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Dipartimento di Biologia
e Biotecnologie
Charles Darwin

Sapienza
Università di Roma

Scientific Report

Second edition
2025

contents

ABOUT US

SERVICES&RESOURCES

RESEARCH

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"MESSAGE FROM THE DEPARTMENT HEAD"

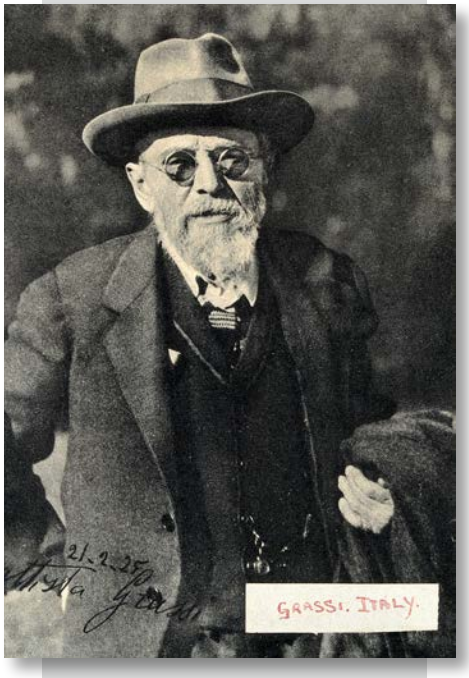
Prof. Rodolfo **Negri**
Full professor of
Molecular Biology
Head of Department

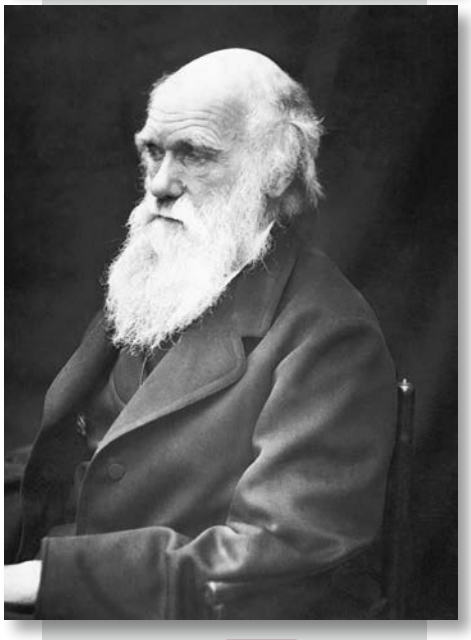
Our Department's aim can be summarized well by the word 'integration'. The Life Sciences are obviously paradigmatic of cultural diversity, spanning the whole diversity of life and a vast array of methodological approaches, which, together with scientists belonging to different areas of the department, offer great opportunities as well as exciting challenges. From the very foundation of the Department, our primary aim has thus been to progressively implement such an integration, regarded – rather than a goal to reach – as an ongoing process to cultivate and continuously keep alive.

The process is hampered by our logistic heritage, with the staff and the facilities operating in several different premises, however the awareness has grown through the years, also thanks to the commitment of my predecessors: the higher the level of integration, the closer we get to the yields of excellence that are in our potential.

Our students belonging to the Bachelor's degrees in Biology and in Biotechnologies as well as the Master's degrees, are a continuous stimulus for all of us to keep our whole work well-rooted into the history of Life Science and our arms projected forwards. Our Department being named after Charles Darwin proves our extensive awareness of the deep and pervasive role of Evolution for Life, and we do our best in order to transmit this message to all our students.

Finally, as the Director of this Department, I want to warmly thank all of its components, from the Administration to the librarians, from the technicians to the scientists/teachers, including all students, for easing a significant part of my work and for sharing with me the goal of making the Department of Biology and Biotechnologies "Charles Darwin" a wonderful place to make and teach Science.





HISTORY | Department BBCD

*The study of Biology in Rome has ancient roots. It is worthwhile to mention here **Giovanni Battista Grassi**, with his research spanning from Zoology to Developmental Biology, from Epidemiology to Ecology. It was in this furrow that in July 2010, the Department of Biology and Biotechnologies was funded, upon the reorganisation of the old biological departments of Sapienza University of Rome ("Animal and Human Biology", "Cellular and Developmental Biology", "Genetics and Molecular Biology" and "Plant Biology"). The new Department took their teaching and research aims forward, perfectly positioning itself within the cultural framework of the Faculty of Science.*

*The Department takes the name of **Charles Darwin**, to affirm the **modern evolutionary matrix**, subtending and permeating almost every theoretical and experimental approaches in research and teaching.*

*Within the Darwin Department many research lines are developed and integrated, which refer to the organisation and the functional analysis of **biodiversity** at different levels: **molecular**, **cellular**, **systemic**, **organismic**, **populational** and **ecosystemic**. Research includes the fundamental aspects of the main biological disciplines, including the **biotechnological** and **applied** aspects. The experimental approaches are largely **interdisciplinary**, as this is increasingly demanded by the complexity of biological problems and by the fast-running methodological innovation. To this aim, the co-existence of a vast array of skills in the various fields within the Department proves crucial.*

The quality and variety of the existing disciplines in the Department allow a vast and highly qualified curriculum that is mostly focused on Biology and Biotechnologies, from Bachelor's to Master's degrees and PhD programmes, but also provide biology-related courses to other Departments' programmes (belonging to the Faculties of Science and Medicine).

COMPARATIVE ANATOMY
GENERAL PHYSIOLOGY
GENETICS
S. LORENZO
ZOOLOGY
PIAZZA VALERIO MASSIMO

THE DEPARTMENT

The Department is located into five major Research Centers (Comparative Anatomy, General Physiology, Genetics, S. Lorenzo and Zoology) that are distributed both inside and in the neighboring areas of the Sapienza University campus. In each Research Center are found research laboratories, offices, facilities, cabled classrooms for teaching, laboratories for didactical experimental practices, conference rooms.
Moreover two Museums belong to the Department, located outside the main campus: the Giovanni Battista Grassi is inside the Comparative Anatomy Center and the Museum of Zoology in the close proximity (Piazza Valerio Massimo).
The administrative staff and the librarians offices are located in the General Physiology and the Anthropology buildings, respectively.

Dipartimento di
BIOLOGIA E BIOTECNOLOGIE
CHARLES DARWIN

HEAD

Rodolfo **Negri**

RAD

Paolo **Valenti**

STAFF MEMBERS

Raffaella **Angeli**
Elvira, Patrizia **Arceri**
Anna **Beneduce**
Giulia **Bernardini**
Fabrizio **Blasi**
Simona **Bucini**
Flavia **Cangelmi**
Michele **Carpino**
Cristina **Corridore**
Elena **De Carolis**
Maria **De Rosa**
Francesca **Fantozzi**
Roberto **Favaroni**
Franca **Iarussi**
Maria **Ippolito**
Carlo **Lico**
Ines **Lonigro**
Claudia **Marchionne**
Stefano **Marotta**
Roberta **Palleschi**
Francesca Papa
Daniele **Recchione**
Francesca **Salvi**
Federica **Spataro**
Paola **Valentini**

LAB TECHNICIANS

Mariangela **Coriandri**
Anna **D'Alfonso**
Angela **Durante**
Martina Leopizzi
Federica **Lucantoni**
Marcella **Marchetti**
Tiziana **Santini**
Andrea **Setini**
Ambra **Tarquini**

IT TECHNICIANS

Riccardo **Bertini**
Carlo **Taricciotti**

ADMINISTRATION AND ACADEMIC AFFAIRS

The head of the Department is the legal representative of the Institution, who guarantes autonomy and cultural unity to the department. The governance of the Department is represented by the Department Council, the Director and the Board. The Chief Administrative Officer (R.A.D.) assists the Director and is responsible for the administrative management and the coordination of the administrative-accounting activities.

Academic Management and Administration

The administrative management is fundamental for coordinating:

- *the accounting management of the funded projects;*
- *the recruitment of contract staff;*
- *the mainteinance departmental offices, laboratories and classrooms;*
- *supporting the activities of the governing bodies;*
- *the updating department's web page and the multimedia equipment.*

Students Affairs

The office supports and provides the student with all the information related to the didactic activities for the courses managed by the BBCD. It represents an interface between students, teachers and the general secretariat of the students; it supports the Coordinators and the Degree Course Councils. The office manages:

- *the first assistance desk;*
- *student counseling and guidance;*
- *the planning of the training and teaching offer;*
- *graduation sessions, in agreement with the student secretariat;*
- *the update of the official website contents.*

Academic Activities

The BBCD Department hosts:

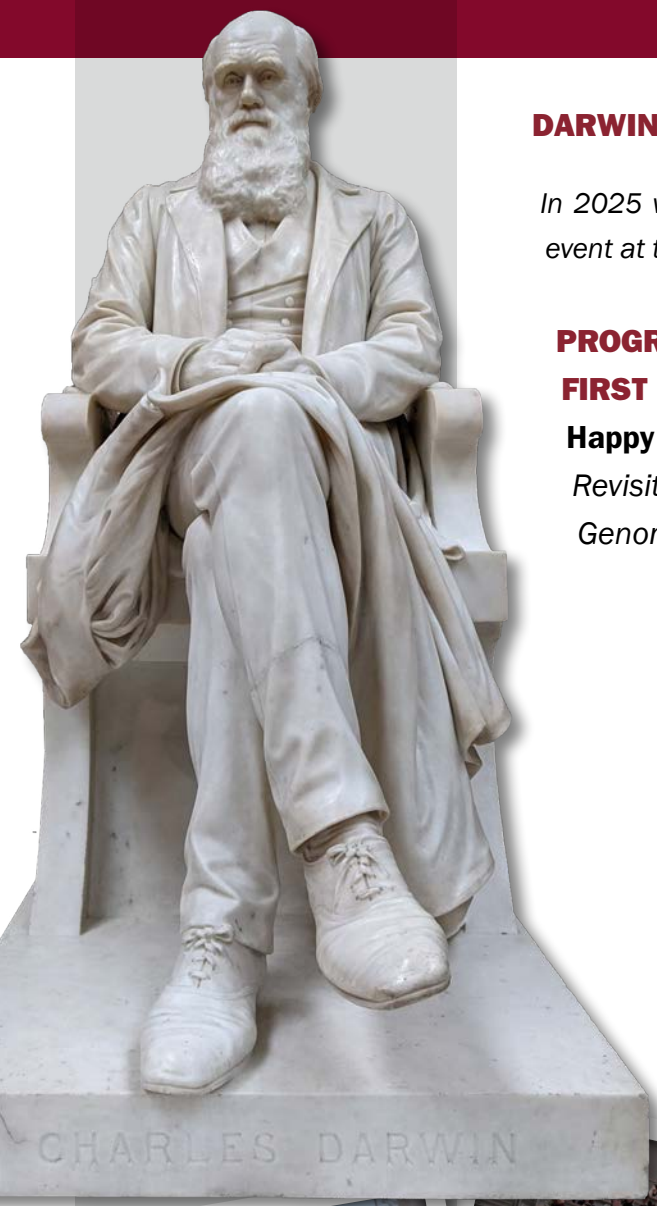
- *the Bachelor's degrees in "Biology" and "Food and Industrial Biotechnology"*
- *five Master's degrees in "Genetics and Molecular Biology", "Neurobiology", "Cell Biology and Technology", "Biotechnology and Genomic for Industry and Environment", "Food Science and Technology" (shared with Tuscia University).*
- *three Doctoral programs:*

  PhD Program in Cell and Developmental Biology
  https://phd.uniroma1.it/web/CELL-AND-DEVELOPMENTAL-BIOLOGY_nD3489_EN.aspx

  PhD Program in Genetics and Molecular Biology
  https://phd.uniroma1.it/web/GENETICS-AND-MOLECULAR-BIOLOGY_nD3506_EN.aspx

  PhD Program in Life Science
  https://phd.uniroma1.it/web/scienze-della-vita_nd3539.aspx

- *three one year graduate Masters in "Scientific Journalism", "Stem Cells and genome editing", "Biology of Nutrition for Human Reproduction".*



DARWIN DAY | Department BBCD

In 2025 we started to organize a Darwin Day celebration with a department event at the crossroads between dissemination and specialized seminar.

PROGRAM OF DARWIN DAY
FIRST EDITION I 12th FEBRUARY 2025

Happy birthday, Charles, how are you?

Revisiting Darwinism in light of the astonishing advances in Genomics, Epigenomics, and Metagenomics.

9 - 13 I Sapienza Università di Roma - Aula La Ginestra
Edificio di Chimica Cannizzaro (CU14)

Keynote address by Prof. R. Faccini, Dean of the Faculty of Sciences and Prof. R. Negri, Head of Department of Biology and Biotechnologies "Charles Darwin", Sapienza University of Rome

Lectures:

Races and we are not taking of dogs
Giovanni Destro Bisol - Prof. of Antropology, Sapienza University of Rome

Genetics and Epigenetics
Nicola Iovino - Research Director, Max Planck Institute of Immunobiology and Epigenetics, Friburgo

Darwin and the "Oblonte theory"
Duccio Cavalieri - Prof. of Microbiology, University of Florence

15 - 18 I Sapienza Università di Roma
Aula Montalenti - Edificio di Genetica (CU022)

Lectures:

In memory of Sergio Pimpinelli
Maurizio Gatti, Prof. Emeritus of Genetics, Sapienza University of Rome

Epigenetic inheritance
Nicola Iovino - Research Director, Max Planck Institute of Immunobiology and Epigenetics, Friburgo

Symbiomes Yeast bacteria interactions and the one health concept
Duccio Cavalieri - Prof. of Microbiology, University of Florence

Lecture Duccio Cavalieri


Lecture Giovanni Destro Bisol

“GIOVANNI BATTISTA GRASSI” MUSEUM OF COMPARATIVE ANATOMY IS THE FIRST OF 10 WINNERS OF WIKIMEDIA ITALIA’S MAB 2025 CALL FOR PROPOSALS

“GLAM&SAPIENZA MUSEUM OF COMPARATIVE ANATOMY”

The wiki project on scientific wall charts is promoted by the Giovanni Battista Grassi Museum of Comparative Anatomy at Sapienza University of Rome in collaboration with the Darwin Library and the IT office of the Charles Darwin Department of Biology and Biotechnology, as part of the GLAM 2025 Wikimedia call for proposals, designed to support Galleries, Libraries, Archives, and Museums in digitizing and sharing their collections under open licenses. Scientific wall charts were a fundamental teaching tool in universities and schools throughout Europe, especially in the period between 1870 and 1920, although examples appeared also in 1820-1830 and in some cases their use continued until the 1960s. Scientific wall charts were educational posters made of paper, sometimes applied to sheets of linen or canvas, characterised by large format - for example, 70x100 cm (27.5x39.3 in.), 100x150 cm (39.3x19.6 in.), or 130x140 cm (51.1x55.1 in.) - and the presence of drawings and illustrations. These were hung on the walls of the classroom where teaching took place, in order to offer learners a visual experience of what was explained during the lesson, a sort of ante-litteram slide projection. The charts (Wandtafeln, wall charts, planches murales), printed in colour using chromolithography, could be purchased from specialised publishers, or alternatively were handmade through the patient work of illustrators or the academic lecturers themselves for their lessons.

Objectives

The museum holds hundreds of wall charts, dating from the last two decades of the nineteenth century to the beginning of the twentieth century, depicting animals from various zoological groups and anatomical parts.

The project proposes:

1. the enhancement, through digitisation, of a sample of 100 plates, appropriately selected among the original hand-drawn ones;

2. digitised images of the plates, carried out by means of photographic acquisition using the camera purchased with project funds, will be uploaded to Wikimedia Commons and provided with metadata, where available;

3. each wall chart uploaded to Wikimedia Commons will also have an item on Wikidata, in its dual role as an “artistic painting” and scientific image, enriched with properties that describe its appearance and content, such as taxonomy, and which create relationships between the charts or other items already present in Wikidata, using the full potential of LOD (Linked Open Data).

Aula Daniel Bovet

Aula Pasquini

Our laboratory

"LIGHTS, CAMERA, ACTION!"

Our department is housed in historical buildings dating back to the 1940s. Some of the classrooms we use for teaching still preserve the original structure of what were once surgical theatres.

In particular, the Zoology section of the department was originally part of the Medical Studies buildings. This explains why the main lecture hall, Aula Pasquini, features the typical amphitheatre layout that was once used for anatomical dissections during medical lessons.
Aula Pasquini, Aula Daniel Bovet, and Aula C in the Physiology building all share the same architectural style: wooden interiors and an amphitheatre design that make them both traditional and charming.

Because of their distinctive atmosphere, our department's classrooms are often chosen by film directors for scenes set in classic university environments.

In 2014 director Sydney Sibilia shot several scenes of the movie "Smetto quando voglio" in our classrooms and one of our laboratories.

In 2023, actor and director Carlo Verdone, filmed some scenes of the TV series "Vita da Carlo 2", while recently he filmed some scenes for his upcoming movie "Scuola di seduzione" in our buildings, precisely in the Aula Daniel Bovet.

Aula Daniel Bovet

Aula Daniel Bovet

MUSEUM OF COMPARATIVE ANATOMY

“ GIOVANNI BATTISTA GRASSI „

The Museum of Comparative Anatomy “Giovanni Battista Grassi” preserves the relics and the archive of the great Italian zoologist **Giovanni Battista Grassi** (1854 - 1925).
The collection includes objects belonging to the celebrated “Kircheriana” exhibition of the 17th century, ancient papier-mâché anatomical models by Jérôme Auzoux (1797-1880) and embryological wax models by Friedrich Ziegler (1860-1936).
Part of the museum is dedicated to the microscopic analysis with ancient instruments from the late 1700s up to the transmission and scanning electron microscopes of the 70s and includes the ancient istoteca with about 3000 slides.

The richest part of the exhibition is certainly the osteological collection which includes complete skeletons of large cetaceans and describes the balance between the evolutionary continuity of all vertebrates and adaptations to different environments.
The scientific collection has been implemented, in more recent years, with collections of small mammals and reptiles, especially from Italy, Africa, Central and South America, thanks to samples carried out by researchers belonging to the Comparative Anatomy headquarters.
The Museum carries out scientific dissemination activities for schools and it is open to the public two days a week.
The collections are used for research activities related to the study of evolutionary morphology and molecular phylogeny of vertebrates.

“ MUSEUM OF ZOOLOGY „

Awareness of the importance of global biodiversity as part of our natural heritage is growing in the society. Therefore, senior scientists and biology students must be given easy access to workable natural history collections for studies with traditional and innovative approaches, including both morphological and molecular methodologies. Metazoans represent a vast majority of the world's known living organisms, as well as of those still to be discovered. In this context, zoological museums represent cornerstones for the future of research in the field of natural history. The University Museum of Zoology (MZUR) is one of the oldest scientific museums in Rome. It hosts around one million specimens (both dry- and ethanol-preserved) belonging to all metazoan phyla, with a special focus on vertebrates and arthropods. MZUR preserves historical collections inherited from the Archiginnasio Pontificio as well as a large amount of material collected during the last decades by researchers during field campaigns. MZUR promotes and triggers high quality and collaborative research activities for scientific projects in nature conservation and biodiversity inventorying, currently with a main focus on insects. These activities include worldwide collecting fieldwork, and laboratory work for sorting, preparing, labelling, loan processing, management of supplies and equipment, as well as species identification (using both morphological and molecular approaches). Through these projects MZUR has seen its collections and international reputation significantly grown. Zoological collections at MZUR represent a big source of historical data which are critical to understand the impact of climate change on ecosystems.

Curatorial philosophy at MZUR

Researchers and technicians at MZUR give priority to networking with all major homologous institutions and taxonomists around the world and are involved with producing high-impact taxonomic revisions and monographs (at regional and global scale). Collections are essential for taxonomy and taxonomy is in turn inalienable from both pure and applied biology. A convincing communication of this concept at every education level is a contemporary challenge in order to highlight the role of natural history collections.

Our curatorial goals are:

- Enhancing the production of matrix-based interactive keys for taxa identification, supported by high quality specimen images and detailed distribution maps;
- Augmenting the arthropod collections through collaborative research programs, mainly focused on areas with high rate of biodiversity loss, e.g. South America, Africa and Australasia;
- Setting up different specimen preservation methods in order to further both morphological and molecular studies and widen the spectrum of possible collaborations.

In line with the objectives of the Sapienza Strategic Plan, BBCD aims to integrate the excellence of scientific research with THIRD MISSION ACTIVITIES. A complete list of BBCD third mission activities is available on the dedicated web page

http://bbcd.bio.uniroma1.it/it/terzamissione/iniziative

“THIRD MISSION”

The activity of BBCD towards society and the world of work is exemplified by the Master “Life sciences in journalistic practice” (**www.mastersgp.it**), which since 2006 has achieved excellent results in job placement. With this Master, BBCD has earned recognition from the National Order of Journalists as a continuing education institution, bringing over 100 journalists/year to Sapienza.

BBCD members are also active in consultancy open to citizens, media, and the University Press Office on scientific and applied issues, as well as involved in Citizen Science projects. BBCD researchers hold numerous international patents in biology and biotechnology and maintain collaborative agreements with private companies for research exchanges.

The organization contributes to schools through the National Science Degree Plan, a 2004 initiative by MIUR, Sciences and Confindustria, aimed at increasing student enrollment in science degrees through professional teacher development and course alignment between school, university and work. BBCD has also carried out numerous school-work alternation programs and joined the School Project with the Pasteur Italia Institute.

In the museum field, BBCD collaborates with the Museums of Comparative Anatomy and Zoology, offering guided tours to hundreds of students and teachers annually. BBCD promotes public engagement through dissemination projects like the SCOPUS-indexed journal “Fragmenta entomologica”, the Italian Fauna Committee, and the “Fauna Europaea” project (**https://www.gbif.org/dataset/90d9e8a6-0ce1-472d-b682-3451095dbc5a**). Since 2014, it has been a partner of the International Union for Conservation of Nature for the global database of endangered species and contributes to the Intergovernmental Platform on Biodiversity and Ecosystem Services. Among its key outreach projects is the exhibition Elogio della diversità, which celebrates biodiversity as a vital scientific and cultural resource, bringing attention to the richness of life forms and their evolutionary paths. BBCD and the Master SGP group also founded **StaR**, a magazine dedicated to science dissemination and the promotion of Sapienza’s research excellence, which highlights innovative projects and fosters dialogue between science and society.

BBCD is further engaged in Erasmus programs, double degrees and seasonal schools with Spain, France, UK, Denmark and Germany, and has established an exchange with Singapore.

In postgraduate training, its doctoral and master’s programs involve international networks, with visiting scholars and co-tutors from abroad.

BBCD researchers also collaborate in research agreements with institutions in Australia, Germany, the Netherlands, UK, Russia, France, Switzerland, China, Iran, Georgia, Mozambique, the US and Singapore.

“LIBRARY”

Dipartimento di BIOLOGIA E BIOTECNOLOGIE CHARLES DARWIN
BIBLIOTECA

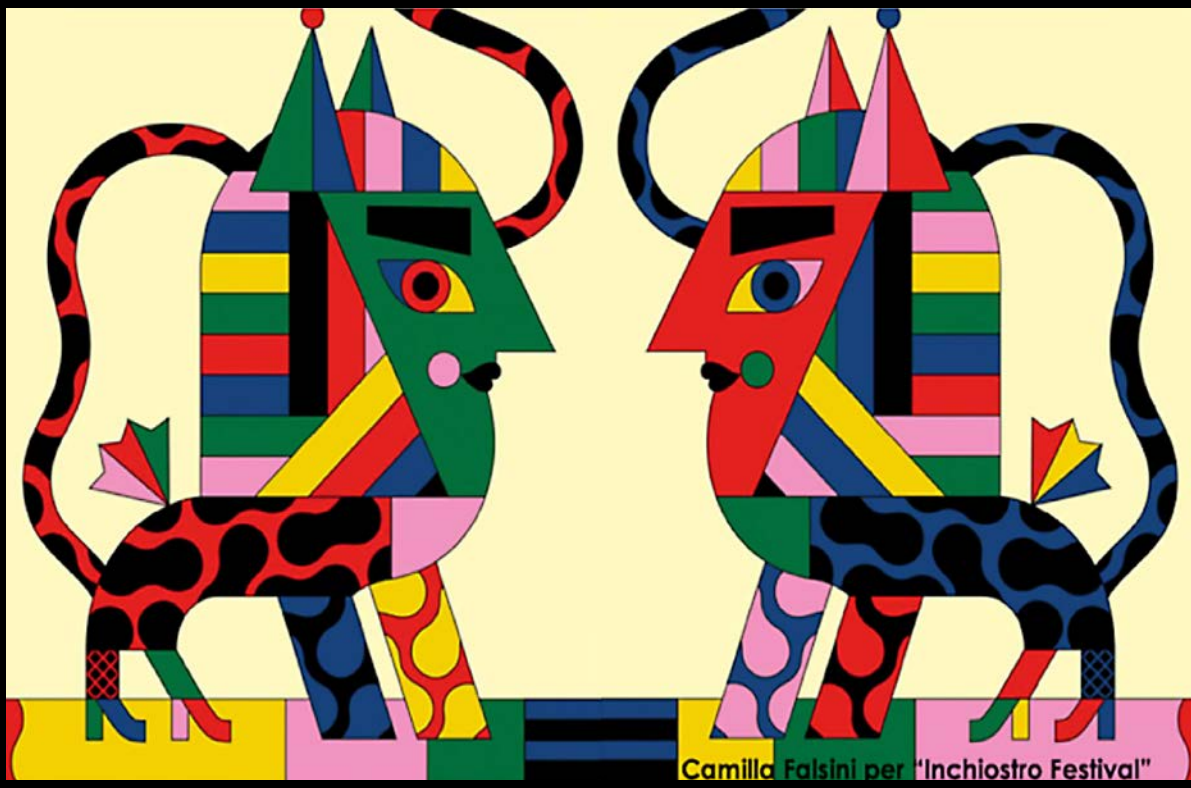
Charles Darwin Library’s staff works actively to support research, learning and teaching and play the role of bridge-building within the academic community.
We offer fertile and innovative ground mix ideas between science and everyday life and we want to be the space for multidisciplinary meetings and exchanges. All this beside offering the core library services: acquisition, cataloguing, technical services, care of physical and virtual collections, scholarly communication, institutional repositories, open data management, open science policies, national and international interlibrary loan and document delivery services, user education and information literacy activities to increase the students’ skills to improve learning and to undertake research independently (es. PubMed-Labs). We are in a transition phase that is leading us to resemble a hub where our users can find opportunities to take part in conversations about books, or their scientific interests and much more besides: “the true collection of a library is not made up of documents or manuscripts, but in the innovation, experience, and brilliance of the community served”. (R. David Lankes, Libraries for learning <http://davidlankes.org/libraries-for-learning>). Whether it is information literacy or support in the evaluation of research, we want to foster the birth of a community based on the sense of belonging, trust and good sharing practices. In the welcoming and friendly context we are building, the participation of our students, PhDs, teachers and researchers becomes the cornerstone of every activity. We work with the purpose to facilitate the meeting and the inclusion and we pay particular attention to the international students. In our library you can find traditional services as loan, reading rooms, etc. but also spaces suitable for meeting, sharing an active and collaborative learning (e.g. group study rooms, Tandem Language Exchange, reading groups).

Library desk

To contact us: email website facebook instagram

Staff:

Elena **De Carolis** | *Director*
Raffaella **Angeli** | *Interlibrary Loan; Cataloguing Services*
Michele **Carpino** | *Third Mission activities; social pages; Institutional Repository.*
Ines **Lonigro** | *Third Mission activities; social pages; Institutional Repository.*
Roberta **Palleschi** | *Reference Services; Institutional Repository; PubMed Labs*



Contact
gep.bbcd@uniroma1.it
laura.ciapponi@uniroma1.it

“ GEP COMMITTEE ”

The Gender Equality Plan (GEP) **Committee of the Department of Biology and Biotechnology “Charles Darwin”** is a group of people dedicated to promoting a culture of respect and inclusion, actively opposing all forms of discrimination, including those based on gender, race, religion, or disability. The Committee’s goal is to implement concrete initiatives, in line with the **University’s Gender Equality Plan**, to create a more equitable and welcoming environment for everyone. Through its work, the Committee aims to raise awareness within the academic community on gender equality issues, prevent situations of disparity and harassment, and celebrate personal and social diversity.

GEP MAIL BOX

Anonymous Spaces to Share and Change

The GEP “mailbox” provides a safe and anonymous space to report discrimination, violence, and microaggressions. A new virtual option - a confidential Google form accessible via QR code - makes it easy to share experiences, and the group can also be contacted by email (gep.bbcd@uniroma1.it). Reports are not limited to violence or broad discrimination but also cover disrespectful or stereotypical behaviours toward women, especially in science and research. These tools give voice to often overlooked situations and help the Department develop more effective and informed inclusion policies.

SAFE ZONE PROJECT

Safe Zones are spaces and trained people who promote inclusion and support for LGBTQ+ individuals. They create an environment where everyone can fully express themselves socially, emotionally, and intellectually. Look for the Safe Zone logo in our Department’s spaces—you’ll find people ready to listen and provide support on issues related to gender, sexual orientation, and gender identity.

CINEFORUM – Beyond the Screen: Gender Stories

Beyond the Screen: Gender Stories is a film series offering a space for reflection and discussion on gender equality, inclusion, and diversity. Through selected films, it explores topics such as gender roles and stereotypes, discrimination, female empowerment, identity, rights, and inequalities, with a focus on women in science and research. Each screening is followed by an open discussion with expert guests, encouraging critical reflection and dialogue. The series aims to use cinema as a tool to inspire new perspectives, questions, and a more inclusive culture.

“RESEARCH&FACILITIES„

Researchers in the Department are engaged in a broad range of investigations at all levels of biological complexity, from molecular mechanisms to entire species communities. Their expertise spans diverse fields, including Molecular Biology, Biochemistry, Bioinformatics, Genetics, Microbiology, Cell Biology, Immunology, Neurobiology, Plant Physiology, Zoology, Comparative Anatomy, Nanobiotechnologies, and Nanoscale Imaging.
This rich interdisciplinarity creates a dynamic environment that fosters innovation and technological progress. The Department’s various buildings house well-equipped facilities - also open to external users - and shared infrastructure and instrumentation that support the cutting-edge experimental research of its members.

