidics. The physicochemical properties of the nanoparticles were assessed over time to monitor stability, and its efficacy was evaluated in two NSCLC cell lines, with a normal fibroblast line used as a control.



## **P14 - The bioarchaeology of Nuragic children and infants: demography and society of bronze age Sardinia**

<sup>1,2\*</sup>R., Anedda.

[roberta.anedda@unica.it](mailto:roberta.anedda@unica.it)

<sup>1</sup> Aix-Marseille University, Laboratoire Méditerranéen de Préhistoire Europe Afrique (LAMPEA, UMR 7269), 5, Rue Château de l'Horloge, 13090, Aix-en-Provence, France

<sup>2</sup> University of Cagliari, Department of Life and Environmental Sciences, SS 554 km4 5, 09042, Monserrato, Italy

How societies develop and adapt when they face cultural changes are core topics of archaeological debate, and bioarchaeology offers a unique approach to explore them. During the Bronze Age, the Nuragic culture rose and spread rapidly throughout Sardinia. While elsewhere population increase led to the intensification of social stratification, in Sardinia the proxies hinting towards either hierarchical or an egalitarian society are not clear. By combining multiple methods, I will investigate the demographic and social aspects of the Nuragic people by focusing on immature remains. Indeed, early life circumstances provide the biological blueprint for adulthood, reflecting thus the wellbeing of the population. Anthropological study of subadult dentition and estimation of age at death investigate the demographic parameters of infant mortality and survivorship as well as the physiological stress and health conditions of children with the analysis of dental defect. The biogeochemical analysis of C, N, and S stable isotopes along the incremental dentine infers about breastfeeding and weaning timing, fundamental to understanding the span between pregnancies, parental care and the variation of diet in children of both sexes. Mobility and whether it was restricted (like in patrilocal societies) is investigated through Sr isotopes. Biological sex is investigated with amelogenin analysis. These results will be compared to modern data using human biology databases, putting them within a human evolutionary and behavioral ecology perspective. This research will add to the debate on Nuragic culture and test new scenarios for the investigation of isolated communities and local developments of social complexities within protohistoric Europe.



## **P15 - Maternal lineages and population dynamics in the Western Mediterranean: a mtDNA study of Sardinia, Sicily, and Corsica**

<sup>1\*</sup>L., Flore; <sup>2</sup>R., Boscolo Agostini; <sup>3</sup>E., Seferidou; <sup>3</sup>K., Nägele; <sup>4</sup>L., Sineo; <sup>4</sup>F., Meli; <sup>5</sup>M., Sazzini; <sup>6</sup>L., Pratesi; <sup>6</sup>M., Vanni; <sup>6</sup>S., Vai; <sup>2</sup>S., Ghirotto; <sup>1</sup>P., Francalacci; <sup>1</sup>C.M., Calò; <sup>1</sup>C. Barbieri.

[laura.flore@unica.it](mailto:laura.flore@unica.it)

<sup>1</sup>Dept. Life and Environment Sciences, University of Cagliari, 09042 Cagliari, Italy

<sup>2</sup>Dept. Archaeogenetics, Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany

<sup>3</sup>Dept. Biological, Chemical and Pharmaceutical Sciences and Technologies, University of Palermo, Italy

<sup>4</sup>Dept. Life Sciences and Biotechnology, University of Ferrara, 44121, Ferrara, Italy

<sup>5</sup>Dept. BIGEA, University of Bologna, 40126 Bologna, Italy

<sup>6</sup>Dept. of Biology, University of Florence, 50122 Firenze, Italy

This study reconstructs the maternal genetic history of the main Western Mediterranean islands (Sardinia, Sicily, and Corsica), through a comparative analysis of ancient and modern mitochondrial DNA (mtDNA) genomes, aiming to explore the roles of migration, colonization, and long-term isolation in shaping insular populations. We analyzed ancient individuals from Sardinian and Sicilian archaeological contexts (Upper Paleolithic–16th century), 17 Sardinians and 10 Sicilians, and 105 modern samples from Sicily, Sardinia, and Corsica. These data were integrated with published sequences, generating a database of 2,272 individuals (538 ancient, 1,734 modern). We reconstructed mitochondrial genomes, assigned haplogroups, and performed phylogenetic network analyses. Our results reveal high maternal diversity in both ancient Sardinia and Sicily, dominated by common Euro-Mediterranean haplogroups such as H and J, but also including rarer lineages (HV, W, U1, X, K, T, U5) reflecting complex demographic histories and Mediterranean contacts. Strong genetic continuity is observed between ancient and modern island populations, particularly in Sardinia, where isolated regions preserve ancient maternal components. Corsican haplotypes are embedded within a broader Mediterranean framework, showing close affinities with Sardinia and Sicily across multiple haplogroups, including H, HV, T, and V. Overall, these findings support a model of long-term insular continuity combined with regional sub-structure and recurrent genetic exchanges across the Western Mediterranean.