FACILITIES

STEM CELLS AND ORGANOIDS
https://bbcd.bio.uniroma1.it/en/stem-cells-and-organoids

This facility, located in the “Fisiologia Generale” building and open to internal and external users, supports stem cell and organoid generation, culture, genome editing, and characterization. Equipment includes an IVF laminar flow hood with stereomicroscope, heated stage, and orbital incubator shakers for long-term organoid culture.

IMAGING
https://bbcd.bio.uniroma1.it/en/imaging

The Imaging Facility of the Department of Biology and Biotechnologies “C. Darwin” offers advanced microscopy and slide scanning technologies to support high-resolution imaging and analysis across multiple spatial scales, using conventional fluorophores and routine sample preparation protocols. The facility hosts in the “Via dei Sardi” Building a ZEISS LSM 900 laser scanning confocal microscope equipped with a super-resolution module, enabling high-resolution, three-dimensional imaging of biological specimens. The facility hosts in the “Fisiologia Generale” Building a Nikon ECLIPSE Ti2-E inverted microscope, integrated with the CrestOptics X-Light V3 spinning disk confocal system and DeepSIM super-resolution module, providing fast, high-throughput, and high-resolution imaging of both fixed and live samples. For large-scale slide digitization, the facility offers the NanoZoomer S60 NDP slide scanner, which allows automated, high-resolution brightfield and fluorescence slides imaging. Additionally, an image analysis workstation equipped with the NIS-Elements (NIS-A) software suite, including high-performance computing and machine learning algorithms (including 2D and 3D deconvolution modules using fast, non-blind, and Landweber algorithms), supports advanced image processing, quantification, and 3D reconstruction. Research activities are supported by specialized technicians responsible for routine maintenance, user assistance, and user training on all imaging systems. The facility is accessible to all department members and available to external users, subject to availability and applicable fees.

SHARED INFRASTRUCTURES AND INSTRUMENTS

PHYSIOLOGY - Building CU026

Animal facility
https://bbcd.bio.uniroma1.it/en/animal-facility

The Animal Facility supports in vivo research activities in full compliance with Legislative Decree 26/2014, which implements the EU Directive 2010/63/EU on the protection of animal used for scientific purposes. The facility houses multiple strains of Mus musculus and Rattus norvegicus, is licensed for in vivo administration of viral vectors under Biosafety Level 1 (BSL-1) conditions, and includes dedicated rooms for behavioral testing and surgical procedures. Research activities are supported by a designated veterinarian and specialized technicians responsible for ensuring animal welfare, in coordination with the Department's Animal Welfare Body (Organismo Preposto al Benessere Animale, OPBA). All procedures are carried out in strict accordance with current regulations, with animal welfare as a primary objective. Scientific activities are guided by rigorous harm-benefit assessments and the application of the 3Rs principles (Reduction, Refinement, Replacement). Access to the facility is granted to the Department's professors and researchers who meet all relevant legal and ethical requirements.

Biosafety Level 2 (BSL-2) Biological Laboratory
BSL-2 laboratory provides enhanced containment and safety measures for handling moderately hazardous biological agents (e.g. lentivirus). It combines controlled access and specialized equipment ensuring both user protection and environmental safety.

Thermostated Incubator 30 °C
Room dedicated to the cultivation of microorganisms at 30 °C.

Refrigerated Chamber 4 °C
Room dedicated to the storage of sample and to run experiments that require low temperatures.

Fluorescence Microscopy Room
Two Microscopes Zeiss (upright microscopes) with fluorescence, objectives 10X, 40X, 100X, UV-GFP-Texas Red filters.

Beckman Centrifuges J-25 and J-26XP
Model J-25 furnished with two rotors for small volumes; Model J-26XP equipped with 1 rotor for large volumes.

Tissue sectioning instruments
Ultramicrotome (Reichert) for cutting ultrathin sections. Microtome LKB for sectioning paraffin-embedded samples. Cryostat Microtome (Leica) for cutting free-floating tissue sections from frozen specimen (thickness from 5 to 50 µm). Vibratome for cutting free-floating tissue sections from fresh or fixed specimens (thickness from 30 to 500 µm).

Real-Time PCR System
Real time PCR System (Applied Biosystem).

Cell Counter
LUNA-FX7™ automated cell counter (Logos Biosystems) for cell counting and viability measurement.

ChemiDoc Imaging System
CCD-based imaging system for detecting proteins on Western blots using ECL chemiluminescence.

Plant growth infrastructure
Walk-in room and cabinets for plant growth

Temperature-controlled rooms at 4°C and 28°C

Next generation sequencing for single small molecules Nanopore MinION (Oxford Nanopore Technologies)

COMPARATIVE ANATOMY - Building RM057

Zeiss Axiophot Epifluorescence Microscope
Equipped with filter sets for FITC, TRITC, and DAPI. It is also equipped with a Sensyn monochrome digital camera for high-resolution gray-scale image acquisition.

Two independent refrigerated chambers (4–16 °C)
Dedicated to the storage of biological samples and reagents, as well as to the performance of experiments requiring controlled low temperatures.

ZOOLOGY - Building CU008

High Performance Computing (HPC) Cluster
Three-node (0,5-1.5 Tb RAM) general-purpose computing cluster for Big Data analyses, contributing to Sapienza TeraStat3 supercomputing cluster.

Molecular Systematics Lab
Including an automated nucleic acid extraction/purification station, PCR thermocyclers, and all equipment for research of DNA-barcoding, phylogenetics, and population genetics.

Zoological Digitalization Platform
Including photogrammetry stations, Artec Micro e macro Scanner, and a Phenom XL II SEM, for digitalization of zoological vouchers.

GENETICS - Building CU022

RAdiation and microgRavITY(Rarity)
Equipped with a monoblock X-Ray generator (MHD200, Gilardoni) and a perfusion RWV bioreactor, installed inside the X-ray cabinet to expose samples to IR in a reduced-gravity environment.

SAN LORENZO - Building RM024

Three refrigerated chambers 4°C
Rooms dedicated to the storage of biological samples and reagents, and to run experiments that require low temperatures.

Three temperature-controlled room (22°C, 28°C and 37°C
Rooms dedicated to the growth of microorganisms and insects

Bioruptur Pico (Diagenode)
A next-generation ultra-sonication instrument for high-quality sample preparation for studies in genomics and epigenomics, proteomics, cancer research, stem cells and many more.

ChemiDoc MP imaging system (Biorad)
for quantifying proteins and nucleic acids in western blotting or gels by far red/near infrared fluorescence and chemiluminescence detection.

Real-time PCR system
StepOne PCR (Thermo Fisher) and QIAcuity ONE digital PCR (Biorad)

Two-laser ScanArray Gx PLUS
(Perkin Elmer) for transcriptomic and proteomic studies.

Orbitrap LC-MS
(Thermo Fisher) for high-resolution mass spectrometry.

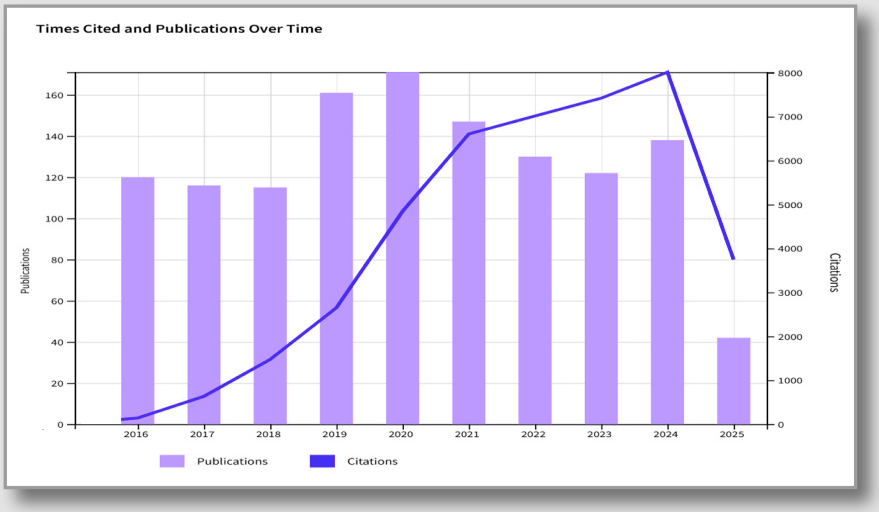
CITATION REPORT FOR 1.262 RESULTS (WEB OF SCIENCE CORE COLLECTION) | 2016-25

Total Publications
1.262
From 2016 to 2025

h-index
88
Average citations per item
33.74

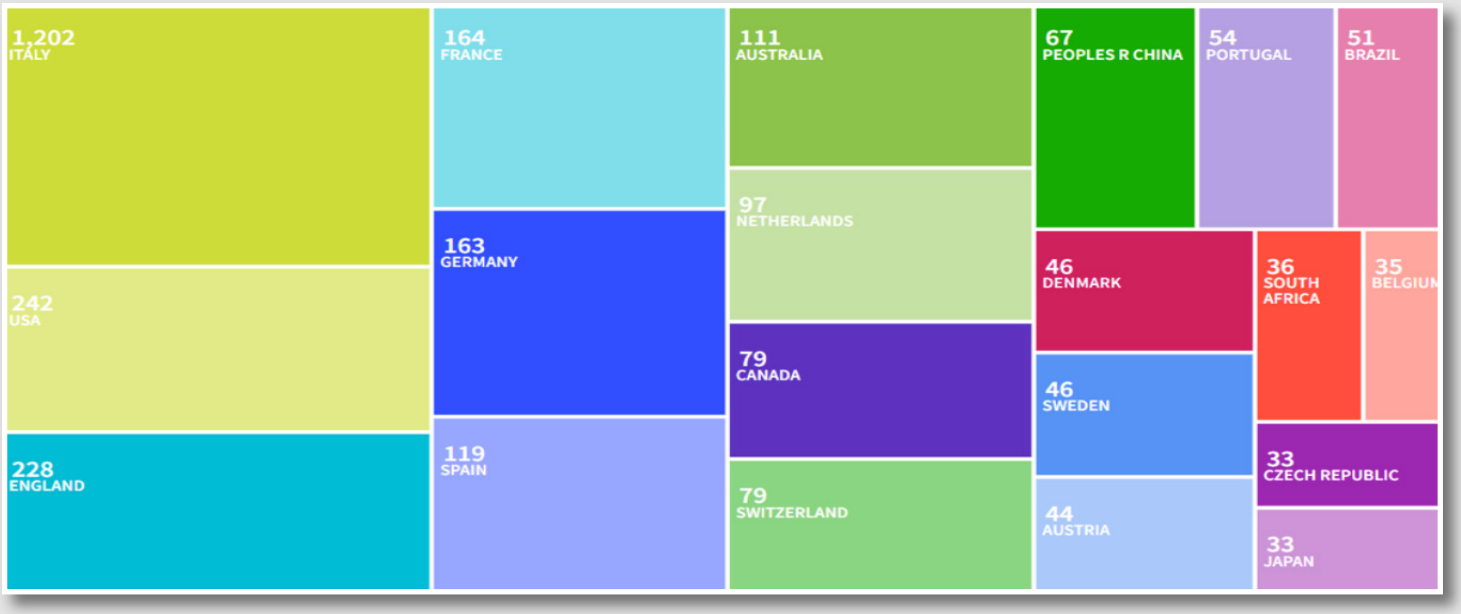
Times Cited
42.574
Total
Without self citations
40.162

Citing Articles
35.363
Total
Without self citations
34.575



TOP TWENTY WEB OF SCIENCE CATEGORY VALUES | 2016-25

TOP TWENTY COOPERATING COUNTRIES | 2016-25



Iris Web Site

"INSTITUTIONAL RESEARCH INFORMATION SYSTEM"

IRIS is an IT system which purpose is to valorize the research published in Italy and favor its wider dissemination into the scientific community. The research works included in the catalogue of the publications and the profiles of the researchers affiliated to the single institutions, provide high visibility and strong impact on increasing the number of citations, collaborations and shared projects. The system indeed is interoperable because of its interface with the data management.
Our department has embraced since the very beginning the use of the IRIS catalogue for its members. Research referents and librarians have trained and helped researchers for inserting the publications in the system and for curating and validating the publication catalogue. In line with Sapienza policy for Open Access (https://www.uniroma1.it/it/pagina/sapienza-lopen-access), our department supports the "open science" concept based on transparency, sharing and re-use of the data, and it encourages the open access publication of the scientific data obtained with public funding.

Prodotti per dipartimento

CENTRO INTERUNIVERSITARIO DI RICERCA "HIGH TECH RECYCLING"	3
CENTRO INTERUNIVERSITARIO DI RICERCA DI PSICOLOGIA AMBIENTALE - CIRPA	3
CENTRO INTERUNIVERSITARIO DI RICERCA SULLA ELABORAZIONE COGNITIVA IN SISTEMI NATURALI E ARTIFICIALI	15
CENTRO INTERUNIVERSITARIO PER LA RICERCA SULLA GENESI E SULLO SVILUPPO DELLE MOTIVAZIONI PROSOCIALI E ANTISOCIALI	17
DIPARTIMENTO "ISTITUTO ITALIANO DI STUDI ORIENTALI - ISO"	5644
DIPARTIMENTO DI ARCHITETTURA E PROGETTO	15333
DIPARTIMENTO DI BIOLOGIA AMBIENTALE	9283
DIPARTIMENTO DI BIOLOGIA E BIOTECNOLOGIE "CHARLES DARWIN"	8441
DIPARTIMENTO DI CHIMICA	11710
DIPARTIMENTO DI CHIMICA E TECNOLOGIE DEL FARMACO	5563

Prodotti per autore

GIAGU, Stefano	1810
DEL RE, Daniele	1661
ORGANTINI, Giovanni	1642
RAHATLOU, SHAHRAM	1619
PARAMATTI, Riccardo	1474
GENTILE, Simonetta	1368
LUCI, Claudio	1336
SANTANASTASIO, FRANCESCO	1270
LONGO, Egidio	1263
RAGNAIA, Paolo	1254

Prodotti per anno di pubblicazione

In corso di stampa	1432
2026	10
2025	6462
2024	17223
2023	19544
2022	19903
2021	20220
2020	21028
2019	20320
2018	19728

Updated August 25th, 2025

SAPIENZA
UNIVERSITÀ DI ROMA

Dipartimento di
BIOLOGIA E BIOTECNOLOGIE
CHARLES DARWIN

RESEARCH CENTERS

COMPARATIVE ANATOMY
Via Borelli, 50

PHYSIOLOGY
University Campus
Piazzale Aldo Moro, 5

ZOOLOGY
Viale dell'Università, 32

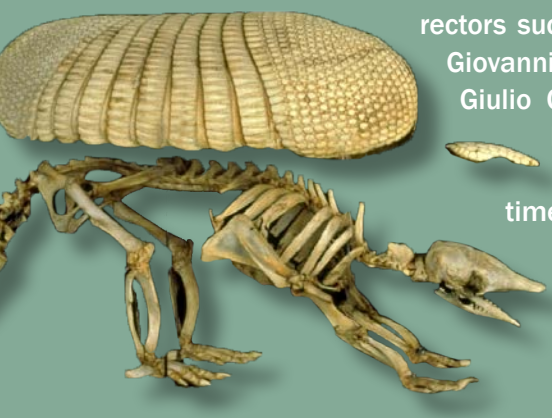
GENETICS
University Campus
Piazzale Aldo Moro, 5

S. LORENZO
Via dei Sardi, 70
Via degli Apuli, 4

“COMPARATIVE ANATOMY”

The headquarters of Comparative Anatomy has very ancient origins, dating back to the first half of the nineteenth century, when Comparative Anatomy and Zoology were associated in the same “Gabinetto di Zoologia e Anatomia Comparativa con annesso Museo” of the “Pontificio Archiginnasio della Sapienza”.

After the unification of Italy and the reorganization of the university in the “Regia Università di Roma”, in 1883, the “Istituto di Anatomia Comparata” was established in via De Pretis 97, in the university area of via Panisperna. Following the demolition of the building, in 1926, the Comparative Anatomy was housed, provisionally, in the new centre of Human Anatomy in via Borelli 50, where the headquarters of Comparative Anatomy is still located. Throughout its history, the institute has had prestigious directors such as Franz Böll, Giovanni Battista Grassi, Giulio Cotronei and Alberto Stefanelli.



In more recent times, since the 70s, two lines of research have emerged: the first on Comparative Neuroanatomy which then developed research concerning the effects of environmental stressors and the role of synucleins in the nervous system of non-mammalian vertebrates; the second on Comparative Cytogenetics of Vertebrates, which has been integrated with molecular phylogenetics/systematics and geometric morphometry approaches. At present the laboratories of the headquarters include an immunohistochemical laboratory, a Molecular Biology laboratory dedicated to systematics, and a cytogenetics laboratory.

Moreover, the facilities include cold rooms for the storage of biological samples, cell culture and a fluorescence microscope. There is also a meeting room equipped with a projector.

Riccardo
Castiglia
Associate Professor

ORCID

RESEARCH LINES

- Evolutionary biology of the house mouse
- Phylogeography of small mammals and reptiles in the Mediterranean region
- Taxonomy and chromosomal evolution of small mammals and reptiles in areas of high biodiversity
- Scientific museology

STAFF | COLLABORATORS

Francesco Gallozzi,
Post-doc (BBCD, Sapienza)
Emanuela Solano,
Researcher (CNR, Monterotondo)
Paolo Colangelo,
Researcher (CNR, Monterotondo)
Alexandra M.R. Bezerra,
Researcher (Museu Paraense E. Goeldi, Belém)

RESEARCH ACTIVITY

Evolutionary biology of the house mouse
The house mouse, *Mus domesticus*, has numerous chromosomal races distributed in various European and non-European regions, characterized by a diploid number between 38 and 22 chromosomes.
The research focuses on the mechanisms that determined the origin of these races and on the effect of chromosomal differences on gene flow. In particular, the chromosomal evolution of the races settled in central Italy, Sicily and the Aeolian archipelago is the object of the research line, through i) the identification of chromosome markers (metacentric Robertsonian), ii) phylogeny with molecular markers iii) analysis of gene flow in areas of natural hybridization (maternal and bi-parental molecular markers), and iv) analysis of fertility in natural hybrids for the study of the effect of structural heterozygosity at the individual level.

Phylogeography of small mammals and reptiles in the Mediterranean region
The objective of this line of research is to investigate the role of paleogeographic and paleoclimatic events of the Pleistocene on the distribution of genetic variability and speciation in some species of small mammals and reptiles in the Mediterranean area. The approach used is the phylogeography, through nuclear and mitochondrial genetic markers.

Taxonomy and chromosomal evolution of small mammals and reptiles in areas of high biodiversity
The research line addresses the taxonomy of small mammals (Rodentia and Soricomorpha) and reptiles (Squamata) in the tropical regions of East Africa and the tropical forest along the Pacific coast of Mexico, mainly using the information obtained from the karyotype study (cytotaxonomy). Furthermore, the patterns of chromosomal evolution have been described in some genera.

Fig. 1 Lake Bagno dell'Acqua (Pantelleria). In the inset, an image of the Mediterranean shrew (Crocidura pachyura). Terrestrial vertebrates on the island have been studied from multiple perspectives, including the origin of their populations (native vs. non-native), taxonomic status, and assessment of threats to biodiversity conservation.

Scientific Museology
Engaged in multiple scientific outreach initiatives ("third mission"), including the publication of data papers and opinion articles, in the role as Director of the Museum of Comparative Anatomy "Giovanni Battista Grassi" (2016-2025).

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3. Di Russo, E., Gippoliti, S., Bezerra, A. M., Aruta, A., Solano, E., & Castiglia, R. (2024) La collezione vertebratologica del Museo di Anatomia Comparata "Giovanni Battista Grassi" di Roma. Museologia Scientifica Memorie, 23:84-92.

Anna Rita
Rossi
Associate Professor

ORCID

RESEARCH LINES

- Evolutionary biology and conservation of Italian freshwater fishes
- Molecular taxonomy and comparative cytogenetics of fishes of the Caribbean and South American area

STAFF | COLLABORATORS

Giovanni Manetti, *PhD (Sapienza)*
Gerardo Petrosino, *Post Doc (Sapienza-Tuscia)*
Lorenzo Tancioni, *Associate Professor (University Tor Vergata)*
Mauro Nirchio, *Full Professor (Machala, Ecuador)*
Paolo Franchini, *Associate Professor (University of Tuscia)*

RESEARCH ACTIVITY

The research in my lab is focused on teleost fishes, from an evolutionary and conservation perspective.

The first research line centers on molecular phylogenetics, phylogeography, and population genetics of Italian freshwater endemic fish. It involves genotyping microsatellite loci, SNPs, and mitochondrial sequences within a conservation biology context. The aim is to disentangle patterns of genetic variability and population structure, and to identify local populations and management units that should be preserved, as many of these species are threatened by habitat degradation and competition with non-native species.
These investigations contribute to reconstructing population connectivity patterns and provide a baseline for identifying fish stocks. They also help infer divergence times, colonization routes of different lineages, historical demography, and the geological and paleoclimatic events associated with them.
As part of this research line, eDNA analysis of freshwater systems is also underway, aimed at developing non-invasive tools and protocols for biodiversity monitoring and quantification.

The second research line combines molecular taxonomy and comparative cytogenetics on species from the Caribbean and South American regions. It includes cytogenetic analysis and chromosomal mapping of repetitive sequences using fluorescence in situ hybridisation (FISH), alongside mitochondrial DNA sequence analysis (Cytochrome Oxidase Subunit I, 16S rDNA, and Cytochrome b) from the same individuals.
The integration of cytogenetic and sequence analysis is essential for accurate molecular identification of karyotyped specimens, particularly in taxa with poorly defined morphological characters. This approach facilitates the association of cytogenetic data with specific taxonomic units and enables the identification of cryptic species. Phylogenetic relationships inferred from molecular data allow for the reconstruction of evolutionary trajectories linked to karyotype diversification both within genera and among closely related fish groups.

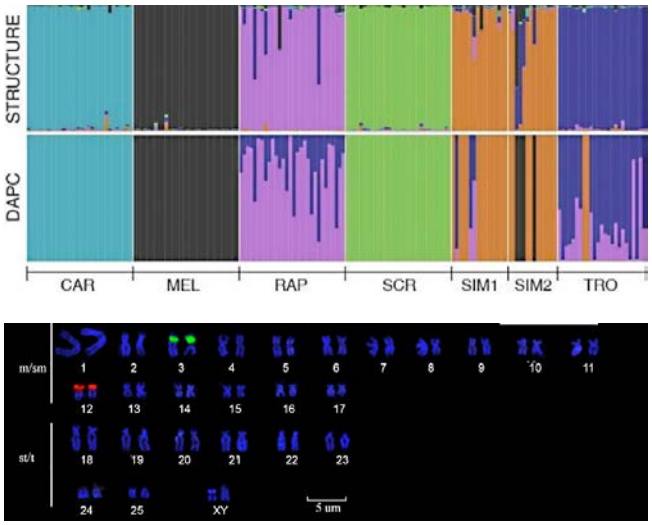

Figure. Upper panel: Barplot of individuals of seven trout populations as obtained through two different clustering analysis (from Rossi et al 2022, Water,14: 937). Lower panel: Double FISH karyotype of Astroblepus mindoensis with 5S rDNA (red) and 18S rDNA (green) probes (from Nirchio et al, 2024: Journal of Fish Biology 1-13).

SCIENTIFIC OUTREACH INITIATIVES (THIRD MISSION)
Coordinator of the PLS (Scientific Degree Plan) project for high school students and teachers, as well as for university students in Biology and Biotechnology.

References

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3. Petrosino G,·Tancioni L, Talarico L, Milana V, Ricci A, Polinori C, Rossi AR (2025). Genetic insight into diversity and population structure provides hints for the conservation of the vulnerable South European roach Sarmarutilus rubilio (Leuciscidae). *Hydrobiologia* 2025, 852, 3599–3614

Mattia
Toni
Associate Professor

ORCID

RESEARCH LINES

- Line 1. Investigation of prion and prion-like proteins (PrPc and synuclein) in mammalian and non-mammalian vertebrates, with a focus on their evolutionary conservation and potential involvement in neurodegenerative processes.
- Line 2. Analysis of the impact of environmental stressors, such as temperature and pollutants, on the nervous system of teleost fish, using integrated neurochemical and behavioural approaches.
- Line 3. Study of the role of neurotrophins, particularly BDNF, in the development, maintenance, and plasticity of the teleost nervous system.

STAFF | COLLABORATORS

Maria Carmela Bonaccorsi di Patti, *Associate Professor (Sapienza)*
Arianna Casini, *Researcher (Sapienza)*
Gabriella Tedeschi, *Full Professor (University of Milan)*
Flavia Frabetti, *Associate Professor (University of Bologna)*
Cristiano Bertolucci, *Full Professor (University of Ferrara)*

RESEARCH ACTIVITY

Line 1 – Synuclein Research Line
Alpha-synuclein (α-syn), along with β- and γ-synuclein, forms a family of proteins predominantly expressed in the nervous system. While α- and β-synuclein are found in the central nervous system (CNS), γ-synuclein is mainly present in the peripheral nervous system (PNS). The term synucleinopathies refers to neurodegenerative disorders characterised by pathological α-syn aggregates in neurons and glial cells of both CNS and PNS. These include Parkinson's disease, dementia with Lewy bodies, multiple system atrophy, and other neuroaxonal dystrophies. Synucleins are evolutionarily conserved across vertebrates, suggesting essential physiological functions. This research line investigates synuclein expression in non-mammalian vertebrates to shed light on its evolutionary roles and to identify alternative animal models for Parkinson's disease research.

Line 2 – Environmental Challenges and the Nervous System
Organisms continuously face environmental stressors, among which pollution and temperature shifts are particularly significant. These factors influence biological systems from the molecular to the population level, ultimately affecting fitness and lifespan. Poikilotherms, such as fish, are especially vulnerable, as their internal temperature mirrors their surroundings. In aquatic ectotherms, water temperature is a major ecophysiological variable, shaping behaviour, physiology, and distribution. This research line explores the impact of environmental fluctuations on the CNS of teleost fish, offering insights into how climate and anthropogenic pressures influence neural function.

Line 3 – BDNF and Brain Function in Zebrafish
Brain-Derived Neurotrophic Factor (BDNF), a key neurotrophin, supports neuronal survival, drives synaptic plasticity, and is essential for the formation and refinement of neural circuits. It is implicated in hippocampal long-term potentiation and experience-dependent plasticity in the visual cortex. Impaired BDNF signalling is linked to several neurological and psychiatric conditions, including depression, schizophrenia, and Alzheimer's disease. This research investigates the effects of partial or complete BDNF deficiency in zebrafish (BDNF+/– and BDNF–/– lines), aiming to elucidate its role in brain development and function.

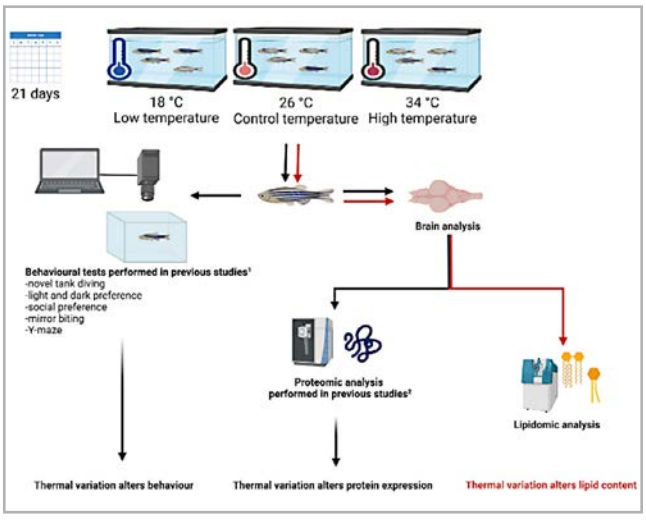

Figure. ***Experimental framework for analysing thermal variation effects in adult zebrafish.*** *Fish were maintained at 18 °C (low temperature), 26 °C (control temperature), or 34 °C (high temperature) for 21 days (chronic exposure). Image reproduced from Maffioli et al., International Journal of Molecular Sciences 2024, 25(17), 9629. https://doi.org/10.3390/ijms25179629.*

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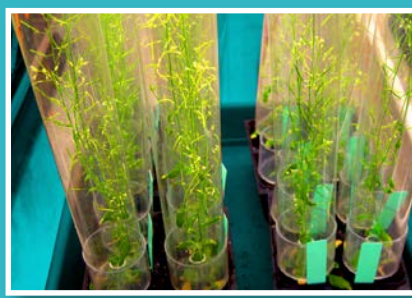
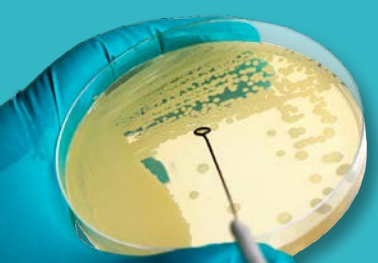
“ PHYSIOLOGY „

The CU026 building, also called the Institute of General Physiology, was built in the 1930s by Arch. Giovanni Michelucci under the supervision of chief Arch. Marcello Piacentini. The building was part of the University campus inaugurated on March 31st, 1935. The functionalism certainly inspired Arch. Michelucci and the rationalist architects who designed the building. It consists of two independent buildings connected to the mezzanine floor. The building comprises several classrooms for the teaching activities of the bachelor degree course in Biological Sciences and the master degrees in Genetics and Molecular Biology, Neurobiology, Cellular Biology and Biotechnology, and Environmental and Industrial Biotechnology. One of these classrooms is dedicated to Prof. Giorgio Tecce, who in 1970 established the first CNR research center for nucleic acids in this building. He was also the “Rettore” of Sapienza from 1988 to 1997. A large amphitheater classroom is centrally located so that it is connected to both buildings. The classroom is dedicated to Prof. Daniel Bovet, who won the Nobel Prize in Medicine in 1957, is one of the fathers of Psychobiology and held the first chair of Psychobiology in 1969. His main discoveries and his contributions to medical science are remembered in the entrance hall of the General Physiology building. Emphasizing the continued importance of basic research in inspiring translational research, the building houses a combination of high quality research groups that study fundamental biological processes of cellular and developmental biology, RNA metabolism, neurobiology, plant biology and microbial biotechnology. Researchers are also involved in first-rate national and international research programs. This highly collaborative approach by investigators in the Department has led to the development of clinical and industrial applications. In addition to the research laboratories, the building contains the administration and teaching offices and their staff, and the library. The Department’s research facilities are well equipped with all the laboratory infrastructure necessary for molecular biology, biochemistry, cell culture, and cell and tissue imaging experiments. An animal facility is also available to researchers for animal breeding and experimental procedures.





Monica
Ballarino
Associate Professor

ORCID

RESEARCH LINES

- Mechanisms of lncRNAs action: modes and interactions
- Disease modeling of lncRNAs in iPSC-derived muscular (skeletal and cardiac) and neuromuscular cells
- LncRNAs as biomarkers and therapeutic targets

STAFF | COLLABORATORS

Marco Simula,
PhD student (Sapienza)
Daniele Durante,
PhD student (Sapienza)
Paolo Tollis, *Researcher (Sapienza)*
Filippo Mirabella, *Researcher (Human Technopole)*
Luca Tesei, *Associate Professor (University of Camerino)*
Letizia Chiodo, *Associate Professor (Campus Bio-Medico)*

GRANTS

ELIXIRxNextGenIT by European Commission NextGenerationEU. PI
HT 24-LI-PILOT. Ion Imaging in Neuromuscular Organoids. PI
MUR PRIN2022, Study of Noncoding RNAs in Organoids for Muscle-Nerve development (NOMeN). PI
MUR PRIN2022-PNRR, RNA secondary structures and their relationship with function: application to non-coding RNAs (RNA2Fun). Co-PI
PNRR CN3 - CN00000041 Sviluppo di terapia genica e farmaci con tecnologia a RNA. PI

RESEARCH ACTIVITY

I specialise in RNA research, with a particular focus on how the intrinsic properties of this molecule define the physiological roles of non-coding RNAs. My experience in RNA-based regulatory mechanisms began during my master's and continued through my doctoral studies in Genetics and Molecular Biology under the mentorship of Prof. Irene Bozzoni (Rome, Italy).
My work contributed significantly to elucidating the nuclear mechanisms involved in miRNA biosynthesis by demonstrating that coupling between transcription and Microprocessor processing promotes efficient expression of this class of non-coding RNA. In 2009, thanks to the Espoirs de la Recherche fellowship awarded by the Fondation pour la Recherche Médicale, I undertook a post-doctoral internship at the Institut de Génétique et de Biologie Moléculaire et Cellulaire (Strasbourg, France) in the lab of Prof. Laszlo Tora. My main project focused on identifying a novel molecular circuit that explains the oncogenic role of the miR-17 locus. During this period, I also served as a visiting scientist at the Ecole Normale Supérieure (Paris, France) where I received training in single-molecule tracking using fluorescence in situ hybridization.
Upon returning to Italy as a tenure-track researcher, my research focus shifted to lncRNA. In collaboration with Anna Tramontano's lab, I pioneered the discovery of novel lncRNA loci, that had been absent from earlier gene annotations. Currently, our research investigates the function of these RNAs through the development and application of dedicated computational pipelines, advanced microscopy techniques, and biochemical approaches. My lab also has substantial expertise in CRISPR-Cas9 methodologies, which have been employed to generate mouse models with targeted mutations in specific non-coding loci. The long-term objective of my laboratory is to unravel how the aberrant regulation of lncRNAs impacts muscle function in humans - both directly, in skeletal and cardiac muscle diseases, and indirectly, in neuromuscular disorders. A paradigmatic example of this line of research is CHARME, a conserved lncRNA that we have extensively characterized in both mouse and human models. Our studies revealed its crucial role in cardiac and skeletal muscle development, and how its misregulation impacts heart function.
To this purpose, we have applied genomic editing technologies to iPSCs, which we are now differentiating into various cell types, including skeletal muscle fibres, cardiac cells, and motor neurons. Fundings from MUR supports the establishment in-house and disease-gene- specific organoids.

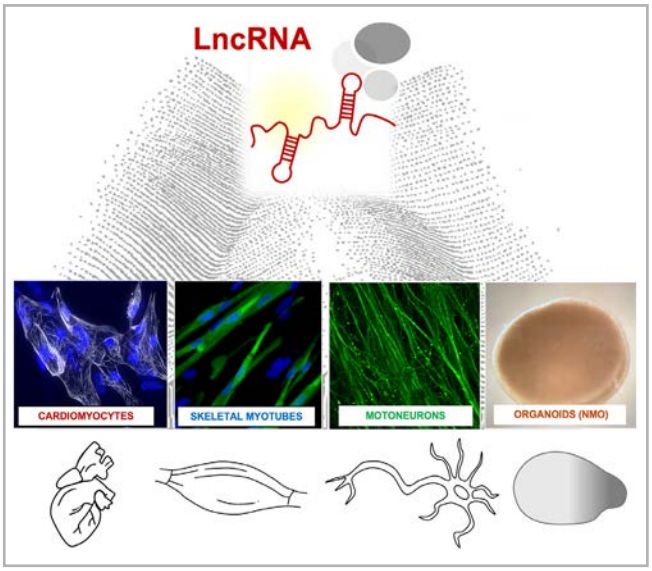


Figure. Examples of iPSC-derived cellular models used to study the role of lncRNA in cell differentiation and disease. From left to right: **cardiomyocytes** *(confocal microscopy, 100× magnification; white: Troponin T2; blue: DAPI),* **skeletal myotubes** *(confocal microscopy, 63× magnification; green: Myosin Heavy Chain, blue: DAPI),* **motoneurons** *(confocal microscopy, 40× magnification, green: Beta-III-tubulin), and* **neuromuscular organoids** *(Day 50 NMOs, stereomicroscopy, 40× magnification).*

References

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3. Desideri F, Cipriano A, Petrezselyova,...Ballarino M. (2020) Intronic Determinants Coordinate Charme lncRNA Nuclear Activity through the Interaction with MATR3 and PTBP1 Cell Reports; 33:108548

Michele Maria
Bianchi
Associate Professor

ORCID

RESEARCH LINES

- Regulation of metabolism in yeast
- Stress response in yeast
- Biotechnological applications of yeast

STAFF | COLLABORATORS

Cristina Mazzoni,
Associate Professor (Sapienza)
Arianna Montanari,
Researcher (Sapienza)
Massimo Reverberi,
Full Professor (Sapienza)
Andrea Martinelli,
Associate Professor (Sapienza)

RESEARCH ACTIVITY

The research studies the effects of environmental factors on metabolism regulation and the identification of involved regulatory proteins. The evolution of aerobic organisms and respiratory metabolism, characterized by electron transfer to oxygen, depends on the appearance and accumulation of oxygen in the biosphere. On the other hand, oxygen becomes scarce or its concentration largely fluctuates in several environments: organism adaptation to these environments depends on the metabolic regulation between respiration and fermentation, governed by oxygen availability. Other environmental factors influence and regulate metabolism: among them, light has an extremely important role, either for energy supply to the biosynthetic metabolism, either for all metabolic activities related to the circadian cycle. Photosynthetic organisms and organisms entrained to the day/night cycle are strongly dependent on light.

The research is performed on yeasts, which are eukaryotic organisms extensively used in basic research as well as in biotechnological applications and in industrial scale productions. Yeast physiology and metabolism are tightly linked to growth conditions, in particular to oxygen concentration and the kind and the amount of carbon sources. The research focuses on the connections between oxygen and glucose regulations in the Kluyveromyces lactis, in particular on the hypoxic regulation of glycolysis and the fermentative metabolism and the hypoxic regulation of lipid biosynthesis. Proteins mediating the hypoxic response have been identified (Rag4, Sck1, KlMga2).

Light response is a well-studied mechanism in filamentous fungi like Neurospora crassa. However little is known about the light response in yeasts which are apparently lacking proteins with light sensitive domains. In the yeast Saccharomyces cerevisiae, light induce ROS formation and the displacement of the stress factors Crz1 and Msn2 from cytoplasm to nucleus. The role of these regulatory proteins are under current investigation in K. lactis, especially in relation to fatty acids desaturation that, in plants, is under the control of light dependent genes. Interestingly, the hypoxic regulator protein KlMga2 was found as a mediator of light stress response.

In addition to basic studies, K. lactis is also suitable to technological applications. A recombinant strain expressing a fungal laccase has been proved to be effective in oxidative deterioration of plastics (polypropylene) in the presence of opportune redox mediators (Figure).

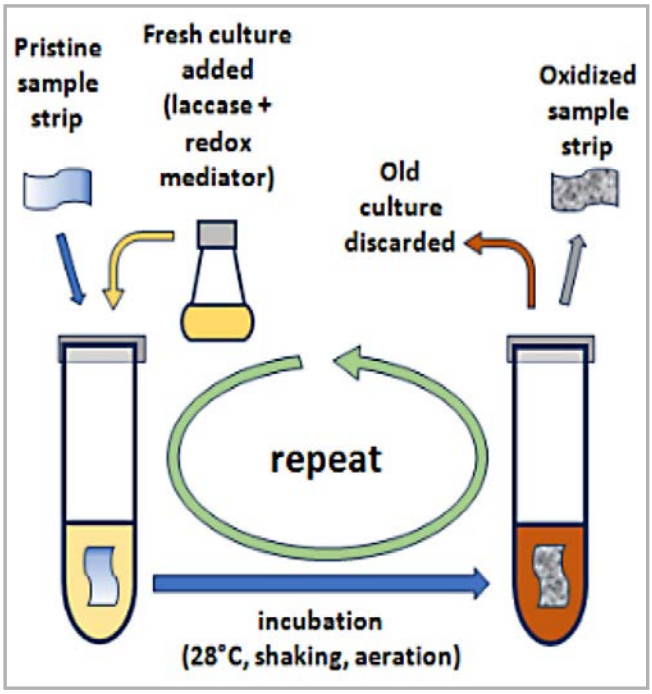

Figure. Repeated plastic incubations with recombinant yeast cultures and redox mediator.

References

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Stefano
Cacchione
Associate Professor

ORCID

RESEARCH LINES

- Structure and function of human telomeric chromatin
- Epigenetic status of human telomeres in normal and cancer cells
- Structural organization of drosophila telomeres
- Impact of the space environment on telomeres

STAFF | COLLABORATORS

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GRANTS

European Space Agency/Coenzyme Q10 prevents proton beam radiation-induced damages in retinal pigment epithelial, Muller, photoreceptor and endothelial cells, € 32.000.
PI: Matteo Lulli, Stefano Cacchione

RESEARCH ACTIVITY

In humans, telomeres are critical regulators of cell fate. At birth, they are 10-15 kb long, composed of thousands of TTAGGG repeats in a compact chromatin structure, bound by the six-protein shelterin complex. While the enzyme telomerase maintains telomere length in germline and embryonic stem cells, it is inactive in somatic cells. This inactivity leads to telomere shortening with each replication cycle, eventually triggering a DNA damage response (DDR) and permanent cell cycle arrest. To proliferate indefinitely, cancer cells must acquire a telomere maintenance mechanism—most often by reactivating telomerase, but in about 10–15% of tumours, an alternative lengthening of telomeres (ALT) mechanism based on homologous recombination is used.
Approximately 80% of telomeric DNA is organized into nucleosomes with an unusually short spacing, enriched with the histone variant H3.3, which is deposited in a replication-independent manner by the ATRX/DAXX complex.

Our current work focuses on the role of H3.3 at telomeres. Strikingly, dominant mutations in H3.3 are frequently found in pediatric ALT cancers, often coupled with the loss of ATRX. The inherent length heterogeneity of human telomeres and their uniformly repeated sequence make it challenging to map their structural organization and understand how this structure changes as telomeres shorten and lose their protective cap. Even powerful techniques such as ChIP-seq can detect H3.3 at telomeres but cannot precisely identify its location.
To overcome these challenges, we are developing new tools and strategies to map the organization of nucleosomes—particularly those containing H3.3—at human telomeres. Our approach includes specific chemical cleavage combined with single-molecule sequencing of long telomeric fragments using Oxford Nanopore technology. The long-read capability of Nanopore sequencing is a game-changer, as it will allow us to analyse H3.3 positioning within repetitive telomeric regions. This combined approach will provide independent lines of evidence for H3.3 localization and offer a comprehensive understanding of its genomic distribution and enrichment at telomeres, and possibly shed light on H3.3's role in telomere biology and the pathology of ALT cancers.

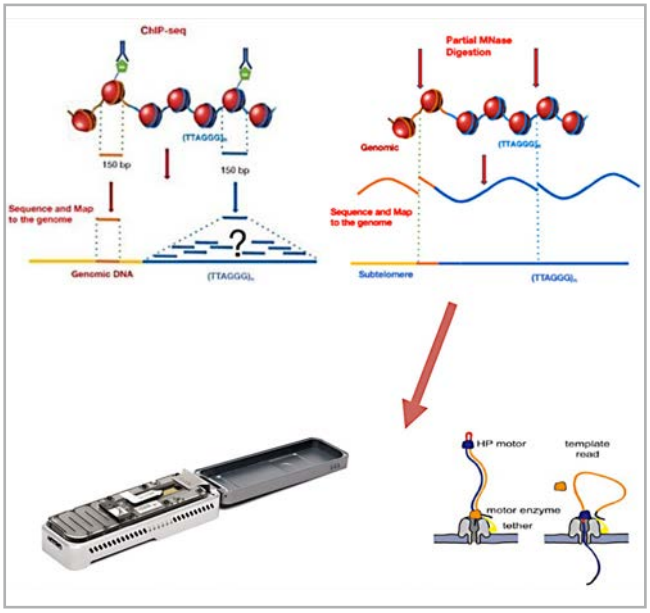

Figure. This schematic illustrates the challenges of nucleosome mapping in the highly repetitive telomeric DNA (top left) and our approach using long-read nanopore sequencing to achieve a more precise map (top right and bottom).

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Emanuele
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RESEARCH LINES

- Contribution of wild type and R451C NLG3 mutated proteins to the regulation of neural stem cell properties and adult hippocampal neurogenesis
- Effects of neuroinflammatory cells (i.e. microglia and astrocytes) on differentiation and survival of neural stem cells and neurons.

STAFF | COLLABORATORS

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Maria Antonietta Ajmone Cat,
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RESEARCH ACTIVITY

Analysis of adult neurogenesis in a mouse model of autism spectrum disorder (ASD)
Dysregulation in adult dentate gyrus (DG) neurogenesis has been observed in mice carrying mutations in genes linked to autism spectrum disorders (ASDs). In a recent study, we found that DG neurogenesis was impaired in the ventral portion of the dentate gyrus of mice expressing the R451C mutation in the NLGN3 gene (Fig. 1), a mutation found in a Swedish family affected by ASDs gene. Fluoxetine treatment partially restored activated adult-born neurons in the ventral DG and improved social behavior in Nlgn3 KI mice, suggesting a functional link between adult neurogenesis and social deficits (Gioia et al, 2023).
The mechanisms behind the neurogenic deficit in knock-in mice remain unclear, and it is uncertain whether it reflects cell-autonomous effects of the R451C Nlgn3 mutation in neural stem/progenitor cells or non-cell-autonomous changes.
To address this question we are studying neural stem cells (NSCs) from wild type and Knock-in mice. Neurons derived from knock-in NSCs show reduced Nlgn3 expression and altered depolarization responses, indicating a possible direct effect of the mutated protein on neuronal maturation and function (Diamanti et al, 2024).

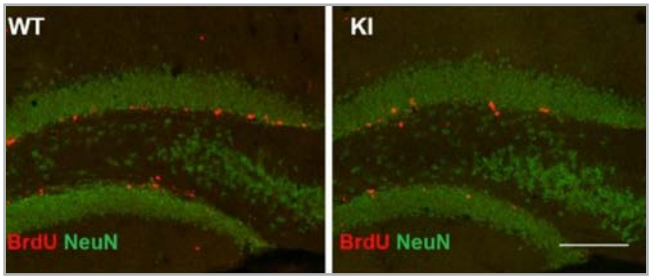

Figure. Detection of newly born neurons in the DG of adult mice. Mature neurons newly generated in the adult DG are immunolabeled with BrdU (red) and NeuN (green). A consistent reduction in the number of double-labelled neurons is observed in KI with respect to WT mice.

As Nlgn3 is expressed at significant level also in NSCs, it may influence neural stem/progenitor cell properties through non-canonical functions beyond its synaptic role. Supporting this, activity-dependent NLGN3 release has been shown to regulate proliferation in glioblastoma models. We are currently investigating how the R451C mutation affects NSC proliferation and differentiation. Since this mutation disrupts protein trafficking and reduces Nlgn3 levels, we have also generated Nlgn3 knockout NSC lines to distinguish between gain- and loss-of-function effects.
We expect that functional and molecular analyses will help shed light on previously unknown non-canonical functions of proteins traditionally associated with synaptic formation.

Effects of glial cells (i.e. microglia and astrocytes) on NSC properties
One of the main goals in stem cell biology is to understand how neural stem cells (NSCs) interact with the various cell types that make up the specialized microenvironment known as the stem cell niche. Among these, microglia and astrocytes play key roles in modulating NSC behavior under both physiological and pathological conditions. NSCs can be efficiently differentiated into astrocyte-like cells in vitro, providing a valuable model to study astrocyte function. Previous work from our group has shown that both human and mouse astrocytes expressing a mutated form of the ALS-associated gene FUS display increased reactivity and acquire neurotoxic properties. Our current research focuses on understanding how aging affects astrocyte function, particularly in astrocytes overexpressing Dbx2 or other aging-associated genes. We aim to investigate their production of cytokines, chemokines, and growth factors, their responsiveness to pro- and anti-inflammatory stimuli, and their ability to support NSC proliferation, survival, and differentiation.
This study will provide new insights into the contribution of astrocytes to the age-related decline in adult neurogenesis.

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Antonella
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ORCID

RESEARCH LINES

- Altered cellular pathways in adult and embryonic progenitor neural stem cells expressing the human mutation R451C in NLGN3 associated to ASD.
- In vivo rescue strategies to revert social deficits of the R451C NLGN3 mouse model of ASD

STAFF | COLLABORATORS

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RESEARCH ACTIVITY

Our research interest focuses on mutations in genes encoding for cell adhesion synaptic proteins that are linked to Autism Spectrum Disorders (ASD).
ASD are neurodevelopmental syndromes characterized by behavioural deficits with a strong genetic background. Several risk genes encode for molecules playing a role in maturation and functioning of the synapses.
Neuroligins (NLGNs) are cell adhesion molecules anchored at the post-synaptic membrane, where they act as synaptic organizers. The ASD-linked reference mutation in NLGNs genes is the amino acid substitution Arg451Cys in the extracellular domain of NLGN3 which causes a local misfolding, the retention of the mutated protein in the endoplasmic reticulum (ER) and a defective trafficking to the cell surface. We established the first evidence between the retention of the R451C NLGN3 in the ER and the activation of UPR both in vitro, in inducible PC12 cell lines, and in vivo, in the cerebellum of the Knock-In (KI) mouse model of ASD carrying the R451C mutation in the endogenous NLGN3 gene.
Recently we have identified a group of compounds (mainly glucocorticoids) that "correct" the defective trafficking of the mutant protein and favors its cell surface trafficking thus reducing the activation of UPR in cellular model systems in vitro (1,3). Next step will be represented by testing Dexamethasone (DEX) in vivo in the mouse expressing the R451C NLGN3 protein as endogenous protein, monogenic mouse model of ASD. While we have shown fluoxetine treatment rescues impaired neurogenesis in the hippocampus of adult mice expressing the mutation in comparison to wild type strain (2). On the other hand, in order to rescue social deficits, we are testing different treatments for the R451C NLGN3 mice: four different probiotic strains and the pro-social hormone oxytocin in order to evaluate whether they have any effects on ameliorating social deficits and aggressivity that characterize this model of ASD.
In order to study cellular alterations in some cellular pathways due to the mutation, we have generated neural progenitor cell lines derived from stem niches of the adult hippocampus (3) and from the embryonal cortical niches. The advantage of these cell populations is that they express the R451C NLGN3 as the endogenous protein and can be differentiated to a neuronal-like phenotype (figure).

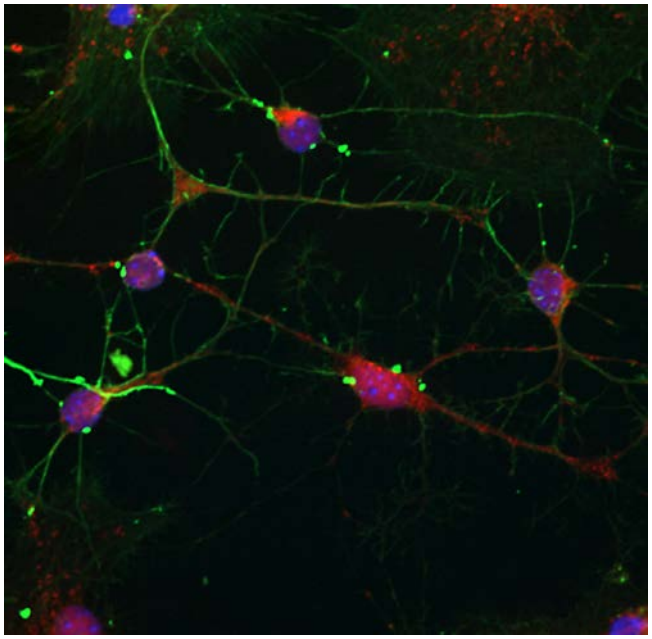

Figure. Neural stem cells derived from adult hippocampus of Neuroligin3 R451C mice. (DAPI: blue; RED: mitotracker; GREEN: phalloidin).

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Maria Egle
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ORCID

RESEARCH LINES

- Neurodevelopmental alterations in the Duchenne Muscular Dystrophy
- Sensory-motor interactin in Duchenne Muscular Dystrophy
- Neuroinflammation in aging and neurodegenerative diseases

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GRANTS

2025-2027 Duchenne Parent Project PP2023GA1.
Muscle – spinal cord interaction in Duchenne muscular dystrophy Co-PI with Prof. F. Grassi (Sapienza)

RESEARCH ACTIVITY

The research activity of the laboratory focuses on the neurodevelopmental alterations associated with Duchenne Muscular Dystrophy (DMD), a severe X-linked disorder primarily affecting muscle tissue but also impacting the nervous system. DMD is caused by the absence of full-length dystrophin (Dp427), a key cytoskeletal protein expressed not only in muscle fibers but also in selected neuronal populations within both the central and peripheral nervous systems.

Over the years, Prof. De Stefano's group has demonstrated that dystrophin plays a crucial role in several neurobiological processes, including: i) synaptic organization in autonomic neurons; ii) axonal growth and regeneration; iii) glucocorticoid receptor stability and stress regulation in hippocampal neurons; iv) adult hippocampal neurogenesis and retinal cell differentiation. Recent studies have revealed a link between altered metabolism of D-amino acids (such as D-serine and D-aspartate) in the hippocampus and the neurophysiological changes observed in dystrophic mice (mdx mouse model). Additional work on the sciatic nerve has shown reduced peripheral myelination, impaired nerve conduction, and possibly altered Schwann cell-axon communication. This is supported by a significant downregulation of key molecular components (including receptors and biosynthetic enzymes) involved in the well-characterized Schwann cell GABAergic autocrine/paracrine loop, concomitant with a disruption of dystrophin-associated protein complex (Figure). The current focus of the lab is on how DMD affects the spinal sensorimotor circuit, particularly proprioception—the body's ability to sense its own position and movement. Emerging evidence suggests that children with DMD perform motor tasks normally with visual guidance but show impaired coordination when relying solely on proprioceptive input.

This may indicate that their frequent falls are due not only to muscle weakness but also to impaired proprioceptive feedback. Since proprioceptive function can be improved through targeted physiotherapy, understanding how it is altered in DMD could lead to better therapeutic strategies.

To this end, we are investigating the structural and functional properties of motor and sensory neurons in mdx mice, aiming to understand how their interactions are disrupted and how this affects locomotion and motor control.

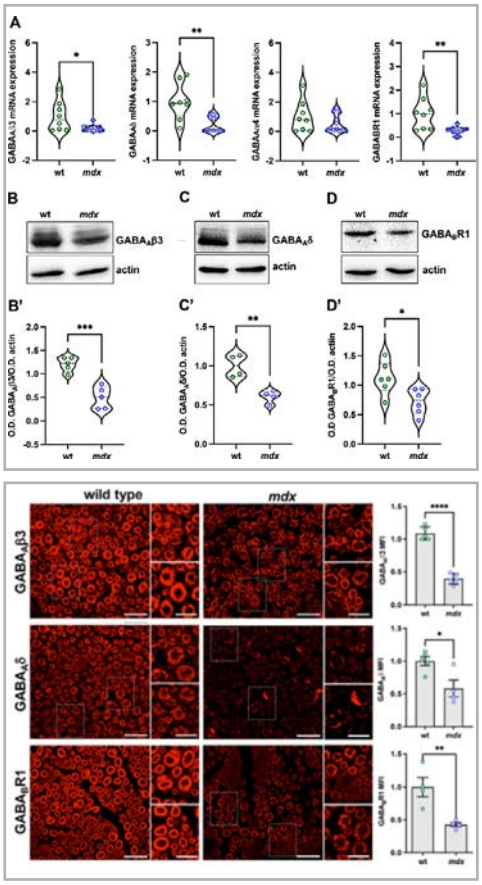

Figure. Decrease in GABAA and GABAB receptor subunits in the sciatic nerve of mdx mice compared to wild type. In the left side: A) real time RT-PCR; B,B') Western immunoblot and densitometric analyses. On the right side: immunofluorescence on sciatic nerve cross sections and mean fluorescent intensity analyses.

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Luciana
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RESEARCH LINES

- Role of extracellular vesicles (EVs) in Amyotrophic lateral sclerosis (ALS)
- Ultrastructural characterization of nanomaterials and EVs

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RESEARCH ACTIVITY

Role of extracellular vesicles in ALS

ALS, is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord, and is characterized by muscle weakness, paralysis and ultimately, respiratory failure. The exact causes of ALS are not understood, though it is believed to combine genetic and environmental factors. Until now, it was admitted that motor neurons (MN) in the brain and spinal cord degenerate, leading to muscle weakness and paralysis. However, as ALS symptoms typically begin with muscle weakness or stiffness, a new hypothesis has recently emerged to explain the development of the pathology, that is, the 'dying back hypothesis', suggesting that this degeneration starts at the connections between MN and muscles, resulting in the loss of muscle function. Over time, this damage extends along with the length of the MN, ultimately affecting their cell bodies in the spinal cord and brain. While the dying back hypothesis provides a potential framework for understanding the progression of ALS, the exact mechanisms underlying the disease remain complex and not fully understood.
We are positioning the role of extracellular vesicles as new actors in ALS development

Ultrastructural characterization of EVs and EVs cryo-EM

Tip-enhanced Raman spectroscopy (TERS) is an advanced technique to perform local chemical analysis of the surface of a sample through the improvement of the sensitivity and the spatial resolution of Raman spectroscopy by plasmonic enhancement of the electromagnetic signal in correspondence with the nanometer-sized tip of an atomic force microscope (AFM). TERS represents an innovative and powerful approach for studying EVs, which are phospholipid bilayer-enclosed vesicles recognized as new mediators in intercellular communication and potential biomarkers of disease. Raman spectroscopy is used to analyze EVs at the micrometric and sub-micrometric scales to obtain a detailed Raman spectrum to identify the EVs characteristic molecular vibrations and, therefore, their chemical compositions. Cryo-EM represents the other technical approaches to visualize the native morphology of EVs.

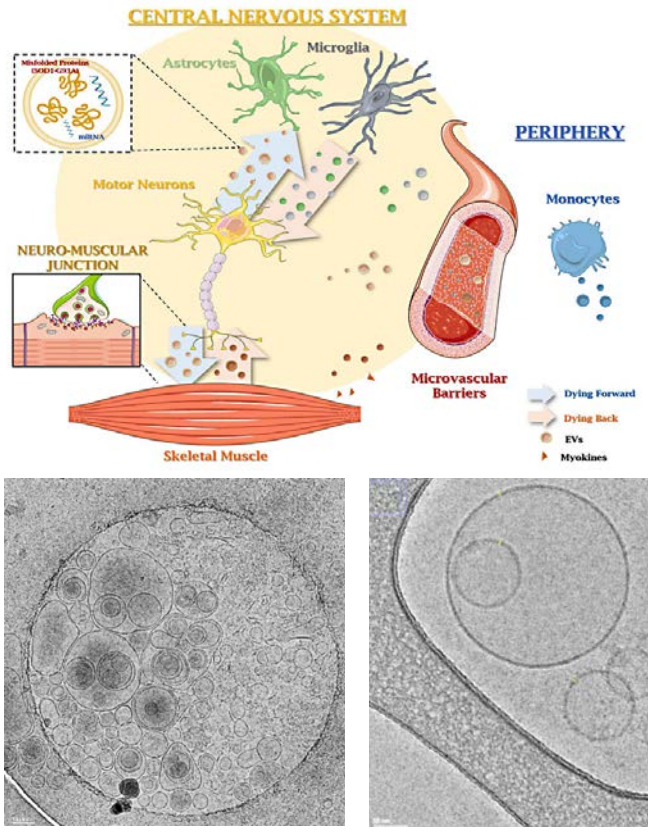

Figure. Upper panel: EVs crosstalk in ALS. In ALS pathogenesis, EVs mediate transfer of misfolded proteins (i.e., SOD1-G93A) and other molecules, such as miRNAs, affecting healthy recipient cells. EVs crosstalk occurs between CNS components (motor neurons, microglia, astrocytes), between motor neurons and skeletal muscle within the Neuro-Muscular Junction, and between CNS and periphery through the microvascular barriers (such as the blood-brain barrier). According to the "dying forward" hypothesis, motor neurons drive EVs towards other cells. However, the emerging "dying back" hypothesis supports that EVs are also driven from other cells, mainly skeletal muscle, to motor neurons.
- Lower panel: Cryo-EM, due to the limitations of available analytical methods, is the best investigation tool to obtain morphological information on isolated EVs. Cryo-EM images of EVs of single, double and multi-layered -membrane vesicles.