## **P16 - BIA International Database (BIAID): results on device technical performance survey**

<sup>1</sup>F., Frau; <sup>2,3</sup>T.R., Silva; <sup>3</sup>G.B., Rosa; <sup>4</sup>J.CK., Wells; <sup>5</sup>L.C., Ward; <sup>3</sup>A.M., Silva; <sup>1</sup>E., Marini.

[federica.frau@unica.it](mailto:federica.frau@unica.it)

<sup>1</sup> Department of Life and Environmental Sciences, University of Cagliari, Monserrato, Italy

<sup>2</sup> Faculty of Nutrition and Food Sciences, University of Porto, Porto, Portugal

<sup>3</sup> Faculdade Motricidade Humana, Universidade de Lisboa, Cruz-Quebrada, Portugal

<sup>4</sup> Population, Policy and Practice Department, UCL Great Ormond Street Institute of Child Health, London, UK

<sup>5</sup> School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, Australia

The BIA International Database (BIAID) is a global, multicentre initiative aimed at supporting methodological standardisation for bioelectrical impedance analysis (BIA) and the development of global reference values. To date, BIAID includes anthropometric and bioelectrical data from approximately 322,000 individuals across multiple countries, encompassing the full lifespan and both healthy and clinical populations. A survey investigating device characteristics and data collection procedures was conducted among researchers who had submitted datasets, in order to evaluate methodological consistency. The questionnaire was distributed between March and December 2025 to 75 invited researchers and responses were self-reported. This exploratory study aims to provide a descriptive overview of the results.

A total of 44 replies were received (response rate ~59%), reporting 27 models of BIA devices, predominantly single-frequency (50%). In most cases, authors declared accuracy around 1% and precision 1-2% for raw data, thus indicating good device reproducibility. Regarding protocols, measurements were performed in the supine position in 72% of cases, while the remaining were conducted in a standing position. Pre-assessment conditions, including fasting, fluid intake, alcohol restriction, high-intensity physical activity avoidance, and environmental temperature varied across centres. These findings provide an overview of the devices and procedures used for data collection, highlighting substantial protocol and methodological heterogeneity and providing essential information to support harmonisation efforts and the development of global reference values.



## **P17 - Violence and conflict at the end of prehistory: from bones to behaviour**

<sup>1</sup>C., Maserati.

[carla.maserati@unica.it](mailto:carla.maserati@unica.it)

<sup>1</sup> University of Cagliari, Department of Life and Environmental Sciences, Cittadella Universitaria di Monserrato  
S.S. 554 bivio per Sestu, 09042 Monserrato (CA), Italy

Between 1200 and 800 BCE, Europe was impacted by a gradual and regionally varied process of social and economic disruption, i.e. the Bronze Age “Collapse”. Archaeological evidence suggests climate stress, plagues, population movements, internal conflict, and the collapse of complex political structures as factors. In Sardinia, during this period nuraghes were progressively abandoned or repurposed, settlements patterns changed, and individual burials became significantly more common. We aim to contribute to the debate by investigating skeletal correlates of health, levels of conflict, and funerary behaviors in remains dated from the Bronze to the Iron age (1400-800 BCE) preserved at the Museo Sardo di Antropologia ed Etnografia. Our analysis focuses on three cave contexts and a polyandric tomb, all of which were used as collective burial contexts.

The work is currently ongoing, therefore results are preliminary. Trauma, both healed and perimortem, was identified or hypothesized for several individuals. Diagnosis is difficult due to the possibility of pseudo-trauma, which is possible in high-energy environments such as funerary caves. In several individuals buried in cave contexts, we identified cut marks potentially related to defleshing activities. These findings suggest the presence of secondary funerary rituals developed through different phases, including decomposition, defleshing, and final deposition. In addition, some individuals exhibit bone alterations compatible with scurvy, suggesting the presence of nutritional stress in prehistoric Sardinian groups. Further analyses and the expansion of the sample will contribute to advancing research on pivotal changes at the end of Sardinian prehistory.