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3 Antonucci, A. Carbon nanotube uptake in cyanobacteria for near-infrared imaging and enhanced bioelectricity generation in living photovoltaics *Nature Nanotechnology* Volume 17, Issue 10, Pages 1111 - 1119October 2022

Alessandro
Fatica
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ORCID

RESEARCH LINES

- RNA modifications in cancer
- Development of combination therapies in cancer

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GRANTS

NextGenerationEU-PNRR M4C2-Investment 1.4- CN00000041

RESEARCH ACTIVITY

Our laboratory is dedicated to understanding how RNA modifications influence cancer and to developing novel therapies. We focus on three core areas:

PCIF1: m6Am mRNA modification and oncogenesis. We investigate PCIF1, the specific methyltransferase that catalyzes N6,2′-O-dimethyladenosine (m6Am) modification at the 5'-end of mRNA and is deregulated in different types of cancer. Using diverse molecular and cellular approaches, we aim to confirm PCIF1 as a promising therapeutic target. Our goal is to identify its specific mRNA targets and the oncogenic pathways it regulates, uncovering novel cancer vulnerabilities.

QTGAL: translational fidelity in cancer. Our work explores the tRNA-modifying enzyme QTGAL, which catalyzes the galactosylation of queuosine (galQ) at the wobble position of tRNA-Tyr. This modification is crucial for translational fidelity. QTGAL is often upregulated in various cancers, including breast cancer. Our research aims to identify precisely how QTGAL activity affects translational efficiency and accuracy in cancer cells and to delineate the impact of its downregulation on cancer growth and progression.

METTL3: m6A modification and anti-cancer therapies. A major focus is developing anti-cancer therapies by targeting METTL3, the catalytic component responsible for installing N6-methyladenosine (m6A) RNA modifications in mRNA. METTL3 is frequently overexpressed and acts as a key oncogene in multiple cancer types, promoting aggressive phenotypes and fostering drug resistance.
As a druggable enzyme, inhibiting METTL3 offers a promising new class of epigenetic drugs. Our aim is to lay the groundwork for developing effective combination therapies, enhancing therapeutic responses and overcoming resistance mechanisms in cancer treatment.

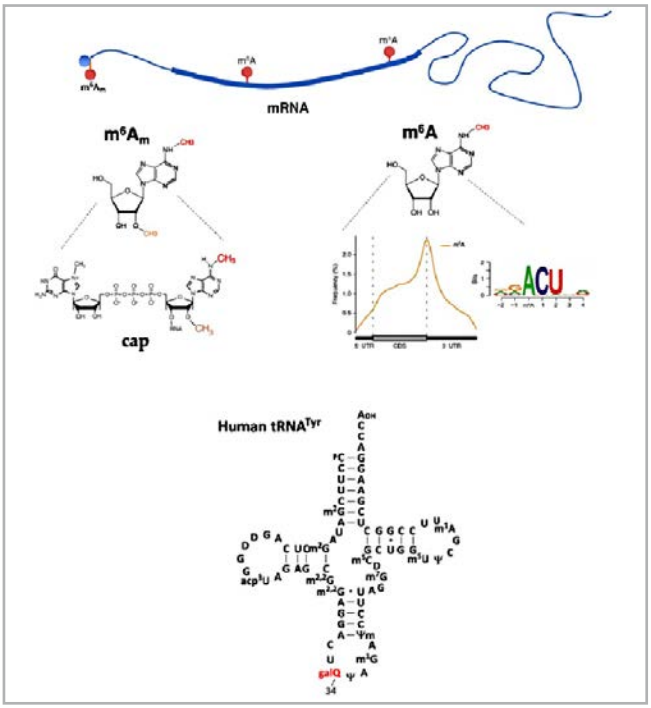

Figure. Upper panel: Schematic illustrating the key RNA modifications, m6A and m6Am, and their characteristic locations within mRNA transcripts. Lower panel: Schematic illustrating human tRNATyr with the galactosyl-queuosine (galQ) modification at the wobble position.

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Valentina
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ORCID

RESEARCH LINES

- Behavioral and physiological characterization of developmental trajectories in mouse models of neuropsychiatric conditions
- Effect of endogenous and exogenous oxytocin modulation on mice sociability and cognition across development
- Analysis of brain–immune system interactions in the regulation of social behavior

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GRANTS

Autism Research Institute 2025-2027: Investigating the Interplay between Oxytocin and Neuroinflammation in the Effects of Social Buffering in a mouse model of 22q11.2DS

RESEARCH ACTIVITY

My research focuses on uncovering the biological underpinnings of behavior, with particular emphasis on how the brain integrates external information at the neuronal and circuit levels to generate complex behavioral outputs. I investigate the neural substrates of social behavior by studying oxytocin-mediated brain circuits, employing a multidisciplinary approach that combines genetic, pharmacological, and behavioral methods.

A central aim of my work is to elucidate the contribution of specific brain regions and networks to social behavior and cognition, with the broader goal of developing novel tools and translational strategies for early detection and intervention in mouse models carrying mutations associated with neuropsychiatric disorders characterized by social and cognitive deficits.

In collaboration with the Italian Institute of Technology (IIT) in Genoa, we use in vivo imaging and electrophysiological techniques to characterize the neural activity patterns underlying social behavior and to identify how these patterns are altered in models of neuropsychiatric conditions.

Recently, I have focused on studying the interaction between genetic factors and immune responses. Genetic alterations, such as copy number variants, and early-life immune dysregulation, play a key role in the pathogenesis of neurodevelopmental and psychiatric disorders—such as ADHD, autism spectrum disorders, and schizophrenia—yet the underlying mechanisms remain unclear. We are currently investigating how 22q11.2 deletion syndrome (22q11.2DS) induces alterations in developmental pathways and affects immune responses. We are also exploring the effects of oxytocin supplementation and a behavioral therapy aimed at enhancing endogenous oxytocin levels, to assess their potential in preventing or rescuing abnormal developmental trajectories.

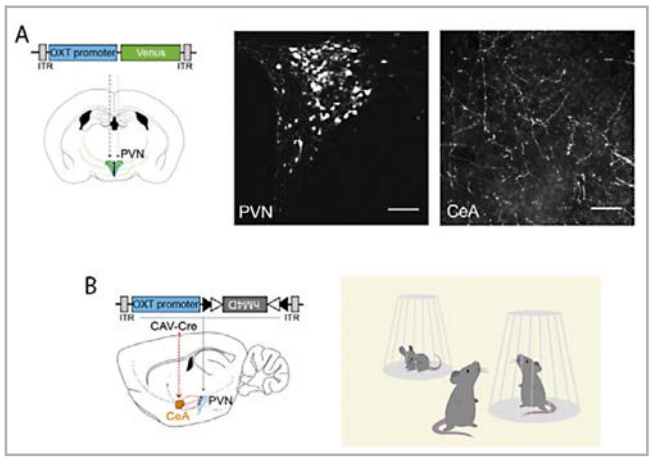

Figure 1. Representative approaches used. A. AAV-mediated tracing of OXT brain fibers in the brain (PVN and Amygdal). B. AAV-mediated functional dissection of selective OXT pathways (PVN-CeA) in a social cognition test.

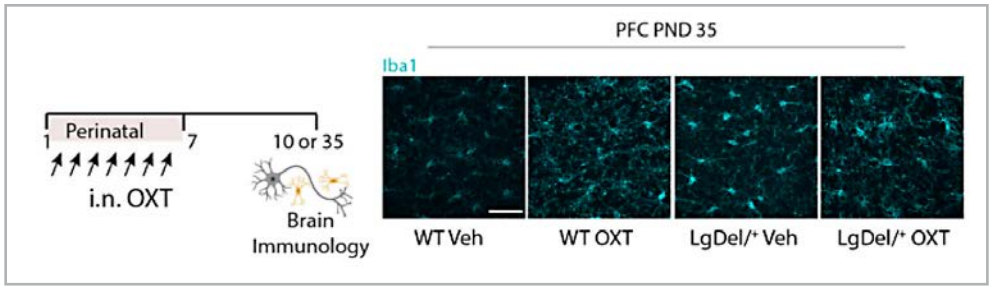

Figure 2. Effect of early life administration of intranasal OXT on microglia reactivity in the medial Prefrontal cortex during adolescence.

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Marco
Fidaleo
Associate Professor

ORCID

RESEARCH LINES

- Neural Resilience and Micronutrient-Driven Recovery
- AI-Driven Correlative Analysis for Cellular and Metabolic Insight

STAFF | COLLABORATORS

Daniele Passeri,
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Livia Angeloni,
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Ada Maria Tata,
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Virve Cavallucci, *Assistant Professor (Catholic University of the Sacred Heart)*
Piergiorgio La Rosa,
Assistant Professor (Catholic University of the Sacred Heart)

RESEARCH ACTIVITY

Our research investigates the mechanisms underlying cellular recovery, with a particular emphasis on the role of nutrients as active modulators of repair and adaptation processes, especially in neural models exposed to oxidative stress or harboring rare metabolic mutations. We study how micronutrients—at both physiological and pharmacological doses—affect neural-like cells, focusing on metabolism as a potential upstream modulator rather than a downstream consequence.

Using in vitro models and in silico analyses, we aim to identify molecular targets that may improve recovery from micronutrient deficiencies or act synergistically in metabolic disorders. These efforts are supported by NMR-based metabolomics and structural analysis through Raman microscopy and fluorescence imaging.

We also develop integrative, non-destructive approaches to explore biological processes in their native spatial context. Raman microscopy plays a key role in capturing label-free molecular data; however, spectral overlap and complexity require sophisticated interpretative tools. To address this, we apply neuro-symbolic artificial intelligence, which merges data-driven learning with symbolic reasoning. This hybrid AI approach enables more transparent, structured, and biologically meaningful interpretations of spectral and spatial data.

Through correlative analysis combining spectral information, fluorescent imaging, and AI-driven modeling, we seek to uncover how molecular and metabolic pathways are modulated by micronutrients in recovery processes.

This interdisciplinary framework not only sheds light on the connection between metabolism, gene regulation, and cell architecture, but also builds scalable tools for predictive analysis.

Ultimately, our goal is to support data-driven precision strategies and identify new molecular targets in the context of neural resilience and micronutrient-related diseases.

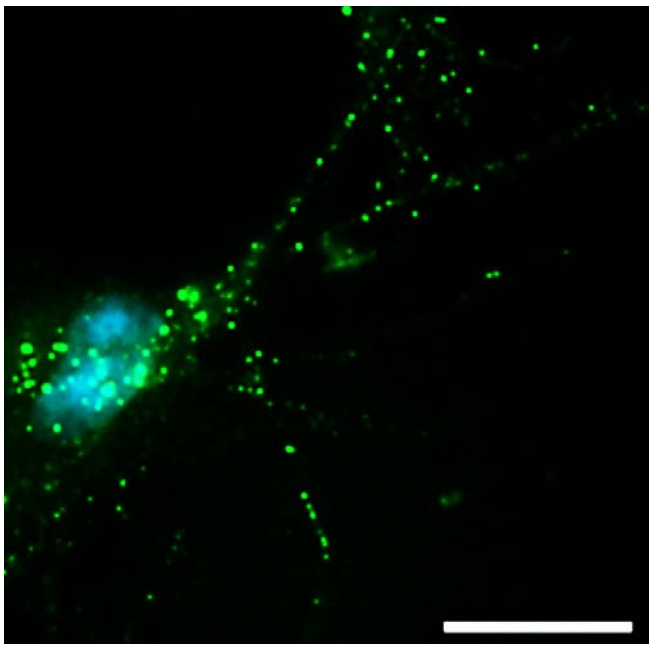

Figure. Retinoic acid-differentiated SH-SY5Y cells stained with phalloidin (red) and anti-GAP43 antibody (green). GAP43 marks neurite elongation and is used to assess treatment effects on regeneration. Scale bar corresponds to a length of 20 µm

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Mauro
Giorgi
Associate Professor

ORCID

RESEARCH LINES

- Phosphodiesterase 4D depletion/ inhibition exters anti-oncogenic properties in hepatocellular carcinoma.
- Oligomeric assembly of PDE5: a putative role in the regulation of function.
- Role of PDE2A expression in pathology and physiology of central nervous system.

STAFF | COLLABORATORS

Silvia Cardarelli, Michele Saliola, Ana Gabriela de Oliveira do Rego, *Technician (Sapienza)*
Mara Massimi, *Associate Professor (University of L'Aquila)*
Viviana Trezza, *Assistant professor (Univ. Roma 3)*
Manuela Pellegrini, Researcher *(IBBC-CNR)*

RESEARCH ACTIVITY

Phosphodiesterase 4D Exerts Anti-Oncogenic Properties in Hepatocellular Carcinoma Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related mortality worldwide. Drug resistance is a serious problem in the treatment of HCC. Therefore, it is of high clinical impact to discover targeted therapies that may improve the survival of patients affected by HCC. We investigated the role of isoform PDE4D in HCC development and progression. We found that PDE4D is over-expressed in HCCs both in vitro and in vivo and the gene silencing or the pharmacological inhibition of protein activity exerted anti-tumorigenic activities.

The oligomeric assembly of PDE5: A putative role in the regulation of function. cGMP-specific PDE5 being a regulator of vascular smooth muscle contraction is the molecular target of several drugs used to treat erectile dysfunction and pulmonary hypertension. Production of full-length murine PDE5A isoforms in Kluyveromyces lactis showed that the quaternary assembly of MmPDE5A1 is a mixture of dimers and tetramers, while MmPDE5A2 and MmPDE5A3 only assembled as dimers. We showed that the N-terminal peptide is responsible for the different assembly and for its mitochondrial localization. Overexpression of the three isoforms alters the cAMP/cGMP equilibrium and induces a metabolic switch from oxidative to fermentative. We also analyzed MmPDE5A1, A2 and A3 using many biochemical techniques pointed towards the role of a few specific cysteines in the isoforms' oligomeric assembly and in the enzymatic activity.

Role of PDE2A expression in the central nervous system at physiological and pathological levels. PDE2A has recently been proposed involved for Fragile X Syndrome (FXS), the leading monogenic cause of Autism (ASD). We investigated the role of PDE2A in ASD pathogenesis using two rat models. We found an altered regulation of PDE2A activity in the brain at an early developmental age. Inhibitors of PDE2A normalized social and cognitive impairment displayed on model rats. From these experiments PDE2A inhibition has emerged as a promising pharmacological approach for the deficits common to both FXS and ASD. We also studied the behavior of heterozygous PDE2A+/- (HET) adult mice. HET exhibited greater tendency to explore novel environments in comparison to WT, while sociability was similar. Therefore, we investigated the involvement of neuronal nitric oxide synthase (nNOS) expression. The neuroanatomical correlation between striatal nNOS upregulation and the behavioral phenotype in HET mice is advanced.

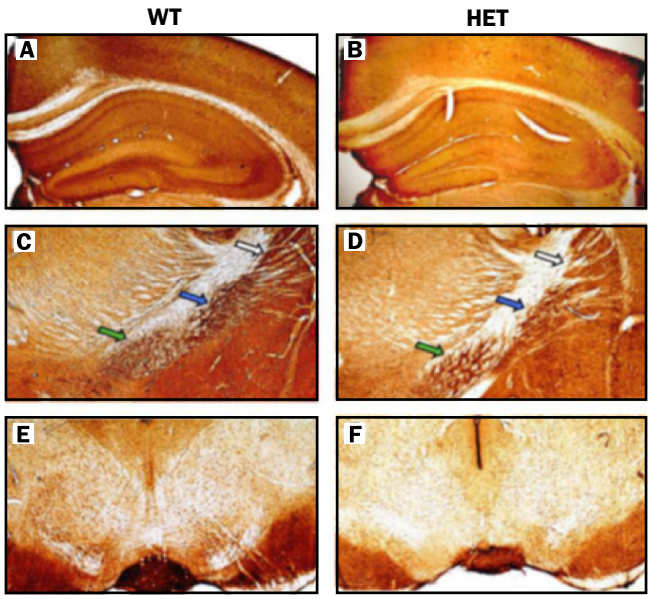

Figure. PDE2A immunoreactivity in comparative brain sections of WT (A, C, E) and HET B, D, F) mice in: cerebral cortex and hippocampus (A, B), striatum (arrow white), external globus pallidus (arrow blu), entopeduncular nucleus (arrow green) (C, D), substantia nigra and periaqueductal area (E, F). PDE2A staining appears less intense in HET than in corresponding brain areas of WT. Scale bar in H: A-F = 250 µm; G-H = 100 µm.

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Giuseppe
Lupo
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ORCID

RESEARCH LINES

- Transcriptional regulators of neural stem cell quiescence
- Molecular mechanisms of neural stem cell aging
- Developmental basis of neurodegenration

STAFF | COLLABORATORS

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Valerio Licursi, *Researcher (CNR)*
Silvia De Marchis,
Associate Professor
(University of Turin)
Ivan Conte, *Associate Professor*
(Univ. of Naples Federico II)

GRANTS

PRIN 2022 (2022WJFN5X)
Nr2f1-dependent regulation of Mitochondrial Function in Neural Development and Disease.

RESEARCH ACTIVITY

Current research in my lab is focused on investigating the molecular mechanisms that regulate neural stem cell fate, using in vitro culture systems of neural stem cells derived from the embryonic and the adult mouse central nervous system.
Over the last few years, we have studied the intrinsic mechanisms controlling neural stem cell identity during neural development, and those underlying the progressive decline of neural stem cell function during aging.
This work has led to the identification of transcriptional and epigenetic changes in homeobox genes occurring in neural stem cells and potentially associated with neural stem cell modulation during development and aging. In particular, we have shown that Hox genes are differentially regulated, at the transcriptional and epigenetic level, in neural stem cells of the developing rostral and caudal nervous system.
This differential regulation is stably retained during neural development and in the adult brain, which may be important for the maintenance of neural stem cell fates throughout life 1. Furthermore, we have found that another homeobox gene, Dbx2, is upregulated, and its epigenetic regulation is altered, in neural stem cells of the aged mouse brain. Dbx2 overexpression in neural stem cells from young adult mice can phenocopy some of the effects associated with aging, such as the inhibition of neural stem cell proliferation 2,3. We are currently investigating the molecular pathways mediating the function of Dbx2 and of other transcription factors in neural stem cell proliferation, with a focus on the mechanisms promoting neural stem cell quiescence.

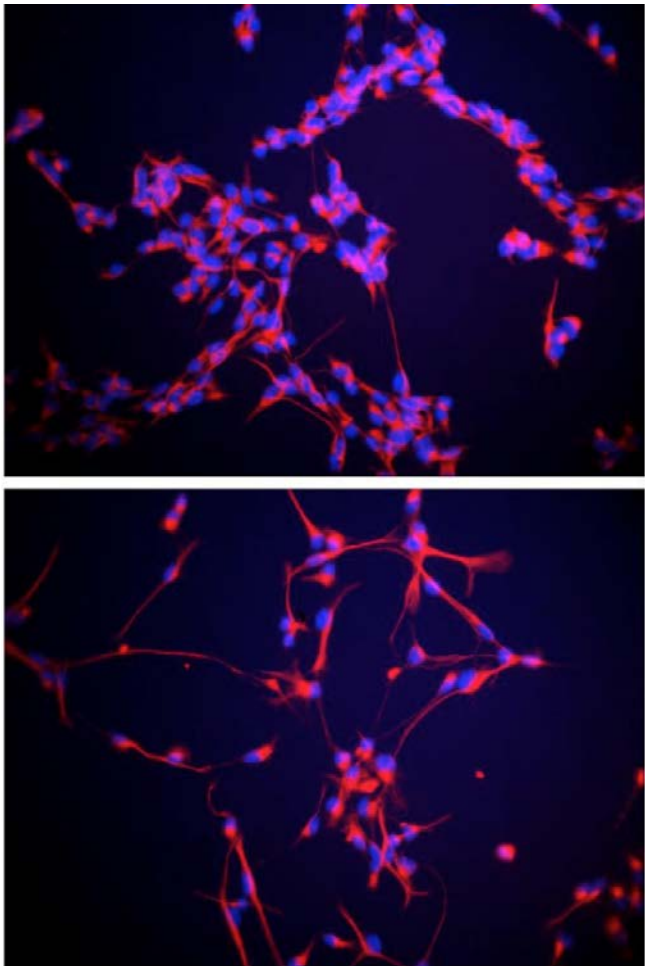

Figure. Transgenic neural stem cultures derived from the young adult mouse brain, which express either the Green Fluorescent Protein as a control (upper panel), or the homeodomain protein Dbx2 (lower panel). Elevated Dbx2 expression levels cause a reduction in the growth of neural stem cell cultures. Red staining shows the expression of the neural stem cell marker Nestin. Blue staining shows cell nuclei.

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Cristina
Mazzoni
Associate Professor

ORCID

RESEARCH LINES

- Mechanisms of cellular aging, cell death and autophagy - Stress response pathways in eukaryotic microbes
- Study of microbial adaptation in extreme environments and its relevance to climate change, biomineralization, and astrobiology.
- Biotechnological applications in food and probiotics

STAFF | COLLABORATORS

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Giovanna Costanzo,
Researcher (IBPM CNR, Rome)
John Morissey, *Researcher (University College Cork, Irland, Yeastime Startup S.r.l.)*
Stefano Fazi,
Researcher (IRSA CNR, Rome)
Marco Ferrari,
researcher (INAF, Rome)

RESEARCH ACTIVITY

Our research focuses on the molecular biology of yeast and microbial ecology, bridging basic research with biotechnological applications.

1. Yeast Genetics, Cellular Stress Responses, Ageing, Autophagy. We investigate cellular stress responses, aging, autophagy and cell death in Saccharomyces cerevisiae using this organisms as eukaryotic models. We explored how mRNA decapping linked LSM genes are linked to ageing, cell death and autophagy. We also use mutant strains to evaluate natural compounds for their protective effects against aging.

2. Microbial Ecology in Extreme Environments. Our recent research includes the study of microbial communities in extreme environments such as the alkaline, hydrothermal Lake Bagno dell'Acqua (Pantelleria, Italy), focusing on microbial adaptation to geochemical gradients, pH tolerance, and carbonate biomineralization inn microbialites. These investigations contribute to understanding life's resilience in changing environments and have implications for the astrobiology research, including the study of Mars terrestrial analogues, origin of life and biosignature detection.

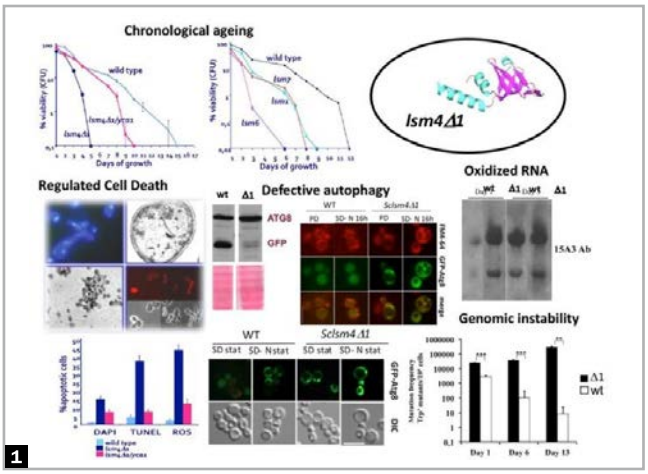

Figure 1. LSM gene mutants age prematurely, fail to activate autophagy, and die via Regulated Cell Death. Adapted from Mazzoni et al., 2003 MCB, Mazzoni et al., 2005 EmboRep, Stirpe et al., 2017 Apoptosis, Caraba et al., 2023 IJMS.

3. Food Biotechnology and Probiotics. We work at the interface of industrial microbiology and biotechnology, isolating potential probiotics from food matrices. We also study methods to increase productivity in fermented food and beverage. Combining yeast genetics, environmental microbiology, and biotechnology, our interdisciplinary research advances both fundamental knowledge and practical solutions in health, food technology, and environmental sustainability.

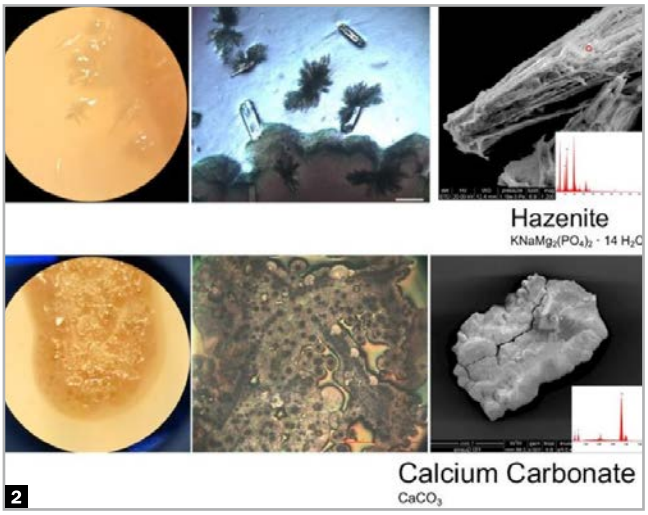

Figure 2. Biomineralization achieved under controlled conditions using bacterial isolates observed by optical and SEM microscopy.

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Andrea
Mele
Full Professor

ORCID

RESEARCH LINES

- Temporal dynamics of experience dependent plasticity
- Neural circuits underlying memory stabilization

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Michele Migliore,
Researcher (C.N.R. - I.B.F.)

GRANTS

PRIN2022 - Neural Mechanisms underlying memory improvement by spaced training in normal and cognitive impaired conditions coPI: Andrea Mele.

RESEARCH ACTIVITY

Learning and memory are two of the most important capabilities of the human mind. Our group has demonstrated that complex associative learning and memory require the activation not only of brain structures associated with the medial temporal lobe but also of different components of the striatal complex (Ferretti et al., 2010). Moreover, we have shown the importance of offline communication between the hippocampus and the ventral striatum (Torromino et al., 2019).
In more recent studies, we investigated distributed training, providing support for the hypothesis that its ability to optimize memory may depend on the engagement of the dorsolateral striatum (DLS), similar to what occurs in extensive training.

Future research

We aim to identify the neural circuits and molecular mechanisms that support learning and memory in both healthy and pathological conditions. In the long term, our findings could contribute to refining theoretical models and may offer new insights into the biological mechanisms underlying learning and memory, as well as support the development of novel therapeutic strategies for mental illnesses.

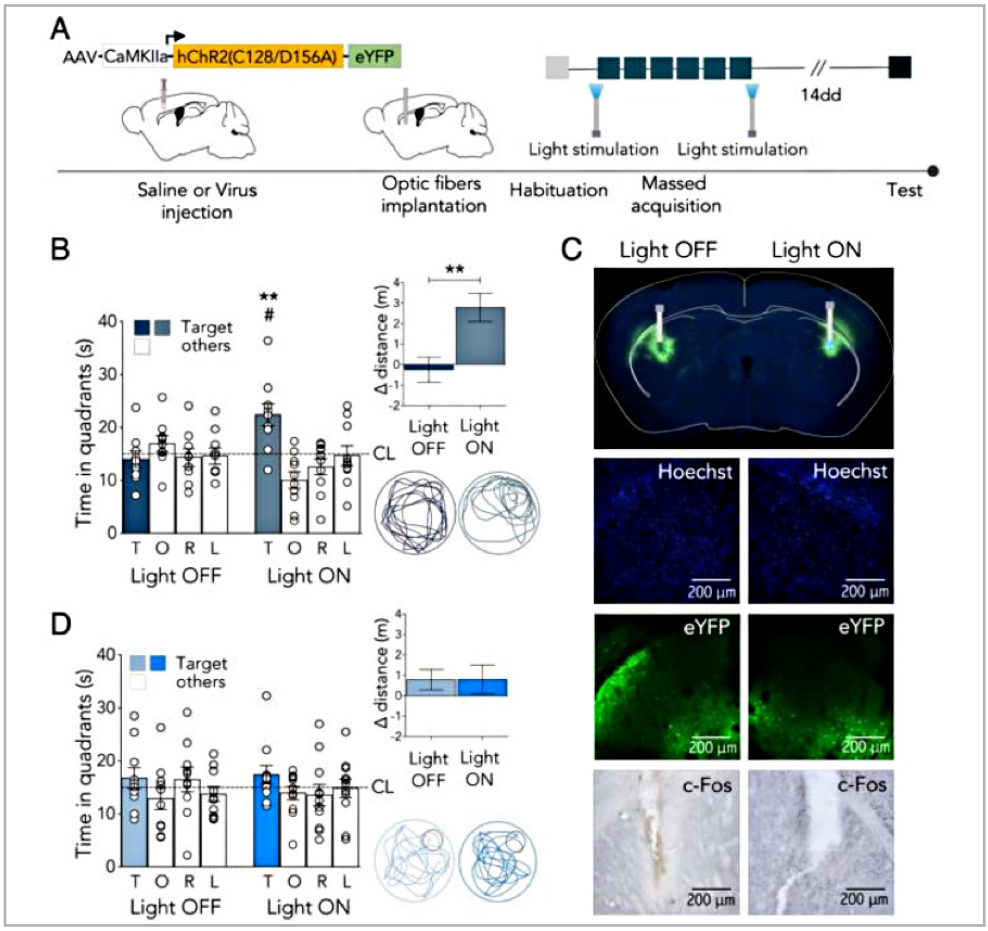

Figure. Optogenetic stimulation of DLS enhances memory stability in massed-trained mice. (A) Schematic illustration of the experimental design. (B) Light delivery in DLS during massed training improved spatial memory; (C) Microphotographs showing ChR2-eYFP expression and representative fiber location in the DLS; (D) Light delivery in mice bilaterally administered with saline did not affect performance in the probe trial 14d after massed training (modified from Mastrorilli et al., 2022).

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Maria Elena
Miranda Banos
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RESEARCH LINES

- Cellular mechanisms of neurodegeneration FENIB
- Monoclonal antibodies to study alpha-1 antitrypsin deficiency

STAFF | COLLABORATORS

Anna Quintiliani, *PhD student (Sapienza)*
Fulvia De Priamo, *Master student (Sapienza)*
Francesca Montemurro, *Master student (Sapienza)*
Annamaria Fra, *Associate Professor (Univ. of Brescia)*
David Lomas, *Professor (UCL, UK)*
Giovanna Galliciotti, *Researcher (UKE Hamburg, Germany)*

GRANTS

Grant from Fondazione Telethon (Italy). Genetic, cellular, and structural basis of the neurodegenerative pathology FENIB (2024-2026, principal investigator).

RESEARCH ACTIVITY

We study two mutant serpins (serine proteinase inhibitors), specifically the neuronal protein neuroserpin and the hepatic serpin alpha-1 antitrypsin. The mechanism of inhibition of serpins requires a high molecular flexibility that renders them very sensitive to destabilising mutations. The mutant variants undergo polymerisation within the endoplasmic reticulum of the cell of synthesis, which prevents their normal trafficking and secretion. This leads to disease with both gain- and lack-of-function phenotypes, due to intracellular polymer accumulation and lack of active serpin in the place of action, respectively.

In the case of neuroserpin, polymerisation causes a very rare neurodegenerative condition called familial encephalopathy with neuroserpin inclusion bodies (FENIB), with an onset of disease that correlates to polymerisation propensity of each variant. We have developed a cell culture model consisting in mouse neural progenitor stem cells overexpressing wild type or polymerogenic neuroserpin, which can be differentiated to neurons in vitro. Using this system, we have shown that neuroserpin polymers cause oxidative stress and mitochondrial alterations, consisting in perinuclear clustering and decrease of the inner membrane potential. Mitochondrial mislocalisation is enhanced by prooxidant molecules and rescued by antioxidants (1). These results highlight the role of oxidative stress and mitochondrial damage in FENIB.

In alpha-1 antitrypsin deficiency, polymerisation of the mutant protein leads to the lack of active alpha-1 antitrypsin in the lungs, causing emphysema, while polymer retention within hepatocytes causes liver disease. We have developed a set of conformation - specific and functional monoclonal antibodies against alpha-1 antitrypsin that we have used in collaboration to study polymer formation and structure, and the role of these polymers in disease (2, 3).

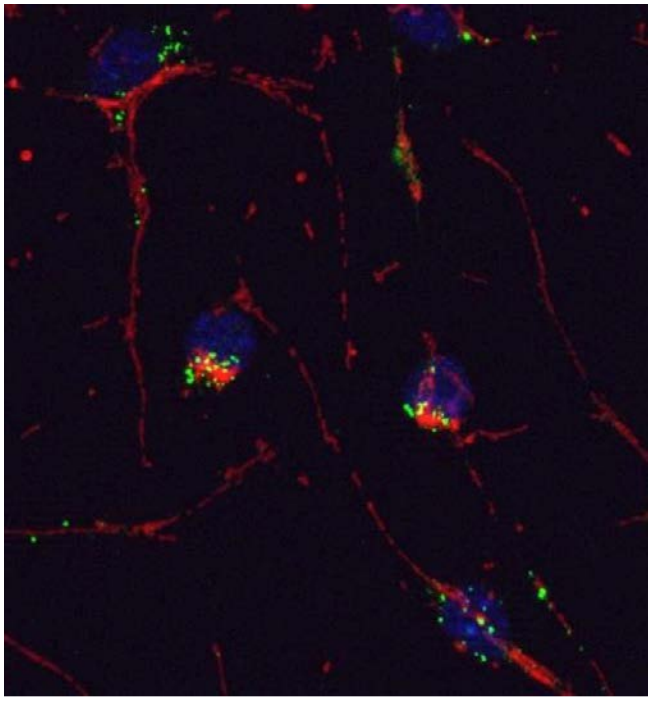

Figure. Mouse neural progenitor stem cells overexpressing mutant G392E neuroserpin, differentiated to neurons in vitro and co-stained for neuroserpin polymers (monoclonal antibody 7C6, green) and mitochondria (anti-Tom20, red). DNA is stained with DAPI (blue).

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Arianna
Montanari
Researcher

ORCID

RESEARCH LINES

- Model systems to analyse mitochondrial dysfunctions;
- Role of epigenetic factors on mitochondrial functionality;
- Characterization of probiotic microorganisms isolated from food samples.

STAFF | COLLABORATORS

Rosalba Carrozzo, *Senior researcher (Bambino Gesù Children's Hospital, IRCCS, Rome)*
Silvana Fiorito, *MD (CNR, Rome)*
J.A. Sánchez-Alcázar, *Full Professor (Universidad Pablo de Olavide, Sevilla, Spain)*

RESEARCH ACTIVITY

The research activity is focused on characterization of the pathogenic effects of mutations that compromise mitochondrial (mt) function and are responsible for serious diseases in humans. For this purpose the fermentative yeast Saccharomyces cerevisiae and nematode Caenorhabditis elegans are used as simple model systems. Several mutations in nuclear or mt genes have been characterized for their ability to alter mt function and this number is continuously increasing.
The use of simple models is validated for the molecular and biochemical analysis of the harmful effects of many isolated mutations. Different genetic strategies are fine-tuned to eliminate or silencing the endogenous genes and to introduce their mutated products into mitochondria. The molecular, phenotypic and physiological effects of the introduced mutations are subsequently studied. It is also possible to verify the therapeutic effect of interest molecules to recover the defective phenotypes.
The use of yeast as a model system allows studying the role of epigenetic factors on mitochondrial functionality. In particular, the involvement of the histone acetyltransferase gcn5 in mt functionality is investigated. The dialogue between nucleus and mitochondria is finely regulated and the alteration of mitochondrial functionality can trigger cellular stress signaling and changes in nuclear gene expression through retrograde regulation.
The epigenetic modifications, which also occur in the mitochondria, regulate gene expression, influencing the maintenance of cellular health through the oxidative stress responses and energy production. Yeast is used to study factors involved in the epigenetic regulation of mt gene expression, such as the stability of mtDNA and the modification of DNA-binding proteins within the mitochondria.
Kluyveromyces lactis is a respiratory yeast requiring functional mitochondria for viability; its metabolic plasticity allows to extend the study of mt mutations to this model and to advance in studies of nuclear-mitochondrial interactions.
K. lactis mt defects are studied in relation to different environmental stress conditions, such as oxidative stress (ROS) and light.
Another research line is aimed to validate microorganisms isolated from fermented foods, as probiotics, They are analyzed for the survival ability in simulated gastrointestinal conditions in vitro, the susceptibility to antibiotics, hydrophobicity, aggregation and inhibition ability the growth of pathogens.

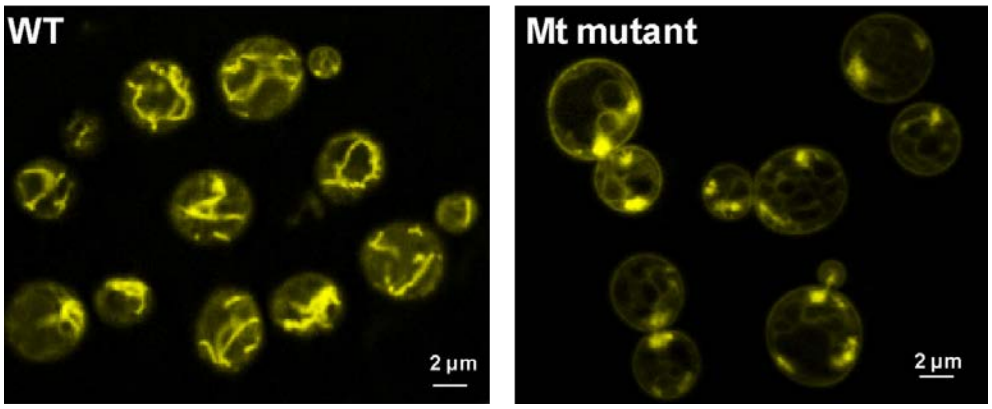

Figure. Fluorescence microscopy of the yeast wild-type (WT) and a mitochondrial (Mt) mutant stained with DASPMI to visualize mt morphology and function. While mitochondria of the WT are well-stained and branched, in the Mt mutant are poorly stained and collapsed.

References

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Mariangela
Morlando
Associate Professor

ORCID

RESEARCH LINES

- Non-coding RNAs function in neurons (physiological vs pathological conditions)
- RNA therapeutics in neurodevelopmental disorders
- Small molecules development with anti-cancer activity

STAFF | COLLABORATORS

Nicolò Salvi, *PhD student (Sapienza)*
Valentina Silenzi, *senior Post-doc (Sapienza)*
Zoya Ignatova, *Full Professor (University of Hamburg)*
Annalisa Fico, *Researcher (IGB-CNR Naples)*
Letizia Barreca, *Associate Professor (University of Perugia)*

GRANTS

2025-2028 AFM-Telethon Scientific grant. Targeting IRF2BPL non-sense mutartons with suppressor tRNAs. 103.100 Euro

RESEARCH ACTIVITY

My laboratory investigates RNA molecules, from their fundamental biology to their therapeutic potential, within the context of neurodevelopmental and neuromuscular disorders. We mainly focus on non-coding RNAs and on unveil their mechanism of action in regulating gene expression.

I started to investigate the biogenesis of microRNA (miRNA) during my PhD (Roma Tre) and my Post-doc (Oxford University, UK). I conducted pioneering research demonstrating that initial miRNA processing occurs very early during transcription. This has established a fundamental concept in the field, revealing the temporal dynamics of miRNA maturation. More recently, I developed a medicinal chemistry approach, identifying quinolone compounds that stimulate miRNA biogenesis, showcasing the innovative idea of targeting miRNA maturation with small molecules for cancer therapy.

A key area of our research involves investigating how the non-coding transcriptome contributes to neurodegeneration, particularly in Amyotrophic Lateral Sclerosis (ALS) associated with FUS mutations. Using patient-derived iPSCs, we determined how FUS mutations alter the biogenesis of specific miRNAs and long non-coding RNAs (lncRNAs and circRNAs). Our recent work on circDLC1(2), a conserved circRNA, demonstrated its ability to regulate glutamatergic synapses and to impact the cortical-striatal circuitry in a murine in vivo model. This has significant implications for ALS, since cortical hyperexcitability and striatal alterations have been observed in the disease. We are currently generating human iPSC models lacking circDlc1(2) expression to translate this observation to human.

Furthermore, leveraging an active collaboration with two Italian physicians and Prof. Zoya Ignatova, we have initiated a new project on NEDAMSS, a neurodevelopmental disorder caused by nonsense mutations in IRF2BPL gene. We are currently generating patient-derived iPSCs to model the disease and establishing a specific differentiation procedure to obtain mature and functional cortical neurons in vitro. A key goal of this project is to develop a novel therapeutic strategy using engineered suppressor tRNAs (sup-tRNA) to restore full-length protein synthesis. Notably, we have generated preliminary evidence showing that an engineered sup-tRNAArg is able to suppress a premature stop codon in IRF2BPL caused by pArg188Ter mutation, thus rescuing protein translation.

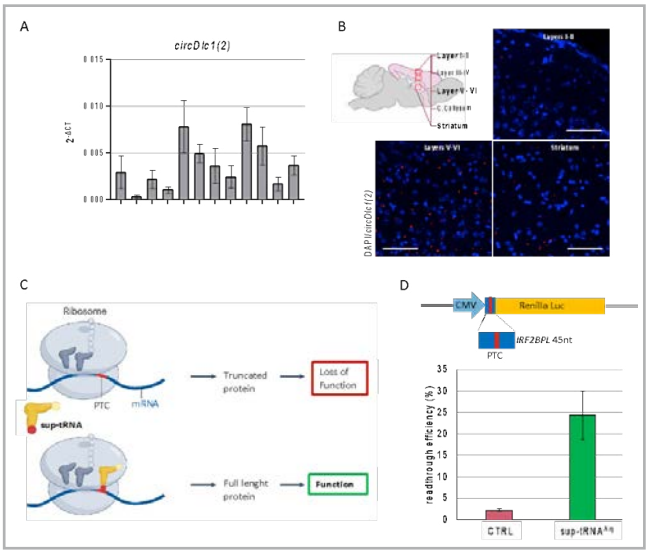

Figure. CircDlc1(2) expression in murine neuronal tissues measured by quantitative RT-PCR (A) and in murine brain by in situ hybridization (B). C) mechanism of action of a sup-tRNA. D) Graph showing the rescue of the luciferase expression from constructs bearing the IRFBPL-PTC (pArg188Ter) by addition of sup-tRNAArg.

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Chiara
Mozzetta
Associate Professor

ORCID

RESEARCH LINES

- Nuclear Lamina-Chromatin interactions in muscle regeneration and aging
- Epigenetic regulation of multipotent stromal cells in striated muscles
- Pre-clinical development of epigenetic drugs in murine models of muscular dystrophies.
- Epigenetic control of rhabdomyosarcoma

STAFF | COLLABORATORS

Valeria Bianconi, *Snr Postdoc (Sapienza)*
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Emilia Skafida, *Post-doc (Sapienza)*
Andrea Menicucci, *PhD st. (Sapienza)*
Alessandra Guidi, *Research Scientist (IBPM-CNR)*

GRANTS

2025-2027. Pasteur-Cenci Bolognetti Anna Tramontano. Epigenetic Reprogramming of Genome Nuclear Lamina Interactions in Fibro-Adipogenic Progenitors During Regeneration and Aging. 40000€.

2023-2028. Investigator Grant from AIRC. Aberrant chromatin-nuclear lamina interactions in stromal cells as underlying mechanism of rhabdomyosarcoma initiation. 630000€

2022-2026. MDA. Assessing the role of Fibro-Adipogenic Progenitors in EDMD. 279300$

RESEARCH ACTIVITY

Our laboratory investigates the epigenetic regulation of muscle regeneration and disease, with a strong translational focus on neuromuscular disorders such as Duchenne (DMD) and Lamin A/C-related muscular dystrophies.
We are particularly interested in how histone-modifying enzymes shape alternative transcriptional programs in muscle progenitor cells by organizing nuclear 3D architecture and chromatin topology. Our goal is to understand how these mechanisms direct cell-type-specific gene expression during tissue repair and how their dysregulation contributes to disease-associated aberrant cell fate decisions.
A central line of research focuses on muscle-resident progenitor populations—muscle stem cells (MuSCs) and fibro-adipogenic progenitors (FAPs)—and how epigenetic mechanisms govern their fate under physiological and pathological conditions. We have contributed to the identification of epigenetic drugs, such as histone deacetylase (HDAC) and G9a/GLP methyltransferase inhibitors, that reprogram FAP plasticity to promote muscle regeneration and limit fibrosis in dystrophic settings.
Our work also explores how the interplay between heterochromatin and nuclear lamins affects nuclear architecture and gene regulation, with implications for muscle degeneration in diseases involving nuclear envelope dysfunction.
More recently, we have extended our studies to investigate the epigenetic underpinnings of rhabdomyosarcoma (RMS), the most common pediatric soft tissue sarcoma of muscle origin. We aim to uncover how oncogenic transformations hijack developmental epigenetic programs in muscle progenitors, leading to uncontrolled proliferation and impaired differentiation.
Our research combines in vivo mouse models, human and murine primary cells, and advanced genomic, epigenomic, and imaging approaches to dissect how chromatin dynamics, nuclear structure, and signaling pathways interact to control muscle progenitor behavior. Ultimately, we aim to apply this knowledge to develop next-generation therapeutic strategies that modulate cell identity and regenerative capacity in both degenerative and neoplastic muscle diseases.

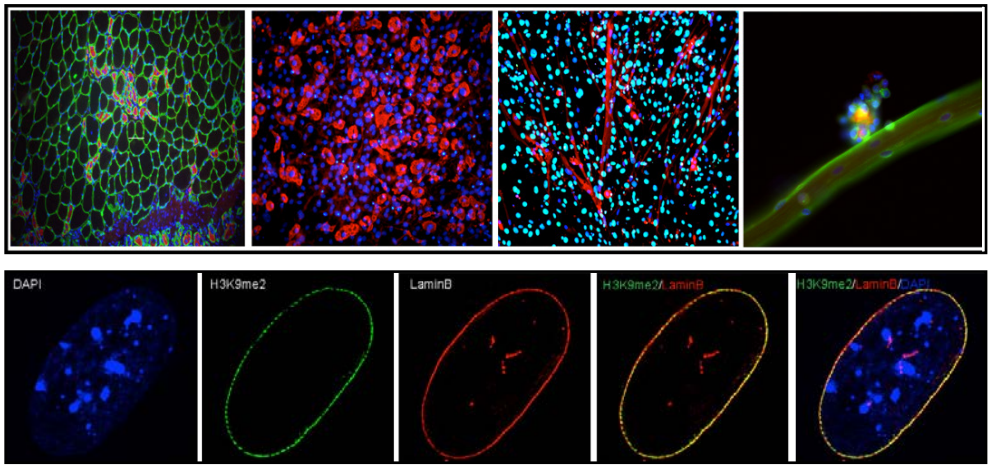

Figure. Upper panel: Representative models used in the laboratory, shown from left to right: a cryosection of regenerating skeletal muscle; stromal cells differentiated into adipocytes; cultured myotubes; and isolated single myofibers with associated muscle stem cells. Lower panel: Super-resolution immunofluorescence images depicting DNA (blue), heterochromatin (green) and nuclear lamina (red) within the nucleus of a muscle stromal cells.

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Arianna
Rinaldi
Associate Professor

ORCID

RESEARCH LINES

- Neural basis of anxiety
- Spatial memory circuits in neurodegenerative disorders

STAFF | COLLABORATORS

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De Jaco Antonella,
Associate Professor (Sapienza)
Giulia Torromino,
Research Tenure Track (Sapienza)
Giuseppina Amadoro,
Researcher (IFT-CNR and EBRI)

GRANTS

2022-2026. Alzheimer Association (USA). Stimulation of non-canonical memory circuits to improve memory in AD.

RESEARCH ACTIVITY

Research in my laboratory is characterized by a multidisciplinary and multiscale approach. We combine behavioural, anatomical, molecular and bioinformatics analyses with chemogenetic or optogenetic manipulations of neural activity, with the aim to build a comprehensive understanding of neural circuits in both normal and pathological conditions.

Decoding the neural basis of anxiety: from molecules to neural circuits.
Anxiety is an emotional state characterized by anticipatory concern regarding potential future threats or negative outcomes. However, anxiety becomes maladaptive when it is disproportionate to actual risks, producing threat generalization to non-threatening situations and a persistent state of heightened arousal that interferes with daily functioning and well-being. This pathological shift reflects a breakdown in the neural mechanisms that normally balance assessment of perceived risks and potential gains, influencing approach-avoidance behaviours. We study innate and stress-induced anxiety-like behaviours, at both molecular and circuit level, with the long-term goal to identify new therapeutic targets for the prevention or treatments of anxiety disorders. Our current focus is on the functional role of the dorsomedial striatum (DMS) within the neural circuit that regulates anxiety. We study how manipulations of specific afferent and efferent DMS projections influence approach–avoidance behaviours.

Targeting spatial memory circuits in neurodegenerative disorders.
Spatial navigation is one of the most common and conserved cognitive functions, as the ability to go from one place to another in a complex environment is essential for the survival of most animals. Spatial memory loss is an early clinical sign of Alzheimer's disease (AD) and other types of dementia. Despite intensive research efforts, we have not yet developed effective cures for AD, while the number of people affected is increasing steadily. We study the neural circuits involved in different types of spatial memory, to shed light on network dynamics of memory acquisition, consolidation and storage. We are currently investigating whether stimulation of brain regions non-canonical to memory functions and less vulnerable to AD pathology, such as the dorsolateral striatum (DLS), may improve spatial memory deficits in preclinical models of AD.

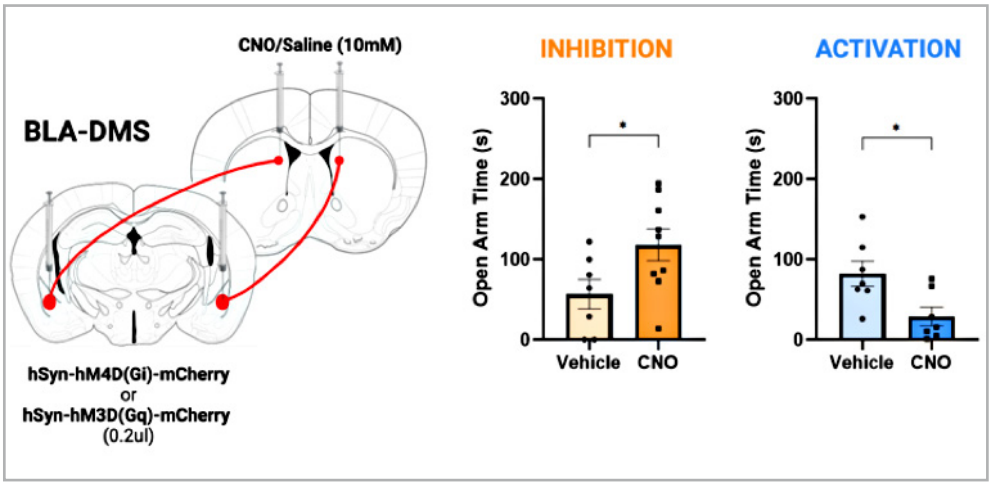

*Figure. Effect of chemogenetic modulation of BLA projections to DMS on anxiety-like behaviours in the elevated plus maze (EPM). Chemogenetic inhibition of BLA-DMS projections is anxiolytic, while activation of BLA-DMS projections is anxiogenic. *p<0.05 (Student's t-test).*

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Teresa
Rinaldi
Associate Professor

ORCID

RESEARCH LINES

- Biotechnology for cultural heritage
- Bacillus cereus group
- Yeast mitochondria

STAFF | COLLABORATORS

Francesca Frasca, *Researcher (Sapienza)*
Marzia Beccaccioli, *Researcher (Sapienza)*
Anita Scipioni, *Researcher (Sapienza)*
Nicoletta La Rocca, *Associate Professor (University of Padua)*
Duccio Cavalieri, *Full Professor (University of Florence).*
Alessia Cemmi, *Researcher (Center Calliope, ENEA)*

RESEARCH ACTIVITY

Biotechnology for cultural heritage.
This research line aims to study the geomicrobiology of hypogeal environments of archaeological interest. The rocks in which these hypogea are carved harbour a dynamic and rich microbial community that has not yet been thoroughly investigated. Nevertheless, the metabolic activity of bacterial and fungal strains could be exploited for biotechnological applications, such as the selection of carbonatogenic bacterial strains for bioconsolidation.

Bacillus cereus group.
The second line of research focuses on selecting molecules and peptides that exhibit antimicrobial activity against the Bacillus cereus group. Many strains of this group are pathogenic, and produce spores, the most resistant form of life. We are selecting green molecules with sporicidal activity to reduce the contamination of spores in specific environments.

Yeast mitochondria.
The aim of this research line is to study the yeast S. cerevisiae to elucidate the pathways activated by molecules of pharmaceutical interest, such as synthetic peptides and small molecules. Specifically, we analyse mitochondrial activity, which is conserved from yeast to human cells, to determine the toxicity of antimicrobial molecules.

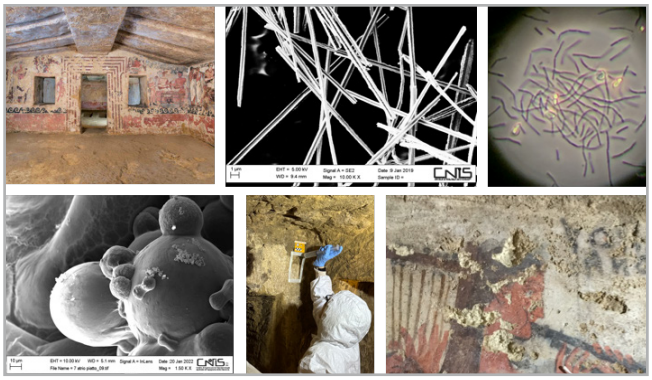

Figure 1. Bioconservation strategy of the hypogeal Etruscan tombs of Tarquinia. Upper panel: bacteria from the moonmilk (calcium carbonate) are selected from the walls of the Tomba degli Scudi. Lower panel: SEM analysis of the biogenic calcium carbonate produced by bacteria- The best strain is inoculated for the bioconsolidation activity.

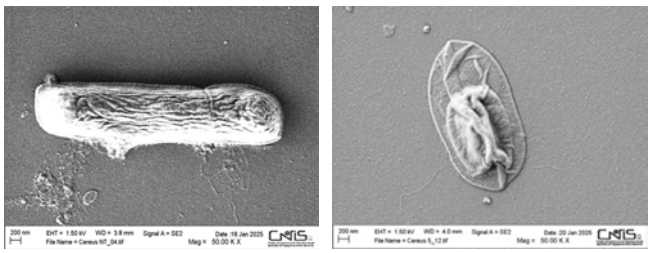

Figure 2. Selection of peptides with sporicidal activity.
Left, purified spores of Bacillus cereus inoculated in complete medium germinate in 4 hours.
Right, the spores in presence of a synthetic peptide, specifically designed to have antimicrobial activity, do not germinate.

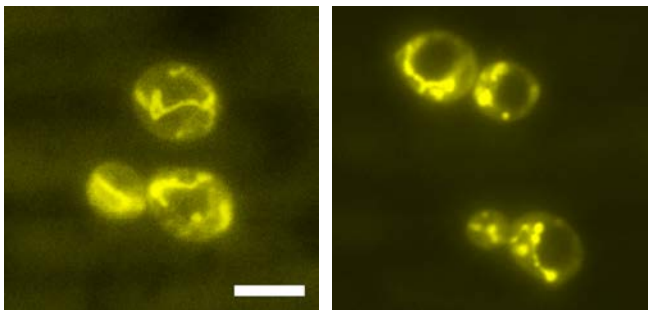

Figure 3. Example of activity of a molecule on yeast mitochondria.
Left, S.cerevisiae cells show a normal dynamic mitochondrial tubular structure.
Right: the addition of a molecule causes a mitochondrial fragmentation and a block of the respiratory activity.

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Alessandro
Rosa
Associate Professor

ORCID

RESEARCH LINES

- RNA and RNA-binding proteins
- Human iPSCs and organoids for disease modeling
- Neurodegenerative and neurodevelopmental diseases

STAFF | COLLABORATORS

Michela Mochi, *Postdoc (Sapienza)*
Margherita Medici,
PhD student (Sapienza)
Beatrice Borhy, *PhD student (Sapienza)*
Serena Carra, *Associate Professor (UNIMORE, Italy)*
Simone Martinelli,
Researcher (ISS, Italy)
Pietro Fratta, *Full Professor (UCL, London, UK)*

GRANTS

PNRR Spoke 3. Sviluppo di terapia genica e farmaci con tecnologia a RNA, 186.025€, PI.
AriSLA 2022. Unraveling the role of SUMO2/3 as a modifier of TDP-43 solubility: a new therapeutic avenue for ALS, 35.200€, Co-PI
MUR PRIN 2022. HSPB3 87.737€, Co-PI.
MUR PRIN 2022 PNRR 120.610€, PI.
AriSLA 2024. StressHUD 60.000€, PI.
Ist. Pasteur Italia - Fondazione Cenci Bolognetti, 40.000€, PI.

RESEARCH ACTIVITY

My research goal is elucidating molecular mechanisms that underlie differentiation, development and neurodegeneration, with a particular focus on the role played by non-coding RNAs and RNA-binding proteins. During my PhD at Sapienza University and my post-doc at Rockefeller University (NY, USA), I have studied the function of miRNAs in blood differentiation and embryonic stem cells, respectively. In 2009-2010 I was appointed director of the Rockefeller University Stem Cell Derivation Core.
My present research lines are based on induced Pluripotent Stem Cells (iPSCs) for the study of molecular mechanisms underlying neurodegenerative and neurodevelopmental diseases in vitro. iPSCs carrying pathogenic variants were derived from patients or produced by gene editing. We developed methods to differentiate them into relevant cell types, including motor and cortical neurons and skeletal muscle cells.
Thus, they represent excellent model systems for the study of the molecular and cellular basis of genetic diseases. In the last years, my laboratory has generated iPSC-based in vitro models of Amyotrophic Lateral Sclerosis (ALS), Fragile X-Syndrome (FXS), and GNAO1 related diseases. We have also set up protocols for differentiating iPSCs in the context of bioprinted models and 3D organoids (Figure 1).
We have found that ALS iPSC-derived motor neurons recapitulate disease phenotypes in vitro and reported changes in the transcriptome, miRNA pathway and FUS interactome in ALS motor neurons. Moreover, we have produced a collection of iPSCs carrying pathogenic variants for the neurodevelopmental diseases caused linked to the GNAO1 gene.

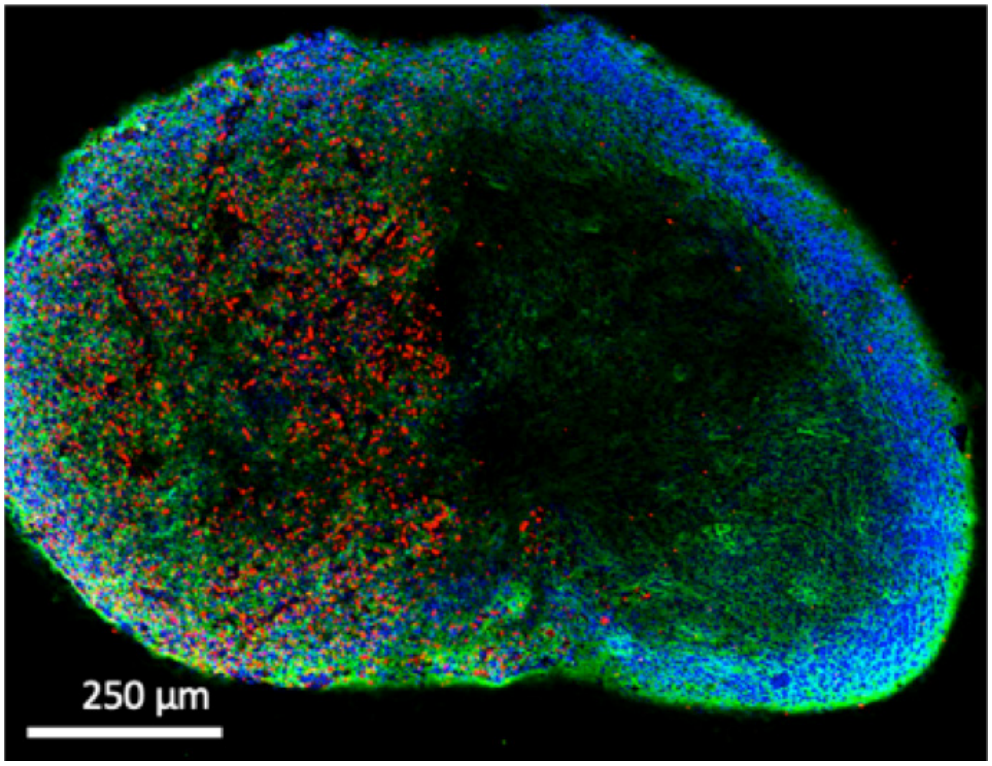

Figure. Neuromuscular organoid derived from human iPSCs. Red: MyHC (muscle); Green: TUJ1 (neurons); Blue: DAPI (nuclei).