## **P18 - Tuning the selective activation of probiotic bacterial carbonic anhydrases to enhance microbiota performance**

<sup>1</sup>A., Deplano; <sup>1</sup> D., Moi; <sup>2</sup> S., Carradori; <sup>2</sup> M., Gallorini; <sup>3</sup> A., Angeli; <sup>2</sup> D., Iacovazzi; <sup>1</sup> V., Onnis; <sup>4</sup> C., Capasso; <sup>3</sup> C. T., Supuran.

[alberto.deplano@unica.it](mailto:alberto.deplano@unica.it)

<sup>1</sup>Dept. of Life and Environmental Sciences, University of Cagliari, University Campus, Monserrato, Italy

<sup>2</sup>Dept. of Pharmacy, University of Chieti-Pescara, Via dei Vestini 31, Chieti, Italy

<sup>3</sup>NEUROFARBA Dept., Sezione di Scienze Farmaceutiche, University of Florence, Via Ugo Schiff 6, Sesto Fiorentino, FI, Italy

<sup>4</sup>Dept. of Biology, Agriculture and Food Sciences, Institute of Biosciences & Bioresources, Naples, Italy

The microbiota is a community of microorganisms establishing a mutualistic and commensal interaction with the host. Alterations in this symbiosis can be related with resistant pathogen infections, with difficulties in their eradication. Bifidobacteria and Lactobacilli are the most employed probiotics able to counteract the colonization of pathogenic bacteria. The administration of antimicrobials might induce an imbalance of gut microbiota (dysbiosis), allowing either the colonization of resistant pathogens and the overgrowth of opportunistic species, promoting the development of several diseases. Thus, developing small molecules that modulate key enzymes in essential bacterial metabolic pathways may be useful for treating dysbiosis and related diseases. In this context, bacterial carbonic anhydrases (CAs) play a crucial role in supporting multiple physiological functions. Therefore, the selective activation of bacterial CAs may result a successful strategy for the improvement of probiotic performances against dysbiosis and microbial infections. On the other hand, despite the structure activity relationships for the develop of CA inhibitors have been extensively studied, the selective activation of these enzymes is still challenging. Herein we report the design, synthesis and evaluation of a new class of bacterial CA activators, designed and prepared from biogenic amines, amino acids and small peptides which are already known as CAs activators. All compounds activated bacterial CAs with a  $K_a$  at low micromolar levels and most important, these new analogues resulted completely inactive against human CAs. The best compounds have been selected for further biological evaluations.



**P19 - Caffeine and Red Bull® differentially modulate alcohol-induced mesocorticolimbic activation: a behavioral, immunohistochemical and neurochemical study**

<sup>1\*</sup>R., Puliga; <sup>2</sup>V., Bassareo; <sup>1</sup>L., Dazzi; <sup>1</sup>E., Acquas.

[roberta.puliga@unica.it](mailto:roberta.puliga@unica.it)

<sup>1</sup> Department of Life and Environmental Sciences, University of Cagliari, Cittadella Universitaria Monserrato, Monserrato, CA, Italy

<sup>2</sup> Department of Biomedical Sciences, University of Cagliari, Cittadella Universitaria Monserrato, Monserrato, CA, Italy

This study investigated the effects of alcohol, caffeine, energy drinks (Red Bull®, RB), alcohol-mixed energy drinks (AMED) and their interaction on the mesocorticolimbic dopaminergic system, a neural circuit involved in reward and motivated behavior and critically vulnerable during brain development. These interactions were examined through an integrated behavioral, neurochemical, and immunohistochemical approach across short- and long-term exposure paradigms. Acute experiments, in adult rats, initially focused on caffeine, the main stimulating component of RB, to assess its influence on alcohol-dependent dopamine transmission in the accumbens shell (AcbSh). Subsequently, acute AMED administration was employed to further examine mesolimbic signaling, together with locomotor activity and pERK-positive cells in the AcbSh. To model adolescent binge-like alcohol and AMED consumption, rats underwent a non-contingent subchronic exposure followed, in adulthood, by the assessment of mesocortical dopaminergic responsiveness and of voluntary alcohol intake. In parallel, chronic operant self-administration, from adolescence to adulthood, was used to evaluate the motivational effects of alcohol and AMED and their impact on mesocorticolimbic dopaminergic transmission under contingent conditions. Overall, the results indicate that under acute exposure caffeine and RB exert inhibitory effects on alcohol-dependent activation of the mesolimbic system, whereas adolescent subchronic and chronic AMED exposure reveal in adulthood a dysregulation of reward circuits that may represent the basis for increased compulsive substance consumption and potentially contribute to the development of alcohol use disorders.