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Giovanna
Serino
Associate Professor

ORCID

RESEARCH LINES

- Regulation of Flower Opening by Light
- Drought-Induced Flowering (Drought Escape)
- Early Responses and Adaptation to Air Drought

STAFF | COLLABORATORS

Serena Farrotti, *post-doc (Sapienza)*
Veronika Balakhnova, *p ost-doc, (Sapienza)*
Ning Wei, *Group leader Soutwest University, China*
Donato Giannino, *Group leader, CNR-IBBA*
Alice Pajoro, *Group leader, CNR-IBPM*

RESEARCH ACTIVITY

Our lab investigates how environmental factors such as drought and light influence plant development at the molecular level. A central focus of our research is on Cullin-RING ubiquitin ligases (CRLs), a family of protein complexes that act as molecular "recycling machines." These CRLs help regulate nearly every aspect of plant physiology and development by controlling the stability — and therefore the activity — of key regulatory proteins. To dissect these processes, we use Arabidopsis thaliana, a model plant widely used in plant biology due to its small size, rapid life cycle, compact genome, and ease of genetic manipulation.

Our current work is organized into three interconnected research lines:

1. Regulation of Flower Opening by Light. While the role of light in controlling flowering time is well established, much less is known about how it affects the process of opeflower opening. We have discovered that light, acting through the hormone auxin, regulates the growth of stamens — the male reproductive organs — by engaging a signaling cascade similar to the one used to control hypocotyl elongation in response to light and temperature. This suggests that evolution has repurposed the same signaling module for different growth processes, enabling plants to adaptively shape organ development based on environmental cues. We are now exploring how this light–auxin pathway interacts with other hormonal signals, particularly brassinosteroids, during flower opening.

2. Drought-Induced Flowering (Drought Escape). When faced with water scarcity, some plants accelerate their reproductive cycle — a survival strategy known as drought escape — to ensure seed production before the stress becomes severe. We study how this process is coordinated by light signals and the stress hormone abscisic acid (ABA). Our recent work implicates the ubiquitin ligase COP1 as a central integrator of these two pathways. We are currently mapping the signaling network downstream of COP1 to better understand how plants make timely decisions under drought conditions.

3. Early Responses and Adaptation to Air Drought. A drop in air humidity is often the first sign of incoming drought stress. We are investigating how plants perceive and respond to this early signal by combining physiological measurements, transcriptomic analysis, and anatomical studies. Our research has identified several genes that contribute to rapid adaptation to dry air and help coordinate the response between above-ground (shoot) and below-ground (root) tissues. This line of work aims to uncover how plants achieve whole-body communication in response to changing environmental conditions. By understanding these mechanisms, we hope to contribute knowledge that can support the development of crops better adapted to climate challenges such as drought and fluctuating light conditions.

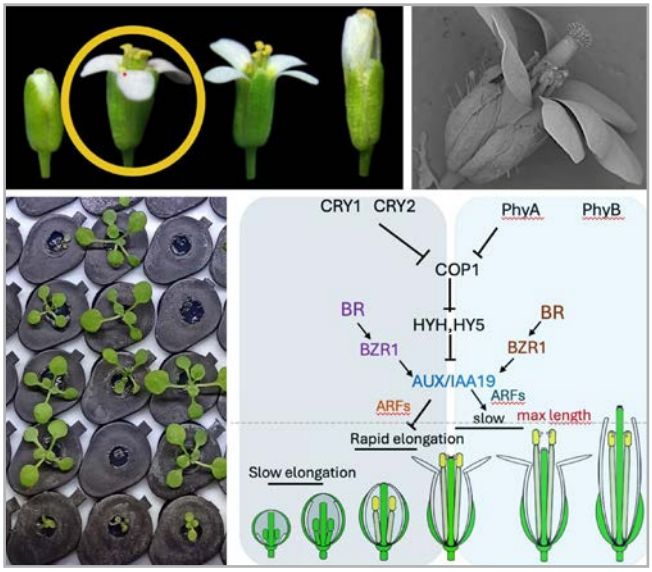

Figure. Top left, different flower stages from Arabidopsis thaliana. Top right, scanning electron micrograph photo of a stage 14 flower. Bottom left, Arabidopsis seedlings grown on hydroponic culture for drought experiments. Bottom right, a model depicting the function of light and hormones ion regulating stamen elongation in opening flowers.

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Stefano
Tacconi
Researcher Tenure Track

ORCID

RESEARCH LINES

- Role of Lipids in Extracellular Vesicles biology
- Extracellular Vesicle-mediated Signaling in Glioblastoma microenvironment
- Bio-based nanoformulations for targeted drug-delivery
- Nanotoxicology of nanostructured systems in cells and model organisms

STAFF | COLLABORATORS

Daniela Uccelletti,
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(University of Chieti/Pescara, Italy)
Sophie Rome, *Researcher*
(University of Lyon, INRAE, France)

GRANTS

2025 - 2026. KERR S.p.a..
Analisi citotossicologiche e valorizzazione nanotecnologica dei digesti.

RESEARCH ACTIVITY

Our research focuses on unraveling diverse aspects of extracellular vesicle (EV)-mediated intercellular communication. This includes the discovery of novel EV-like communication systems, as well as in-depth investigation into the role of lipid cargo in EV biogenesis and function, combining innovative methodologies and high-resolution microscopies. In collaboration with the University of Lyon, we revealed that lipid droplets (LDs) can be secreted by lipid-associated macrophages (LAMs), potentially via CD81-enriched membrane domains, and contribute to cell-to-cell signaling. We aim to define the mechanisms of LD secretion and assess whether this represents a conserved communication pathway. Equally important is our focus on the role of lipid-associated EVs in glioblastoma (GBM) biology, particularly the crosstalk between tumor and glial cells during chemotherapeutic treatment.

Through integrated omics approaches and comprehensive functional analyses, we aim to elucidate how EVs and their molecular cargo influence GBM growth, malignancy, and progression, especially by modulating immune responses. Among our group's activities is the use of EVs derived from waste products for the targeted delivery of drugs or bioactive molecules. Leveraging our solid expertise in the field of nanoformulations, we adapt existing approaches or develop innovative methods for isolating and loading EVs from biological waste matrices, such as bovine milk whey, to produce eco-friendly nanocarriers. As a key component in the development of new nanocarriers, our scientific interest also includes investigating the efficiency, targeting capability, bioavailability, and cytotoxicity of these nanostructured systems, using both in vitro and in vivo models.

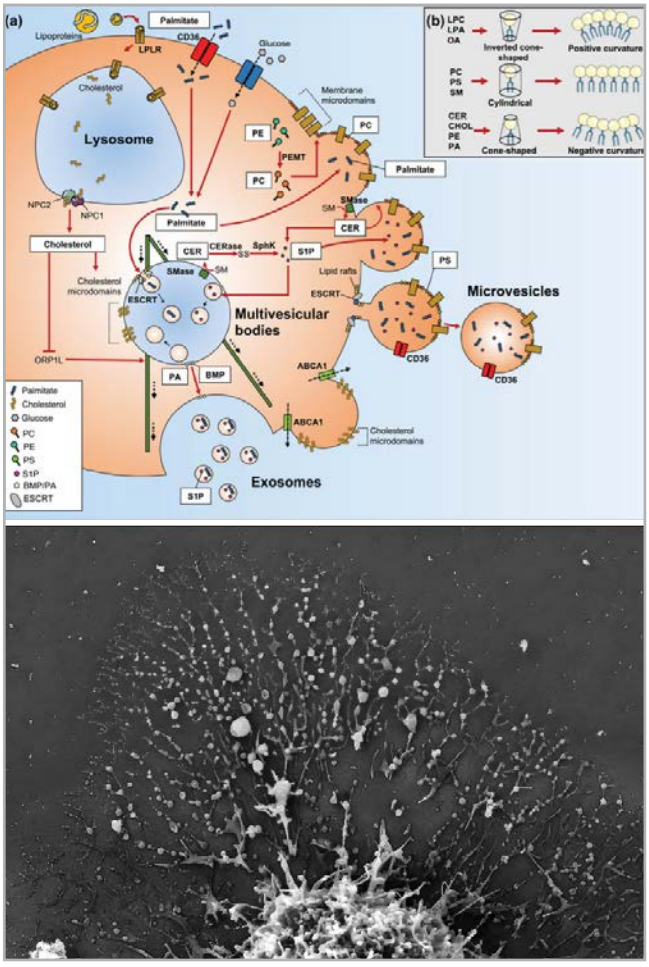

Figure. Upper panel: Role of lipids in EV biogenesis (Rome S and Tacconi S., J Extracell Vesicles. 2024). Lower panel: SEM image of EVs released from lipid-loaded macrophages.

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Ada Maria
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Full Professor

ORCID

RESEARCH LINES

- Effects mediated by naphtalimide derivatives in glioblastoma cancer stem cells.
- Modulation of insulin resistance and anti-inflammatory pathway mediated by Oleoylethanolamide (OEA) in human astrocytes
- Cholinergic modulation of central and peripheral inflammation

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RESEARCH ACTIVITY

Effects mediated by naphtalimide derivatives in glioblastoma cancer stem cells.
Glioblastoma (GBM), the most aggressive brain tumour, still today presents poorly effective treatments. In fact, pharmacological therapies failed to impact patient survival. Therefore, the identification of new drugs capable of counteracting malignancy remains a promising challenge in Glioblastoma treatment. To this aim, we investigated the role of naphthalimide derivatives in inhibiting GBM cell proliferation and survival. Interestingly, the dualsteric agonist Iper-8-Naphthalimide (N8), binding both allosteric and orthosteric binding sites of M2R, can induce “biased agonism” downstream receptor activation and promote a strong effect upon low-dose treatment. Recently, thanks to the addition of an amine group in the allosteric region, we have obtained an autofluorescent N8, named fluo-N8. It seems very useful to better understand the ligands’ functional properties and the interaction with M2R. Moreover, fluo-N8 can allow to follow the fate of naphthalimide derivatives once internalized into tumour cells. A comprehensive characterization of the fluorescent dualsteric agonist Fluo-N-8-Iper as a reliable and biologically active molecular probe for investigating M_2 muscarinic receptor signalling in glioblastoma cells will be analysed through a multidisciplinary approach combining receptor binding assays, molecular docking, cytotoxicity analyses, and confocal microscopy analysis (see Figure). Moreover, we are investigating the ability of naphtalimides derivates to cross the BBB.

Modulation of insulin resistance and anti-inflammatory pathway mediated by Oleoylethanolamide (OEA) in human astrocytes.
The impact of peripheral insulin resistance(IR) on systemic health is well-documented, and its profound effects on brain function and cognition have gained increased attention in recent years. Nutritional intervention with insulin sensitizers/modulators may prevent cognition impairment and dementia. The treatment of in vitro culture of human astrocytes with OEA will be investigated by our group to evaluate its ability to counteract IR and neuroinflammation.

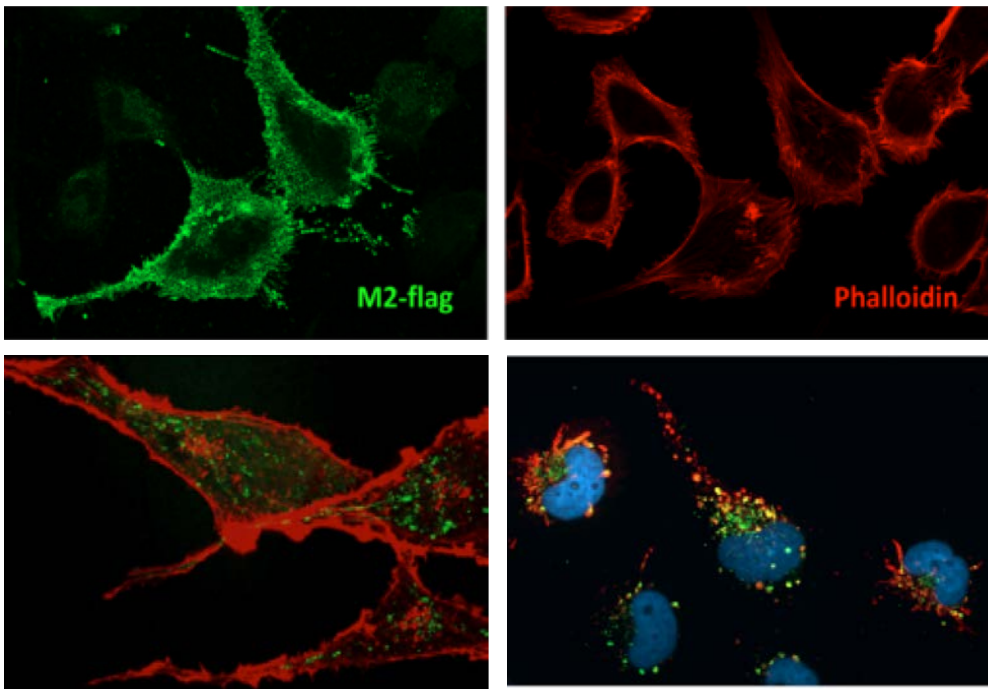

Figure. Upper panel: M2 –flag overspressed n glioma cells (green)-Lower panel N8-ipernaphtalimide-fluo (green) into the glioma cells after 48-72h of treatment. In red the actin staining by phalloidin (on the left) and with mitrotraker (in red) (on the right)

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RESEARCH LINES

- Subcortical-to-cortical networks underlying memory consolidation
- Peripheral Nervous System stimulation for memory enhancement

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RESEARCH ACTIVITY

Memory is a multifaceted process through which living beings can actively retain information acquired through experience for a short- or long-term. In the classical view, memory is conceived as the result of mental representations that arise from the activity of specific cortical areas, among which the hippocampus is the most studied structure precisely because of its role in various types of memory. This classical view is being challenged by evidence that showed the role of different subcortical and peripheral areas in memory formation. Indeed, the emerging perspectives in cognitive neuroscience suggest that human cognitive abilities are mediated by the relationship that our body as a whole generates with the external world, through the activation of sensory and motor systems. This perspective conceives cognition as a function evolved from brain-body interactions and the body as a central agent in the regulation of cognitive functions that can influence brain activity and affect behaviour, be it an action, a thought or a memory.

Touch is a crucial sense for animals that allows to explore and interact with the environment since birth. Interestingly, evidence shows that the somatosensory system might actively modulate memory functions; indeed, tactile stimulation has been shown to elicit hippocampal responses – through the thalamus and the somatosensory cortex (S1) – increasing S1-hippocampus rhythm phase synchronization, stimulating memory-related plasticity in the hippocampus, improving memory performance, and augmenting the survival and differentiation of hippocampal cells in adulthood.

Additionally, transcutaneous electric stimulation (TENS), which is known to activate the somatosensory tactile system, has been shown to modulate the activity of cortical and subcortical brain regions, change neurotransmitters release, modulate neural plasticity pathways and potentiate memory (Fig. 1).

Although these interesting set of evidence, the role of touch in the mechanisms related to memory formation has never been systematically investigated.

Our hypothesis is that stimulation of somatosensory tactile fibres (Fig. 2) from the peripheral nervous system might elicit a neural entrainment and neuromodulatory pathways activation that if applied in specific temporal windows can potentiate memory functions and related molecular changes through mechanisms of heterosynaptic plasticity.

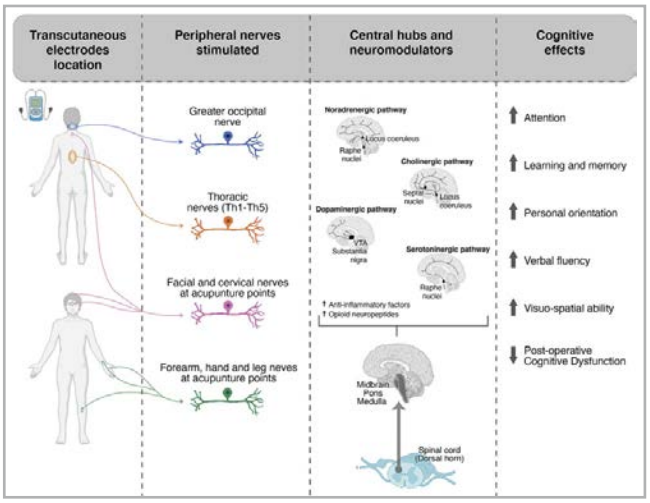

Figure 1. TENS hypothesized mechanism of action on cognitive functions (Fiorentini et al., 2025). The figure shows the different types of peripheral nerves stimulated through TENS, which have been used to modulate cognition, and the neuromodulatory pathways that might be recruited.

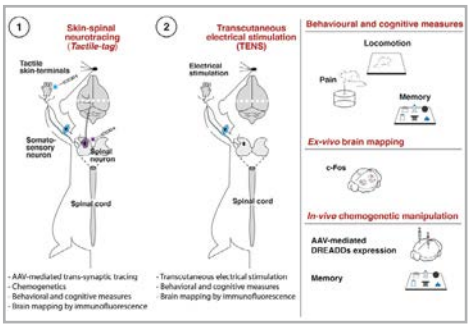

Figure 2. Main experimental approaches that are being developed in the lab for studying the potential of tactile stimulation for memory enhancement.

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RESEARCH LINES

- Host-microrganism interactions in the animal model Caenorhabditis elegans
- Nanobiotechnology for biomedical and environmental applications
- C.elegans as tool in the farm to fork strategy

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GRANTS

2024-2027.
PRIMA 2023 SAFOOD4MED
2022-2026.
AGRITECH CN2 Spoke 9

RESEARCH ACTIVITY

The research activity is based on the various fields of microbial biotechnology and the use of the nematode C.elegans as a model system to study the host-pathogen interaction processes to unveil the mechanisms involved in the innate immunity and in stress response.
Several advantages allow C.elegans to be used as an in vivo infection model. The genome is completely sequenced and it has a defined number of somatic cells and all are visible in the intact living organism under the microscope making the observation of infection possible at the organism level. It is also an excellent genetic model: it has both hermaphrodite and male sexes and is a premiere organism for the use of RNA interference studies allowing rapid targeted investigation of gene function. Currently investigations in the lab regard the glycosylation's role in pathogen recognition as well as in innate immune and in the oxidative stress responses. Key signaling pathways involved in pathogen response using several bacterial strains are studied. Dietary sources, such as bacteria, play an important role in the control of C. elegans lifespan; the bacterial biomass indeed represents the worm food, and although their trophic relationship is different from the synergistic one between mammals and gut microbiota, live bacteria influence the nematode physiology through their metabolites, representing both direct and indirect aspects of a diet (Figure 1).
The nematodes are also utilized to screen for the isolation of potential probiotics deriving from foodborne bacteria.
In recent years, our research has also focused on the field of nanotechnology to characterize the antimicrobial properties of nanomaterials produced by bacteria and utilized in biomedical and cultural heritage fields through multidisciplinary approaches. Specifically, our attention is devoted to study the interactions between the cells and the carbon-based nanopolymers to understand how nanomaterials interact with microrganisms. Nematodes are a very sensitive tool to study sub-lethal responses at the molecular level. The environment directly affects health status and plays a major role in quality of life. In this frame, our research employs C.elegans as a biological model to diagnose environmental quality but also the properties of bioactive molecules from agricultural by-products.

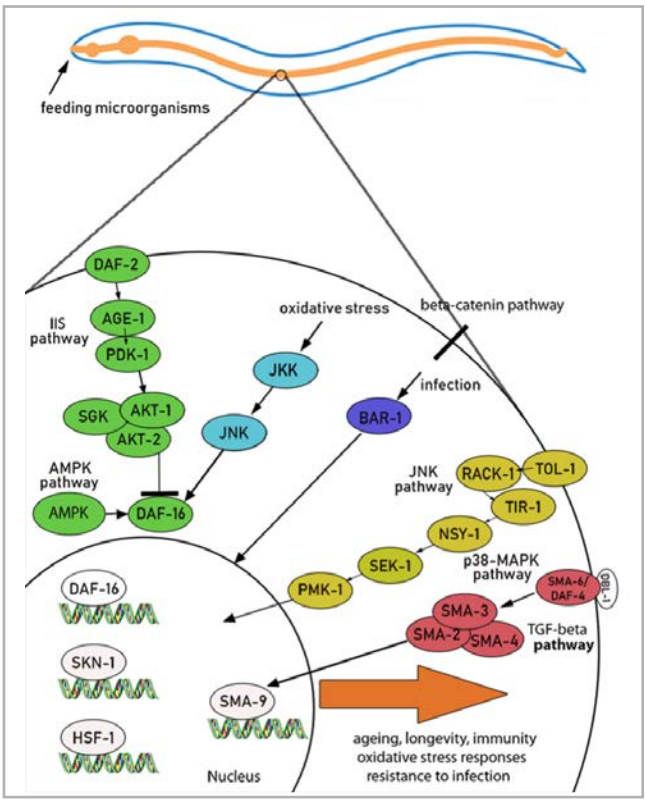

Figure 1. Schematic representation of the most common signaling pathways influenced by microrganisms employed as a diet in C. elegans studies (Modified from Roselli et al., 2019).

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RESEARCH LINES

- Molecular and epigenetic effects of Quadrato Motor Training on healthy subjects and Parkinsonian patients.
- Epigenetics and oxidative stress in Fetal Alcohol Spectrum Disorder.

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GRANTS

SEED-PNR-2022.
Molecular and cognitive effects of Quadrato Motor Training on patients with Parkinson's disease. N. protocollo SP12218475C9037E

RESEARCH ACTIVITY

Quadrato Motor Training (QMT) is a specifically structured sensorimotor training that involves sequences of movements, developed on the base of a neuroscientific research aimed at finding new means of reducing stress while improving cognition and emotional well-being. QMT enhances reflectivity and creativity in healthy subjects, as well as reading skills in dyslexic ones. Electrophysiology has shown that QMT significantly increases inter- and intra-hemispheric EEG alpha coherence and cerebellar oscillatory alpha power in healthy subjects and dyslexics. In addition, increased neuronal connectivity and arborization following daily QMT training was observed by MRI studies. This implies ongoing neuronal remodeling possibly involving molecular modifications.
Neurotrophins are closely related to neuroplasticity and synaptogenesis, representing valuable candidates as mediators of the QMT driven effects. In addition, they are involved in stress, mental health and well-being. Levels of pro-neurotrophins are also considerably changed in neurodegenerative pathologies.
We demonstrated salivary variations of proNGF and proBDNF following QMT practice, that are reciprocally and positively correlated and correlated with improved creativity. A correlation was also found with increased white matter volume and inter-hemispheric connectivity by MRI. Subsequently, methylomics has shown significant CpG methylation changes on Repeated Elements (RE), specifically rDNA clusters and LINE-1 sequences, hypothetically linked to up-regulation of protein synthesis and increased genome stability (1). In addition, preliminary observation suggests a reduction of the pro-inflammatory cytokine IL-1β (2). The study was extended to include a cohort of Parkinsonian patients. Transcriptomics revealed modulation of about 450 genes, some of which involved in the etio-pathogenesis of Parkinson's disease (the manuscript is in preparation). Currently, we are investigating the neurotrophins levels of the PD cohort following QMT, as well as evaluating the possible anti-inflammatory effects of QMT by measuring levels of several cytokines. We are also trying to answer the question of whether QMT could help reduce oxidative stress in PD patients. Finally, methylomics is ongoing to evaluate the possible epigenetic effects of QMT on this pathological population. Our results support the idea that QMT is a useful integrated training that may aid in ameliorating well-being, by activating endogenous resources of the mind-body system (Fig.1). In addition, QMT can be regarded as a powerful non-pharmacological supporting therapy for the treatment of neurodegenerative diseases.

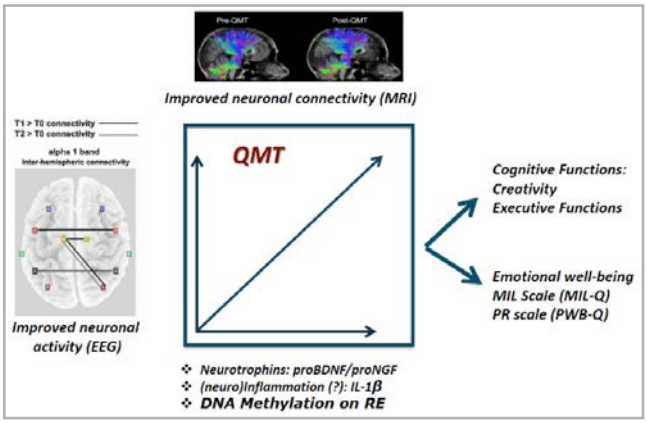

Figure. Summary of the studies and effects related to Quadrato Motor Training (QMT) on healthy subjects. Scheme of the direction of movements inside the Quadrato space (center). Main electrophysiological effects by EEG (left). Morphological outcomes by MRI (top). Molecular and Epigenetic effects (bottom). Cognitive and Psychological outcomes (right).

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RESEARCH LINES

- Molecular and epigenetic control of seed germination in Brassicaceae species
- Pharmacological approaches to increase plant resilience to abiotic stresses
- Stress Granules in Arabidopsis thaliana

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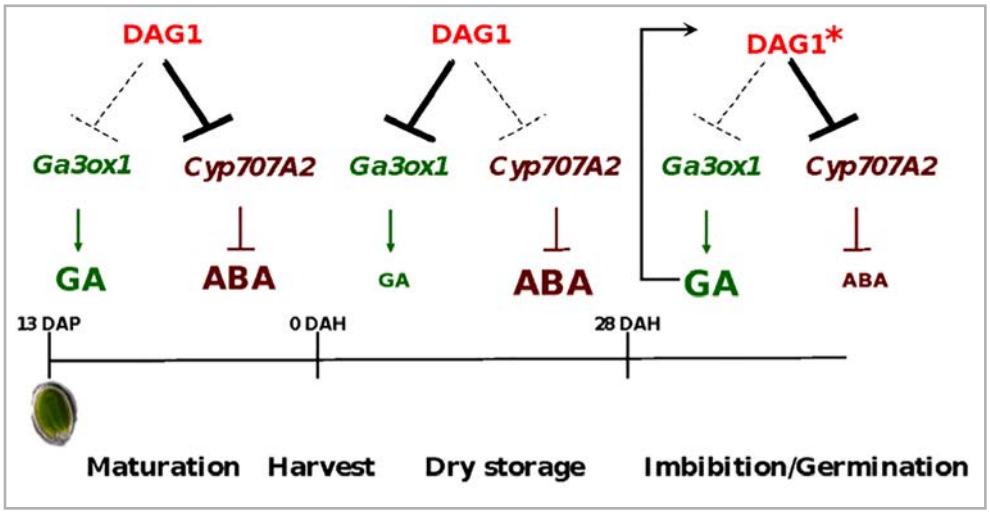
RESEARCH ACTIVITY

The transition from a growth-arrested seed to a germinating seed is a crucial developmental switch in plant life. Arabidopsis seeds develop dormancy during the late stages of their development; abscisic acid (ABA) induces seed dormancy whereas gibberellins (GAs) release dormancy and promote germination. DAG1 is a repressor of the light-mediated seed germination process in Arabidopsis. DAG1 controls the ABA/GA ratio during seed maturation and dormancy by directly repressing GA3ox1 and CYP707A2.



DAG1 mutant seedlings show shorter hypocotyls compared to the WT, suggesting that DAG1 is a negative component of the light-mediated inhibition of hypocotyl elongation. DAG1 promotes hypocotyl elongation acting on ABA, ethylene and auxin signaling. Plants, as sessile organisms, have to survive to changing environmental conditions. ABA has a key role in the adaptation to environmental challenges as in the control of plant development. The response to abiotic stress is mediated by epigenetic reprogramming, which involves the POLYCOMB REPRESSIVE COMPLEX 2 (PRC2). DAG1 is a PRC2 target and is marked by H3K27me3 in seeds and seedlings. Mutations in the catalytic subunit of PRC2 results in a severe phenotype; although the effects of several inhibitors of the PRC2 catalytic subunit (EZH2) have long been tested in animals as anti-cancer therapy, no trial with any inhibitor has ever been reported in plants. Taking advantage of the homology of EZH2 in animals and plants, we assessed the efficacy of a EZH2 inhibitor on Arabidopsis seeds, to provide a powerful tool in studying PRC2 action in plants.

Figure. Upper panel: model illustrating the function of DAG1 during maturation, dormancy and germination of seeds in Arabidopsis thaliana. Lower panel: a new pharmacological approach in Arabidopsis thaliana.

We performed treatments with a compound previously reported as an EZH2 inhibitor in human leukemia cells, and we proved that it is active on the Arabidopsis catalytic subunit of PRC2. Indeed, treatment with the drug reduces the total amount of H3K27me3 in a dose-dependent fashion. The pharmacological approach to inhibit PRC2 is efficient in plants; therefore, this inhibitor could represent a powerful tool to further investigate the effects of the transcriptional control mediated by PRC2 in plants, also in the response to abiotic stresses.

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“GENETICS„

The research activity of the Genetics section of the Department of Biology and Biotechnologies “Charles Darwin” is focused on three main broad areas:

- human population and forensic genetics;
- molecular genetics, gene therapy and cytogenetics of mammalian somatic cells;
- molecular genetics, epigenetics and cell biology of *Drosophila melanogaster*.

These research topics are carried out by Faculty Members in collaboration with researchers of the Institute of Molecular Biology and Pathology (IBPM) of the National Research Council (CNR).

Research on human population genetics traces back to the early times of genetics in Rome, when G. Montalenti and M. Siniscalco used population genetics to study the role of malaria as a selective factor for maintenance of mutant alleles in thalassemia and G6PD genes. There are currently two research groups that exploit human population genetics on ancient and modern samples for studies on human evolution, migrations and the genetics of aging and related diseases. These research activities are also aimed at clarifying the molecular evolution of the human genome and at applying genetic knowledge to address forensic problems and legal proceedings.

Groups currently working on the molecular genetics and cytogenetics of mammalian cells, are mainly interested in development of vectors and strategies for gene therapy, in human telomere and centromere biology and in the control of genome stability, including the structure and origin of chromosomal fragile sites. Current research in human biomedical genetics stems from the human cytogenetics branch set up first by G. Montalenti and then expanded by G. Olivieri.

The research in *Drosophila* genetics, carried out by the Italy’s largest *Drosophila* research pole that was originally founded by two scientifically active emeritus professors, M. Gatti and S. Pimpinelli, embraces different topics. These include the role of transposition in evolution, the epigenetic modifications of chromatin and heterochromatin, the molecular mechanisms of cell division, the analysis of telomere structure and stability, the biological effects of ionizing radiations and the relationship between nutrition, genome integrity and cancer. Some groups also exploit *Drosophila* as a model for different neuromuscular degenerative diseases.

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RESEARCH LINES

- Regulation of telomere capping,
- Unconventional Roles of HP1a
- Biological effects of low-dose/ low-dose rate radiation and mechanisms of radioresistance

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GRANTS

2023-2026. Non-canonical roles of cohesin and Separase, beyond that of cohesion Role PI, MUR, N. 202227SYBW.
2024-2026. Unravelling a conserved role for HP1a in mitochondrial homeostasis (Anna Tramontano Grant, Istituto Pasteur Italia/ Fondazione Cenci Bolognetti.

RESEARCH ACTIVITY

Regulation of telomere capping. G. Cenci has focused most of his research activity on the identification of proteins required for Drosophila telomere protection. His work has contributed to i) the description of Drosophila telomeres as epigenetically determined structures, ii) the identification of a multi-protein complex, dubbed terminin, which specifically associates with Drosophila chromosome ends; iii) the characterization of non-terminin proteins required for telomere protection that have human counterparts involved in telomere maintenance. These findings unveil the potential of Drosophila as a model system or the study of human telomeres, which are currently object of intense investigations due to their involvement in aging and cancer processes.

Unconventional Roles of HP1a. In the last 10 years G. Cenci research has revealed new regulatory mechanisms of HP1a expression that are required for both canonical and non canonical roles of this conserved multifaced protein. In particular, we demonstrated for the first time that in fruit flies Hp1a physically and genetically interacts with H2A.V, the Drosophila ortholog of mammalian H2AX and that this interaction is essential for the regulation of kinetochore-driven k-fiber regrowth. Additional we showed that Hp1 interacts with the Nijmegen Breakage Syndrome 1 (NBS1), a protein involved in DNA repair which also acts as a regulator of Hp1a stability during DNA damage both in flies and human cells. Furthermore, we described that human HP1 coding genes are co amplified with EGFR encoding genes in several human cancers underscoring functional relationships among these factors.

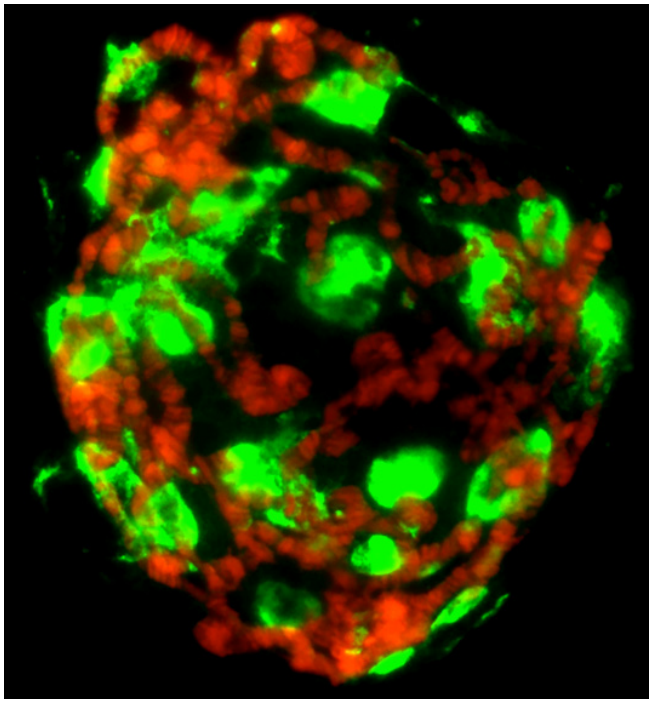

Figure. Localization of mutant TBX3 human proteins (green), associated with ulnar mammary syndrome, in Drosophila larval polytene chromosome formin distinct aggregates on chromosomes (red) doi. org/10.1002/jcp.31440.

Biological effects of low-dose/low-dose rate radiation and mechanisms of radioresistance.
G. Cenci research has also recently focused on the biological effects of low-dose/ low-dose rate radiation (LDR) exposure. His group discovered that prolonged LDR exposure in Drosophila, which induces increased expression of DNA damage response proteins, triggers a radioadaptive response (RAR) that protects against extensive DNA damage. Notably, several genes modulated in radioadapted Drosophila cells are also implicated in stemness regulation and encode Drosophila orthologs of human proteins (e.g., PACT, a member of the RISC complex) with established roles in CSC function and tumor progression. These findings suggest that studying Drosophila RAR could provide valuable insights into CSC radioresistance and its association with DNA damage response.

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Laura
Ciapponi
Associate Professor

ORCID

RESEARCH LINES

- Role of polyamine metabolism in DM2 pathogenesis
- Role of epigenetic regulation of TDP-43 in ALS pathogenesis
- Role of epigenetic dysregulation to the aetiology of primary microcephaly

STAFF | COLLABORATORS

Marta Terribili, *PhD Student (Sapienza)*
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Researcher (CNR-IBPM)
Sonia Coni, *Researcher (Sapienza)*
Gianluca Canettieri,
Full professor (Sapienza)

GRANTS

2023-2025- PRIN MUR code 2022M75NN8 - Dissection of common mechanisms in genetic primary microcephaly. co-PI
2023-2025- PRIN PNRR MUR code P2022S7H3H. Understanding the role of eIF5A and autophagy in Myotonic Dystrophy Type 2 pathogenesis. PI
2023-2026- Telethon 4389 - Understanding the role of CNBP-eIF5A-polyamine metabolism in DM2 pathogenesis. co-PI

RESEARCH ACTIVITY

I've been working with *Drosophila* melanogaster since 1997, when I started my postdoc at EMBL in Heidelberg. My switch to the Drosophila system was love at first sight, a deep and lasting passion that has stayed with me ever since. Even after all these years, my passion for this tiny fly and what it can teach us continues to grow stronger every day (Figure 1).

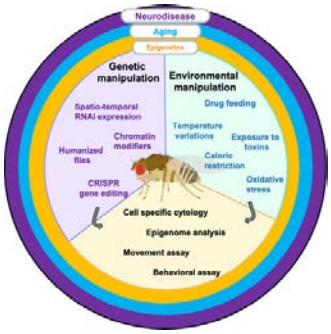

Figure 1. Schematic of genetic and environmental manipulations used in Drosophila models of neurodegeneration and aging. Genetic manipulations (purple) include RNAi knockdown, CRISPR-mediated gene editing, chromatin modification, and humanized transgenes. Environmental interventions (green) comprise drug administration, temperature shifts, caloric restriction, toxin exposure, and oxidative stress. The effects of these manipulations produce measurable phenotypes (yellow), can be assessed via cytological analyses, epigenomic profiling, locomotor assays, and behavioral tests etc.

Line 1. Myotonic Dystrophy Type 2 (DM2) is a genetic multisystemic disorder caused by a CCTG repeat expansion in the CNBP gene, primarily affecting skeletal muscle. We previously showed that loss of the Drosophila CNBP ortholog in muscle impairs polyamine metabolism, leading to locomotor defects. Remarkably, we found that polyamine metabolism is also altered in human DM2 muscle tissues. We are currently investigating whether the reduced CNBP–ODC–polyamine axis impairs muscle function by disrupting eIF5A-dependent translation of autophagy-related targets.

Line 2. Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disorder, characterized by degeneration of motor neurons, related to dysfunction of TDP-43 protein.
Studies in Drosophila and mice show that TDP-43 levels decline with age, leading to locomotor defects. We recently identified that this decline is due to epigenetic silencing of the TDP-43 encoding gene, driven by increased Su(var)3-9–mediated H3K9 methylation. We are using genetic and chemical methodologies to modulate both expression and activity of the Su(var)3-9 histone methyltransferase and analyse the effect on TDP-43 levels, motor neuron degeneration and associated motility phenotypes (Figure 2).

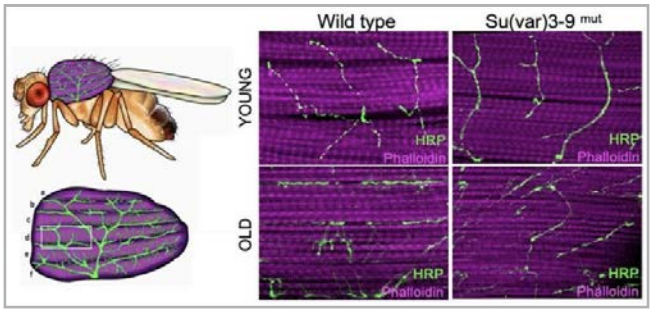

Figure 2. Loss of Su(var)3-9 methyltransferases reduces NMJ aging-dependent decline in Drosophila adult muscles.

Line 3. Primary microcephaly is an invalidating condition characterized by a reduced number of neurons, resulting from alterations of the delicate balance between proliferation, differentiation and death. In the developing brain, the proteins encoded by MCPH genes are required for maintaining genome stability, ensuring a precise temporal order of gene expression patterns and maintaining a correct balance in cell fate commitment. Using Drosophila as model system we are studying whether altered chromatin organization and abnormal transcription profiles are consequences of the reduced function of known MCPH genes, as compared to other genes that have not yet been involved as causal factors.

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Fulvio
Cruciani
Full Professor

ORCID

RESEARCH LINES

- Human population genetics
- Molecular evolution of sex chromosomes
- Forensic genetics

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GRANTS

2023 PRIN MUR. "Tracing North African population structure over time by whole-genome analysis of modern and ancient humans: a resource to understand the relationships between Europe, Africa, and the Levant". (PI, 205000 €)
2021 Regione Lazio. "Genetic analysis of foetal DNA circulating in maternal blood: development of a highly specific non-invasive paternity test". (PI, 150000 €)

RESEARCH ACTIVITY

My group is primarily focused on exploring various aspects of human genetic diversity and evolution. Our research encompasses three major areas: archaeogenetics, sex chromosome molecular evolution and forensic genetics.

Human population genetics. This is the longest-standing research line of our group, which has evolved in parallel with advances in molecular technologies and statistical methods for analyzing genetic diversity. Most of our early studies concentrated on Y chromosome variability, with particular focus on questions related to the origins of our species and migrations driven by cultural evolution and climate change in the African continent. More recently, we have begun analyzing high-coverage whole genomes to unveil past migrations related to the spread of the pastoralism in Africa and the Middle East (D'Atanasio et al. 2023). In collaboration with anthropologists and archaeologists from our institution, we are also conducting genomic analyses of ancient human remains from the Sahara Desert.

Molecular evolution of sex chromosomes. This research line focuses on the role of ectopic gene conversion in the evolution of sex chromosomes. We have shown that X-Y ectopic gene conversion is a widespread phenomenon in the male germline, contributing to the maintenance of sex chromosome integrity. We have also demonstrated that the arms of Y chromosome palindromes have reached a steady-state equilibrium between mutation and gene conversion (Bonito et al. 2021, 2023).

Forensic genetics. This is the most recent line of research developed by our group, aimed to evaluate how population structure and demography affect the discrimination power of rapidly mutating Y-STR used for identification purposes in forensic casework (Della Rocca et al. 2022; Barni et al. 2024). In collaboration with the Reparto di Investigazioni Scientifiche dei Carabinieri, and Eurofins Genoma, we are also currently investigating the application of novel DNP-based NGS panels for non-invasive prenatal paternity testing and for the deconvolution of severely unbalanced forensic DNA mixtures.

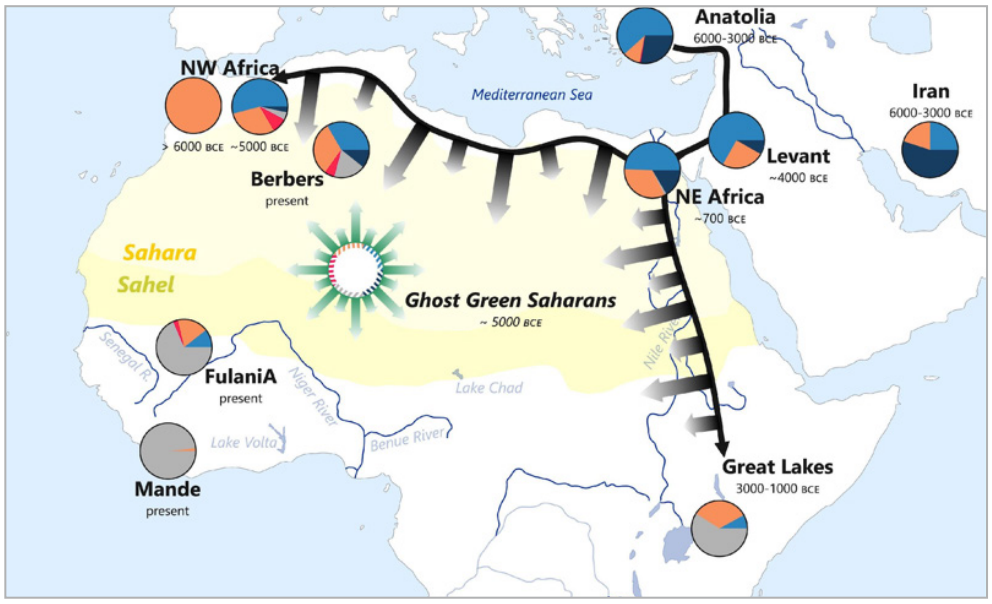

Figure: Movements of main non-sub-Saharan ancestry components in the Green Sahara 8,000–7,000 years BP and a possible scenario for the formation of the Green Saharan populations (from D'Atanasio et al. 2023).

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Laura
Fanti
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ORCID

RESEARCH LINES

- Formation and organization of heterochromatin
- Transposable elements, environmental stress and evolution
- Circadian rhythms, genomic instability and aging
- Epigenetic regulation of the centromere and telomere

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Maria Pia Bozzetti, *Assoc. Professor (University of Salento)*

RESEARCH ACTIVITY

Heterochromatin, transposable elements and evolution.
All my research lines focus on several aspects of the heterochromatic chromosomal domain, using Drosophila melanogaster as a model organism. Heterochromatic regions are mostly composed of repetitive DNA. Among the heterocromatic repetitive sequences, transposable elements (TEs) are relevant components. TE are mobile genetic elements able to jump to different locations along the chromosomes causing mutations. Although cells evolved mechanisms for TE silencing in all organisms, flies exposed to heat stress for some generations during metamorphosis have been shown to display morfological abnormalities (Fig. 1) when they become adults. These abnormalities can become heritable because they are caused by transposition events. The molecular mechanism underlying this phenomenon involves the heat-shock-inducible protein HSP70 and other chaperones, which cause TEs derepression and their transposition. For this reason TEs are considered a motor of evolution capable of inducing genetic variability in populations when strong environmental changes require rapid adaptation of organisms. We are currently studying the involvement of transposons in the adaptations of Drosophila populations and various Drosophila species (1).

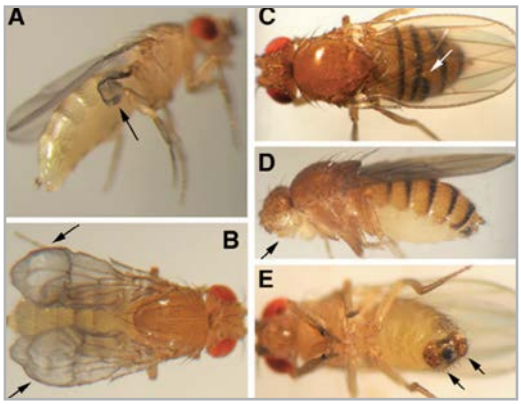

Figure 1. Morphological abnormalities in heat shocked flies.

Circadian rhythms, genomic instability and aging.
This research line focuses on the study of the function of the circadian clock on brain development and the effects of its dysfunction. Recently, we observed that the absence of a functional circadian clock, due to mutations in some of its components, leads to increased genotoxic stress in third-instar larvae compared to controls. This induces double-stranded DNA breaks in the central nervous system and chromosomal aberrations in dividing neuronal precursor cells. Furthermore, the absence of some clock components may result in less condensed chromatin, contributing to DNA damage (2). We are currently studying the effects of circadian clock dysfunction on the adult brain, also in relation to metabolism and aging.

Epigenetic regulation of the centromere.
In recent years, we have shown that some of the Trx-G proteins responsible for maintaining the active state of genes through epigenetic mechanisms, are associated with the centromeric regions. In particular, they are important for the deposition of the CENP-A protein (Fig. 2), a centromeric chromatin-specific histone H3 variant (3).
We are currently studying the epigenetic regulation of the centromere and the effects of stress on its stability and function.

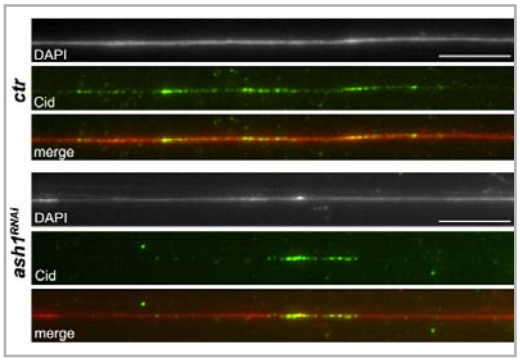

Figure 2. Extended chromatin fibers from larval brains colored with DAPI (red) and immunostained with antibodies against CENP-A (green), from wild-type and Ash1mutant.

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Simona
Giunta
Associate Professor

ORCID

RESEARCH LINES

- Human Centromere Biology
- Repetitive DNA in Human Primary and Cancer Cell Lines
- Genome Stability, Checkpoints & Repair Pathways
- DNA and Chromosome Structure

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Luca Corda, *Ph.D. Student (Sapienza)*
Elena Di Tommaso, *Ph.D. Student (Sapienza)*
Alessia Spurio, *Ph.D. Student (Sapienza)*

GRANTS

ERC-2022-STG
Centrofun 2024-09 to 2029-12.
EUR 1,500,000 PI Simona Giunta .
AIRC StartUp
Investigating the basis of cancer and aging-associated centromere instability in human cells 2020-01 to 2025-12. EUR 1,000,00
PI Simona Giunta .

Giunta Lab Website

RESEARCH ACTIVITY

More than half of our genome is made of repetitive DNA. Long referred to as "junk", many of these regions carry out important functions in our cells. Especially, repetitive DNA at centromeres holds a fundamental paradox: how is this fast-evolving locus maintained stable to perform its essential and conserved function in chromosome segregation? In the Giunta Lab, we investigate different aspects of centromeres spanning three major areas: genomics, DNA mutagenesis, and chromosome dynamics. We use cellular, molecular and structural biology approaches, integrated with cutting edge genomics to bring light into this essential region of the human genome with particular emphasis in understanding why centromeres are mutating rapidly and how these changes can contribute to tumorigenesis, aging and human diseases.

Line 1. Centromere genomics. While we celebrated the completion of the human genome project 20 years ago, our DNA still contains large gaps that lack annotation. Human centromeres are defined as "dark regions" in our DNA, representing one of the biggest challenges in completing the genome assembly. We were one of the first laboratories worldwide to assemble a diploid human reference genome including centromeres of all chromosomes (Volpe et al., 2023). The RPE1v1.1 reference enables innovative CRISPR-based/genome engineering approaches to uncover mutational signatures and centromere pathological variants.

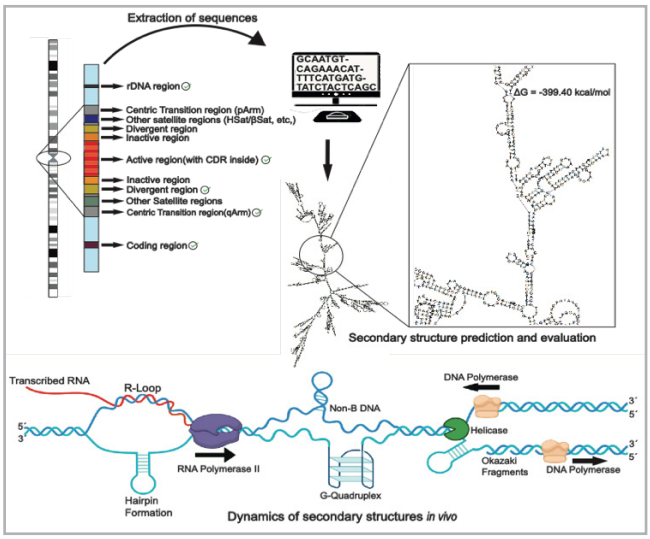

Figure. Diagram of selected human repeats along the chromosome that are sequenced and computationally analysed to understand formation of secondary structures and other dynamic processes causing disease-associated changes in DNA, consequences at cellular/organismal level (Chittoor & Giunta, 2024), with ensuing cancer-like chromosome defects occurring in the following cell cycle (Giunta et al., 2021).

Line 2. Centromere Stability, Maintenance, and Repair. We put forward the concept that human centromeres are inherently unstable due to converging vulnerable features commonly associated with fragile sites, such as: (1) active transcription of long non-coding centromeric RNAS (lnc-cenRNAs); (2) late replication (Giunta et al., 2021); (3) active mitotic recombination resulting in unequal sister chromatids exchange (Giunta & Funabiki 2017); and (4) secondary structures (Chittoor & Giunta, 2024). Our research currently aims to tease apart mutagenic processes and the network of factors protecting repetitive DNA from instability using bioinformatic and experimental approaches.

Line 3. Chromosomes structure-function relationship. How do changes in DNA translate in alterations in chromosome structure and behavior? We have discovered a conserved DNA barcode within centromeres specific to each chromosome (Corda & Giunta, 2025) that enables rapid classification of centromere sequence and architecture. Together with super-resolution imaging like 3D-Structural Illumination and Expansion Microscopy to image centromeric DNA and its constituents under multiple conditions of stress (Di Tommaso & Giunta, 2024; Di Tommaso et al, 2023), we plan to expand our work to genotype-to-phenotype association studies in large cohorts with our international collaborators at Genomics England, The Rockefeller University (NYC), and across the globe.

References

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2. "The complete diploid reference genome of RPE-1 identifies human phased epigenetic landscapes" E Volpe, L Corda, E Di Tommaso, F Pelliccia, R Ottalevi, D Licastro, A Guarracino, M Capulli, G Formenti, E Tassone, S Giunta, bioRxiv (2023) 2023.11.01.565049 doi: https://doi.org/10.1101/2023.11.01.565049
3. "Comparative analysis of predicted DNA secondary structures infers complex human centromere topology" Chittoor SS, S Giunta Am J Hum Genet. (2024) Dec 5;111(12):2707-2719. doi: 10.1016/j.ajhg.2024.10.016. Epub 2024 Nov 18. PMID: 39561771; PMCID: PMC11639080.

Lucia
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ORCID

RESEARCH LINES

- Transposable elements in stress response and genome evolution
- Transposable elements in age-related neurodegenerative diseases
- Epigenetic regulation of adult stem cell function

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Stefano Gustincich, *Full Professor (SISSA and IIT Genova)*
Sonia Manzo,
Senior Researcher (ENEA)

GRANTS

GD Tecnologie Interdisciplinari Farmaceutiche, Contratto Conto Terzi, "Studio dell'efficacia di composti bioattivi naturali nel contrastare il danno genotossico indotto dalle radiazioni UVC in Drosophila melanogaster". PI Lucia Piacentini

RESEARCH ACTIVITY

Transposable elements as environment-sensitive sources of genotypic and phenotypic variability. Transposable elements (TEs) are repetitive mobile genetic elements that represent a large fraction of most eukaryotic genomes and are known to have an important and global impact on genome evolution. TEs are potentially able to modulate host gene expression networks in response to specific environmental stresses thus triggering rapid adaptive phenotypic and genotypic responses. We demonstrated that TE activity can be modulated in response to different types of biotic and abiotic stresses and identified the Hsp70 chaperone as a key positive regulator of stress-induced transposon mobilization. These results shed new light on our understanding of evolutionary dynamics because they establish that the environment acts not only to select the most suitable physiological traits, but also as an inducer of genetic variability through TE activation. (Figure 1). We are currently investigating the molecular mechanisms that regulate the activation of TEs in response to different environmental stressors[1]. Our goal is to evaluate whether TE activation can serve as a sensitive and innovative endpoint for detecting environmental stress exposure, and to assess its integration into safety and risk assessments to improve the monitoring and management of environmental hazards.

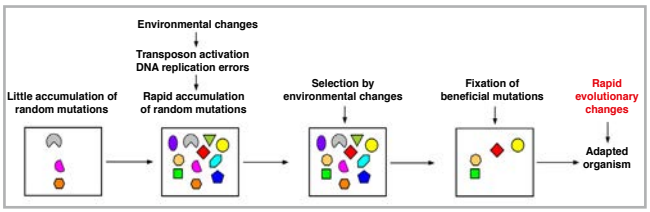

Figure 1. Stress induced transposon activation leads to rapid accumulation of random mutations, generating a new state of 'induced evolutionary plasticity' on which stress selection might act to establish more favorable mutations.

TE activity in neurodegenerative disorders.
Given the growing evidence of an association between unregulated TE activation and diseases of the nervous system, another major focus of the research is to investigate the molecular mechanisms through which TEs contribute to cellular toxicity in neurodegenerative diseases. In detail, we demonstrated that transposable element (TE) expression and mobilization are strongly increased in *Drosophila* models of Huntington's and Alzheimer's disease[2-3]. Notably, inhibiting TE mobilization with reverse transcriptase inhibitors (RTIs) rescues neurodegeneration, supporting the notion that TE activation contributes to neurotoxicity. We are currently investigating TE activation as a potential pharmacological target in neurodegenerative processes.

HP1: Guardian of Stem Cell Identity.
Our studies on Heterochromatin organization and function revealed that Heterochromatin Protein 1 (HP1), an evolutionarily conserved epigenetic adapter, known for its role in heterochromatin formation and gene silencing, also positively regulates gene expression by stabilizing RNA transcripts and protecting them from premature degradation. This novel and unanticipated role of HP1 in post-transcriptional regulation of gene expression allowed us to discover an unexpected function of HP1in maintaining the homeostasis of adult stem cells. We are currently studying the molecular mechanisms through which HP1 regulates the proliferation and differentiation of germline and neural stem cells (Figure 2).

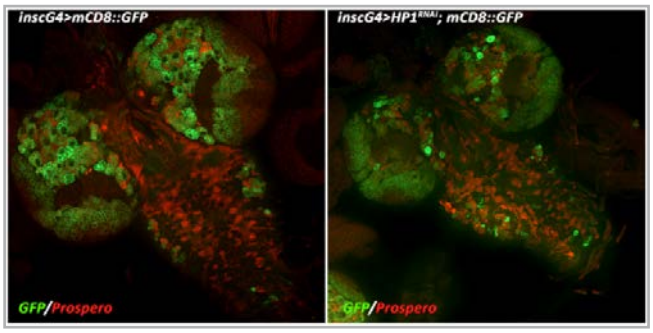

Figure 2. Functional inactivation of HP1 using the insc-Gal4 driver, which is specific for neuroblasts, results in severe neuroblast proliferation defects.

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Grazia Daniela
Raffa
Associate Professor

ORCID

RESEARCH LINES

- Exploring the role of snRNA deregulation, transcriptional stress and DNA damage in Spinal muscular atrophy (SMA)
- Mechanisms of telomere protection in the Drosophila embryo
- Regulation of telomerase and telomere homeostasis in human cells.

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Stefano Cacchione,
Associate Professor (Sapienza)
Maurizio Gatti,
Professor Emeritus (Sapienza)

GRANTS

AIRC-IG 26496 Relationships Between Transcriptional Stress, R-Loops Formation And Genome Instability In Drosophila and Humans. P.I. Grazia Daniela Raffa

RESEARCH ACTIVITY

Line 1. SMA is a severe neurodegenerative disease, characterized by defects in RNA splicing. We recently developed a Drosophila model to identify novel genetic interactors of SMN, the causative factor for SMA. We recently found that systemic depletion of Smn leads to accumulation of RNA:DNA hybrids (R-loops), increased DNA damage, dysregulation of amino acids and sugar metabolism and activation of the innate immune responsePersistent DNA damage in Smn-deficient flies alters cell proliferation rates in larval brains and induces extensive cell death in the developing eye. These phenotypes are rescued by increased expression of human RNAse H1 that stimulates the resolution of RNA:DNA hybrids, Our data suggest that depletion of Smn causes an accumulation of aberrant transcripts and chronic DNA damage, which—along with the altered metabolomic profiles associated with Smn deficiency—trigger systemic inflammatory responses, ultimately affecting neuronal function and survival. Our model recapitulates key pathological features reported in mammalian models and severe SMA patients.

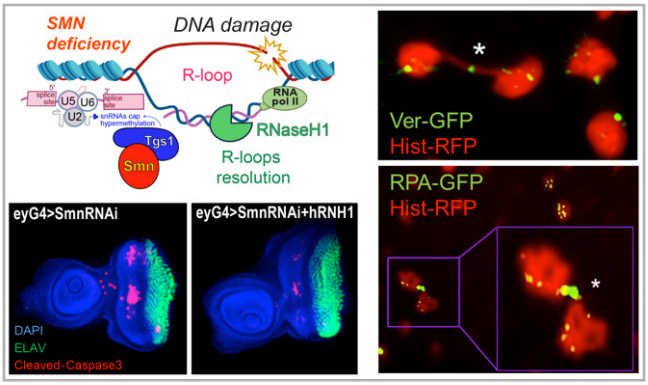

Figure. Left panel: Smn dysfunction disrupts splicing, induces DNA damage and cell death and aberrant morphogenesis in the developing eye. These phenotypes are rescued by reducing RNA:DNA hybrids, by RNaseH1. The two immunofluorescence panels on the left show examples of eye-antennal imaginal discs from Smn-depleted flies with and without overexpression of RNaseH1, which reduces apoptotic signals (Cleaved-Caspase-3) and restores correct photoreceptor development (labeled by ELAV) and defects in eye structure.
Right panels: Defective RNA surveillance pathways induce extensive telomere fusion and genome instability in Drosophila embryos. Still image of representative ana-telophases from time-lapse movies of mutant embryos, RNAi-depleted for two regulators of exosome-mediated retrotransposon degradation pathways and bearing fluorescent markers for histones (Hist-RFP) and telomeres (Ver-GFP) or damaged DNA (RPA-GFP). The asterisk marks a fusion region between two daughter nuclei, which are connected by a bridge. Damaged nuclei undergo asynchronous divisions and accumulate RPA foci, labeling, exposed ssDNA at telomeres.

Line 2. Drosophila telomeres are protected by the Terminin complex and elongated by specific retrotransposons. Terminin comprises rapidly evolving proteins HOAP/HipHop/Moi/Ver/Tea; deficiencies in these proteins lead to telomere fusions. Investigating de novo telomere establishment in embryos, where thousands of telomeres assemble rapidly, provides insights into distinct protection mechanisms in somatic and germline cells. Co-and post-transcriptional regulation of telomeric retrotransposon expression in the germline influences the quality and abundance of transcripts loaded into the embryo, associating with telomeric chromatin and providing a reservoir for telomere establishment during early development. Through in vivo analyses in syncytial blastoderm embryos, we investigate the consequences of depletion in components of the RNA surveillance machinery, which results in defective chromosome segregation, persistent anaphase bridges involving telomeres, robust RPA-associated DNA damage, and nuclear collapse/fusion, underscoring the crucial role of telomere transcripts during early development. Our data support a model wherein the accumulation of TERRA-like telomeric retrotransposon transcripts that evade degradation induces damage and stress, leading to chromosome entanglements involving telomeres. This sheds new light on the intergenerational control of telomere state and the intricate relationship between RNA quality control pathways and telomere assembly in the germline.

Line 3. We have found that one of the Terminin interactors, the TGS1 hypermethylase, is a negative regulator of telomerase activity and telomere length in human cells. We are currently investigating TGS1 inhibitors as potential therapeutic treatments for short-telomere syndromes. Italian patent 102020000012577 with international extensions. Pharmaceutical composition for the chemical inhibition of TGS1 in the therapeutic treatment of telomeropathies.http://www.uniroma1.it/sites/default/files/field_file_allegati/scheda_grafica_tt_340_raffa_en.pdf

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Isabella
Saggio
Full Professor

ORCID

RESEARCH LINES

- Stem cells and gene therapy
- Aging and mechanogenetics

STAFF | COLLABORATORS

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Domenico Flagiello,
Professor (Paris Cité)
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Professor (NTU, Singapore)

GRANTS

2023-26 National spoke coordinator and Sapienza spoke coordinator PNRR CN5-National Biodiversity Future Center. Role PI
2023-2026 Ministry of Health Singapore, National Innovation Challenge (NIC) Role: PI
2020-25 AIRC Five Year Investigator Grant Role PI

www.saggiolab.com

RESEARCH ACTIVITY

Gene and stem cell therapy. During the association with the laboratories of San Raffaele Science Park, I. Saggio has been involved in the study of stem cells and contributed to unravel the characterization of stem cell progenitors as organizers of the hematopoietic microenvironment (Sacchetti et al Cell 2007; Sacchetti et al Stem cell reports 2016). In addition, I. Saggio laboratory has experience in vectors for gene and cell therapies, including lentiviral, adenoviral and humanized phages (patented WO 02/24934). I. Saggio developed growth factor antagonists and expressed them with adenoviral vectors as proof of principle studies of disease customized gene therapy (Saggio et al Gene therapy 1997; Di Marco et al PNAS 1996; and patent on viral vectors WO 98/13383).

Aging and mechanogenetics. I. Saggio identified the first human telomere-associated factor linked with the nuclear envelope. Telomere dysfunction causes genome instability and is a driver of cancer and premature aging (Burla et al Plos Genetics 2015; Cenci et al Plos Genetics 2015; Burla et al Open Biology 2016; La Torre et al Aging Cell 2018, Chen et al. Cell Reports 2019). Building on the link between telomeres and the nuclear envelope, I. Saggio developed new research focusing on the implication of nuclear integrity in aging and cancer. The model systems used by I. Saggio are mammalian cells and mice. In addition, comparative studies were performed in D. melanogaster. Research by I. Saggio and the work of her group have been recognized internationally and she has been funded, as PI, based on open competition and peer reviewing, by national and international agencies, including Telethon, the Progeria Research Foundation USA and AIRC. In a trans-kingdom perspective, our most recent program focuses on a comparative study in plants and mammals to identify common and possibly transplantable genes controlling aging and life-span.

Science and society. I. Saggio is responsible for the spoke Science and society of the national PNRR NBFC center and for the Master in One health and of Science journalism. She published two books dedicated to science and society. In 2025 curated a national exhibition at Palazzo delle Esposizioni, now becoming virtual in a project named Bioverse presented at Expo 2025 in Osaka.

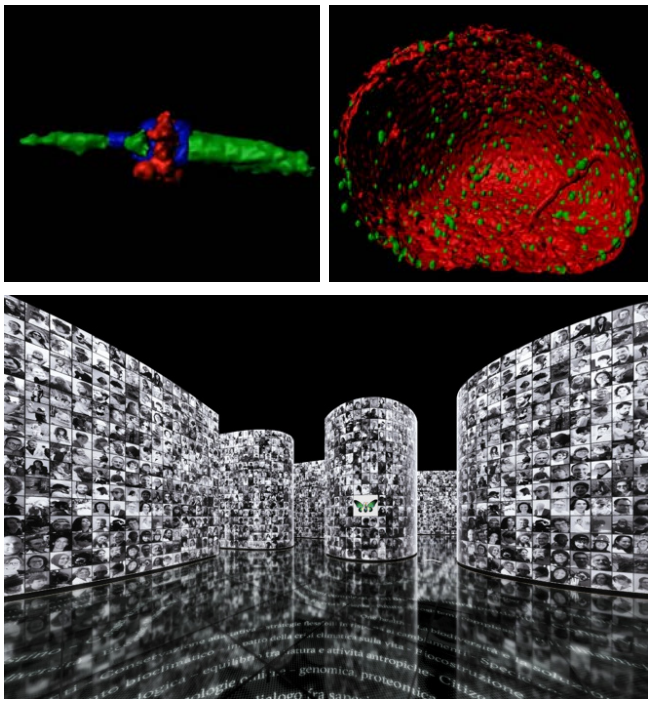

Figure. Upper left: SuperResolution midbody (green tubulin, red AKTIP, blue IST1). Upper right: AKTIP (green) at the nuclear envelope. Bottom: From Bioverse -the scientific world of researchers.

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Beniamino
Trombetta
Associate Professor

ORCID

RESEARCH LINES

- Archeaogenomics
- Genomics of conservation
- Bioinformatics

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Mario Ventura,
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Elisabetta Scungio,
Director of DRM-Lazio (MiC)

GRANTS

PRIN 2022. Telomere-to-telomere sequencing: the new era of Centromere and neocentromere eVolution (CenVolution).
CO-PI

RESEARCH ACTIVITY

I have always worked in the field of population and computational genomics. My lines of research branch out in three main directions.

Line 1. My work braids ancient DNA into the story of Mediterranean archaeology, letting long-silent skeletons speak. I led the first full genomic portrait of the Picene culture, sequencing more than 100 individuals spanning nearly a thousand years; the data reveal a common ancestry among Iron-Age Italic communities, demonstrate that Iron Age was a cosmopolitan era and show how Roman expansion reshaped Italic genetics. A companion study of a late-Republican–period burial pushes the arrival of Near-Eastern ancestry in central Italy back by two centuries. Now, I am mapping the Ionian arc, extracting DNA from roughly 500 Greek and indigenous graves to reconstruct the genetic dialogue between Greeks and local peoples within Magna Graecia. Every project is run with the Italian Ministry of Culture: museums and superintendencies provide the remains and receive in return phenotypic reconstructions and public-engagement events that transform DNA data into clear, compelling stories for visitors.

Line 2. I also focus on conservation genomics, developing tools that underpin concrete strategies for protecting biodiversity. I study the genetic diversity of the Asiatic lion. Our data show how much genetic variation they have lost and provide DNA markers that help with forensic tracking. I have also analysed the DNA of lions excavated from the Colosseum, fusing those ancient genomes with modern datasets to pinpoint the homelands of the lions that once roared in Rome's arena. I apply the same high-resolution approach to orangutans. By marrying long-read sequencing and tight partnerships with zoos and biobanks, I generate the critical evidence base for reintroduction plans, genetic management, and the fight against wildlife trafficking—pushing back against the global tide of biodiversity loss.

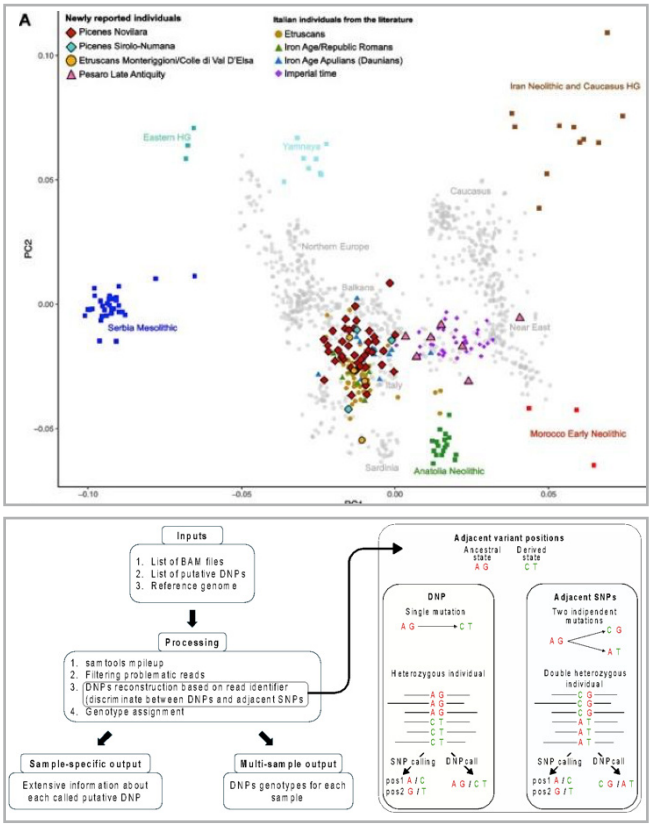

Figure. Upper panel: Population structure of the Italic Iron Age and Late Antiquity period. Lower panel: schematic representation of DNPcall workflow.

Line 3. This line of research is grounded in bioinformatics to crack the human genome's hardest puzzles. I used customized pipelines to analyse segmental duplications, regions where short NGS reads cannot be uniquely mapped. We have developed new tools, including DNPcall, a script that analyze DNPs and delivers reliable genotypes even from limited data. In ancient-DNA contexts we perform imputation of ultra-low-coverage genomes, recovering more than 80 % of markers for kinship analysis and phenotypic trait inference. All my tools are modular, open-source, and reused to tackle new challenges, from forensic genetics to demographic modelling.

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Fiammetta
Vernì
Researcher

ORCID

RESEARCH LINES

- Vitamin B6 deficiency in Cancer Onset and Progression
- Tumor Suppressor Role of Serine hydroxymethyltransferase (SHMT)

STAFF | COLLABORATORS

Giulia Tesoriere,
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Full professor (Sapienza)
Angela Tramonti,
Researcher (CNR/IBPM)
Cinzia Volonté, *Research Director (CNR, Fondazione Santa Lucia)*

RESEARCH ACTIVITY

Our research explores the link between vitamin B6 deficiency and cancer, using Drosophila as a model. While primary B6 deficiency is rare in developed countries due to its widespread presence in food, secondary deficiencies are associated with various conditions including diabetes, malabsorption syndromes, renal diseases, pregnancy, and alcoholism. Furthermore, certain common medications, such as antidepressants and antibiotics, can induce B6 deficiency. Vitamin B6 possesses antioxidant properties, and its active form, pyridoxal 5'-phosphate (PLP), acts as a crucial cofactor for numerous metabolic enzymes (1). Notably, PLP is essential for serine hydroxymethyltransferase (SHMT), an enzyme vital for supplying cells with DNA precursors. Although epidemiological and intervention studies have inversely correlated vitamin B6 intake with cancer risk, particularly colon cancer, the underlying molecular mechanisms remain largely unclear. Our previous work demonstrated that PLP deficiency induces chromosomal aberrations in Drosophila. We also uncovered a significant gene-nutrient interaction between SHMT and vitamin B6 that impacts genome stability (2). Given the strong link between DNA damage and cancer, we started from these findings to investigate the relationship between PLP, DNA damage, and cancer using various Drosophila cancer models, aiming to elucidate the precise molecular mechanisms involved.

The #1 research line investigates the role of PLP depletion in cancer initiation and progression. We recently showed that PLP deficiency increases the risk of cancer onset and progression in Drosophila models of eye imaginal disc cancer (Ras^{V12} and $Ras^{V12}Dlg^{RNAi}$) (3). Crucially, we established a cause-effect relationship between DNA damage and cancer phenotypes in these models and demonstrated that low PLP levels enhance genome instability by both reducing cellular antioxidant defenses and decreasing SHMT activity. We are currently developing a Drosophila colon cancer model to further explore the role of B6 deficiency in relation to Apc and RasV12 genes, with the goal of identifying implicated pathways.

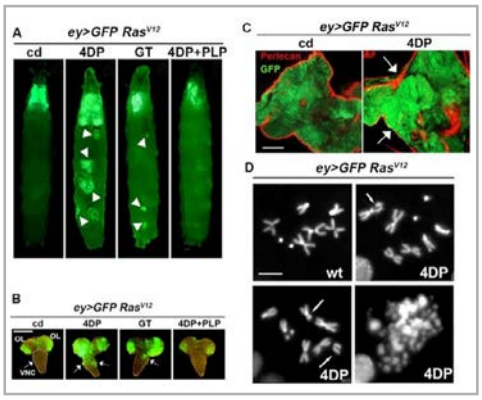

Figure. Vitamin B6 deficiency transforms Ras^{V12} benign cancers in aggressive forms (adapted from (3)). A Examples of larvae with GFP-labeled tumors caused by two PLP antagonists: 4DP=4 deoxypyridoxine and GT=ginkgotoxin. cd=control diet. B Examples of secondary tumors occurring on the ventral nerve cord (VNC) of brain. C 4DP causes gaps in the basement membrane (BM) through which cells spread. α-Perlecan is an antibody which stains the BM. D Examples of chromosome aberrations in eye disc cells from 4DP-treated Ras^{V12} larvae.

The #2 research line focuses on the tumor suppressor role of SHMT and its underlying mechanisms. We are investigating how SHMT depletion, induced by RNA interference, influences the metastatic potential of RasV12DlgRNAi tumors. Concurrently, we are exploring whether the gene-nutrient interaction between PLP and SHMT influences this cancer model. Discovering such gene-nutrient interactions in cancer could open new avenues for personalized nutrition strategies aimed at enhancing health and preventing disease.

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“SAN LORENZO”

The RM024 building is a former brewery built at the beginning of the 20th century in the heart of Rome’s San Lorenzo district. It was first known as the Paszkowsky and later as the Wuhrer building. Like many of the former factory buildings nearby (Vetreria Sciarra, ufficio direzionale delle poste, etc), it was acquired by Sapienza University to face the huge increase in the student number during the years.

Today, the building hosts three University Departments and several research groups from CNR-IBPM (Institute of Molecular Medicine and Pathology) in the framework of an agreement to constitute a joint research collaborative structure between Sapienza and CNR. A section of the Department of Biology and Biotechnologies is located on floors 1, 2 and 3 of the building, where many research groups are studying biological processes in a variety of model organisms. Virology, Immunology, Microbiology, Genetics, Neurobiology, Plant Biology, Epigenetics and RNA metabolism are among the research topics.

On the third floor are three laboratories (Microbiology, Molecular Biology and Cellular Biology) which are considered among the best equipped in Sapienza and are used for practical work training by a large number of students from many different academic Courses.

In collaboration with CNR, which shares a part of the laboratories, the building hosts a “State of the Art” Microscopy Center, inserted in the Microscopy Network of National Interest, that is heavily used by many research groups of Sapienza. Other noteworthy technological infrastructures available in the building include: a transcriptomic platform equipped with a digital PCR (Qiagen) and a hybridization facility (Agilent); a proteomics facility equipped with an FT-Orbitrap mass analyzer; chemidoc; cytofluorimeters; temperature-controlled growth chambers for bacteria and various model organisms; and temperature and light-cycle controlling phytotrons.

A small library is located on the first floor. And a classroom on the second floor is dedicated to the memory of Franco Tatò, an unforgettable brilliant microbiologist.

Nadia Andrea
Andreani
Researcher Tenure Track

ORCID

RESEARCH LINES

- Gut-brain interaction in Anorexia Nervosa
- Microbial adaptation to Inflammation
- Microbiome in health and Disease

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Giulia Matusali, *Researcher Tenure Track (Sapienza)*
John Baines, *Full Professor (Max Planck Institute for Evolutionary Biology and CAU Kiel)*
Jochen Seitz, *Professor (LVR-Klinikum Essen)*
Beate Herpertz-Dahlmann, *Professor (RWTH Aachen)*

RESEARCH ACTIVITY

A unifying theme of research in my lab is to understand how the microbiome contributes to human health and disease, with a particular focus on conditions involving the gut-brain axis and chronic inflammation. The gut microbiota exerts a profound influence on host physiology through its metabolic outputs and immune modulation. My lab explores how microbial functions evolve or become disrupted under extreme physiological conditions, and how this can shape disease trajectories.

A major research line focuses on Anorexia Nervosa (AN), a psychiatric condition increasingly linked to gut microbiota alterations. Within the framework of the MIGBAN consortium (https://www.neuron-eranet.eu/projects/MiGBAN/), we analyze longitudinal and cross-sectional microbiome datasets from patients with AN and healthy controls to identify microbial taxa and functions associated with the disorder. In parallel, we collaborate with scientists at Université de Rouen, RWTH Aachen and UMC Utrecht to apply animal models to investigate the impact of microbial changes on behavior and physiology. Our results confirm the presence of gut dysbiosis in AN, a trend to normalization after weight gain, as well as the presence of taxa with prognostic value that could inform on disease duration and long-term BMI.

A second major line of research investigates Inflammatory Bowel Disease (IBD), where we explore how bacteria adapt during chronic gut inflammation. We apply experimental evolution in-vivo to track genetic changes in commensal strains exposed to inflammatory environments. This study aims to uncover evolutionary strategies that bacteria adopt to persist during inflammation with the aim of developing alternative therapies for IBD, based on evolutionary medicine.

Beyond AN and IBD, I am also interested in the role of the microbiome in other disorders, including other psychiatric and systemic conditions where microbial signaling might play a yet-unrecognized role. My research combines bioinformatic analysis of microbial genomes, metagenomes, and transcriptomes with molecular biology approaches, including strain engineering, in vitro models, and functional assays.

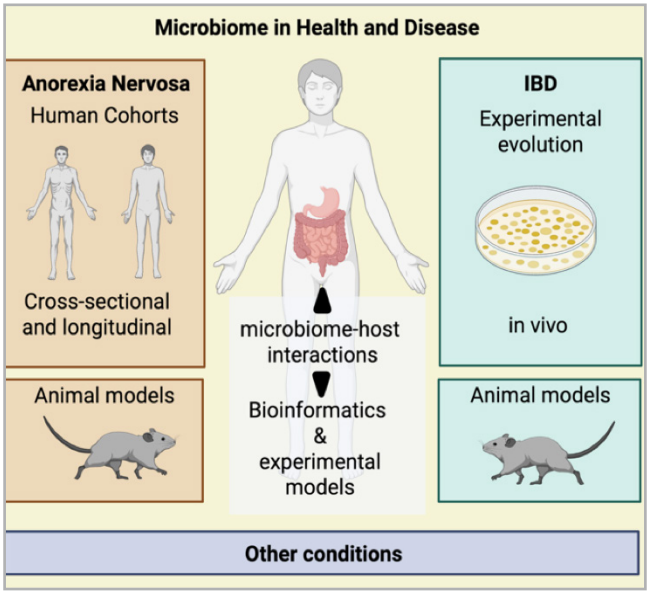

Figure. ***Overview of research lines exploring the role of the microbiome in health and disease.***
Studies on Anorexia Nervosa include cross-sectional and longitudinal analyses in human cohorts as well as animal models. Research on Inflammatory Bowel Disease involves in vivo models and experimental evolution approaches. At the core, bioinformatics and experimental tools are applied to investigate microbiome–host interactions.

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Fiorentina
Ascenzioni
Full Professor

ORCID

RESEARCH LINES

- Molecular mechanisms of antibiotic resistance and identification of drugs that inhibit resistance.
- Biofilms as targets for the selection of antimicrobial drugs.
- Microbicidal mechanisms of phagocytes and the bacterial defense pathways in macrophage and Pseudomonas aeruginosa interaction.

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GRANTS

Fighting antibiotic resistance by exploiting innovative strategies and targets. PI, F. Ascenzioni. Funded by Sapienza, big projects 2023.

RESEARCH ACTIVITY

Multidrug-resistant (MDR) Gram-negative bacteria pose a significant global health challenge as their infections are associated with high rates of morbidity and mortality, extended hospital stays, and increased healthcare costs. Colistin is a last-resort antibiotic against multidrug-resistant Gram-negative bacteria. However, resistance to colistin is spreading and increases the risk that this antibiotic will rapidly become ineffective. Colistin resistance rely on modification of the lipid A component of the outer membrane, which is the target of colistin. In Pseudomonas aeruginosa this is mainly determined by the arn operon, whose last enzyme, the transferase ArnT, mediates the addition of 4-Amino-4-deoxy-l-arabinose to the lipid A. Our group, have identified a natural ent-beyerene diterpene, named FDO, as an ArnT inhibitor, which potentiate colistin activity not only against colistin-resistant Pseudomonas aeruginosa, but also against Klebsiella pneumoniae. Based on this we are now working to simplify the ent-beyerene scaffold up to drug-like synthetic ArnT inhibitors (figure 1). Additionally, as the ArnT inhibitors we have identified are characterized by poor solubility, we are working to the development of nano-vehicle for the co-delivery of colistin and its adjuvant. Bacteria within biofilms appear more tolerant to antibiotics, including colistin, possibly due to protection of the bacteria by the extracellular matrix and low bacterial metabolism. Thus, we are studying the molecular mechanisms involved in the biofilm tolerance to colistin with the final goal to inhibit tolerance and improve colistin activity against P. aeruginosa biofilms.
Cystic Fibrosis, the most common life-limiting genetic disease, is caused by mutations in the CFTR gene, which very recently has been targeted by drugs, the CFTR modulators, that have been designed to recover defective CFTR activity in CF subjects. Based on our previous work leading to the identification of defective microbicidal activity in human macrophages from CF patients against P. aeruginosa, we are now studying the recovery of the microbicidal defects of these cells, in CF subjects in therapy with the CFTR modulators. Our objective is to understand whether CF phagocytic cells are corrected by the CFTR modulators, similarly to airways epithelial cells, the main target of CFTR modulators. We are also investigating the molecular mechanisms involved in the defective microbicidal activity of CF phagocytes against P. aeruginosa.

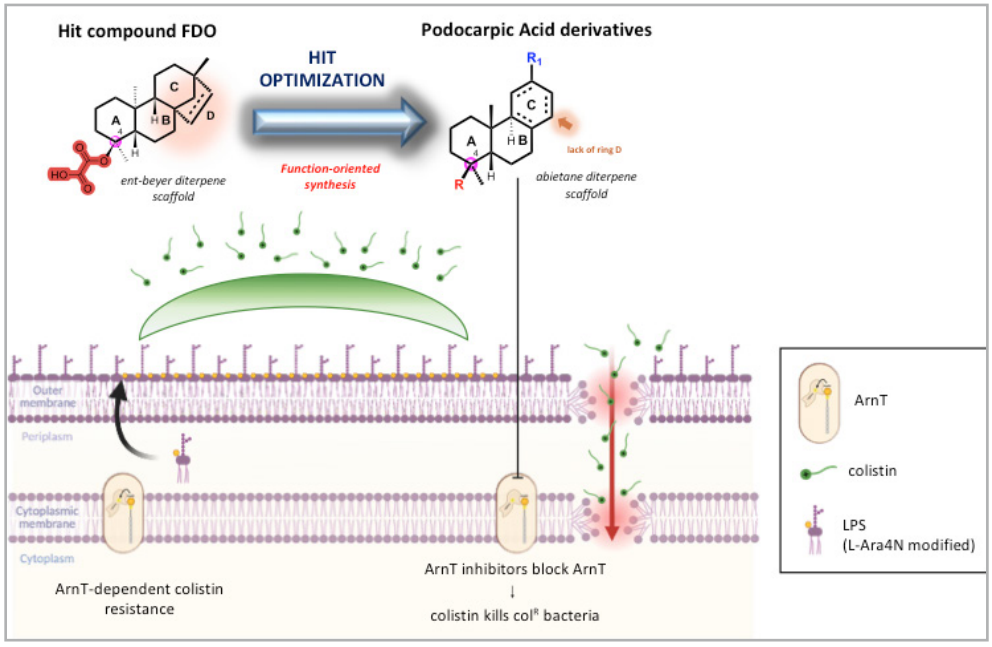

Figure. Schematic representation of the colistin resistance mechanism in P. aeruginosa and the activity of the colistin potentiators, FDO or podocarpic acid derivatives.

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Bianca
Colonna
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ORCID

RESEARCH LINES

- Regulation of MDR efflux pumps in response to intracellular stimuli
- Molecular events in the evolution of Shigella

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GRANTS

MIUR-PRIN 2022 (2022FN 7ANE)

RESEARCH ACTIVITY

Regulation of MDR efflux pumps in response to intracellular stimuli. Efflux pumps (EPs) represent an important and large group of transporter proteins found in all organisms. The importance of efflux pumps resides in their ability to extrude a wide range of antibiotics, resulting in the emergence of multidrug resistance (MDR) in many bacteria. MDR EPs are able to export a large variety of molecules and are emerging as relevant elements in interactions with other bacteria and with plant or animal cells. We have recently analysed the contribution of MDR EPs during the intracellular life of two groups of pathogenic E. coli, Shigella and Ad herent Invasive E. coli (AIEC), characterized by their ability to invade the host cells. The results indicate that the expression of MDR EPs is differentially modulated during the intracellular life of the bacterium and that the MFS-type EmrKY efflux pump of Shigella and the RND-type Md tEF efflux pump of AIEC contribute significantly to bacterial survival in the harsh macrophage environment. Currently we are addressing the following issues: how relevant are MDR EPs for the intracellular life of Shigella and AIEC in epithelial cells? Which regulatory networks allow the activation of specific MDR efflux pumps in response to intracellular environments?

Molecular events in the evolution of *Shigella*. It is well known that Escherichia coli is not only a harmless commensal of the human and animal intestine but also a major cause of morbidity and mortality. The evolution of E. coli towards pathogenic phenotypes has been determined, as in many other bacterial pathogens, mainly by two mechanisms: the acquisition of virulence genes by horizontal gene transfer as parts of plasmids, phages or pathogencity islands, and the silencing of genes of the core genome. In Shigella, currently regarded as an invasive pathogenic E.coli, the critical event towards a pathogenic life-style has been the acquisition a large plasmid (pINV) containing the genes required for inva sion, intracellular survival and spreading through the intestinal mucosa. The ample gain in virulence determinants has been counteracted by a substantial loss of functions that, al though important for the survival in the environment, are redundant or even deleterious for survival inside the host. We have contributed to the characterization of novel antivirulence loci mainly related to the polyamine metabolism (cad, speG). Currently we are investigating whether other housekeeping genes of Shigella have been disrupted or lost to increase the bacterial fitness in the host.

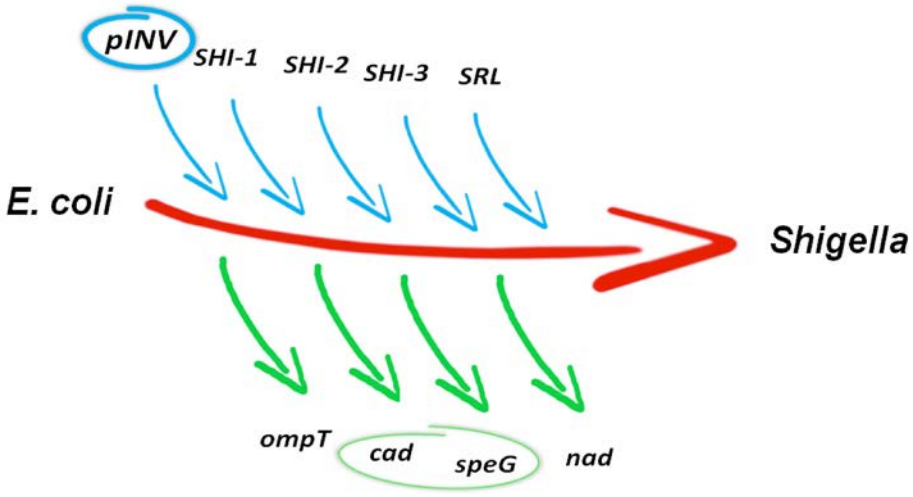

Figure. Genetic events contributing to the evolution of Shigella from ancestral commensal E. coli. The acquisition of the virulence plasmid (pINV) by horizontal gene transfer is a major evolutionary event towards pathogenicity. This has been flanked by the acquisition of the SHI-1, SHI2, SHI 3, and SRL pathogenicity islands. The loss of the antivirulence genes ompT, nad, cad, and speG has contributed to the optimization of the virulent phenotype.

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Giulia
De Lorenzo
Full Professor

ORCID

RESEARCH LINES

- The interplay between plant immune and developmental processes orchestrated by cell wall-derived Damage-Associated Molecular Patterns (DAMPs).
- Homeostasis of cell-wall derived DAMPs.
- Receptor-mediated perception and signaling specificity of CW-DAMPs
- Role of H_2O_2 generated by oligogalacturonide oxidases (OGOXs) in long-distance signaling.
- Regulation of the production of immune-active oligogalacturonides by the complex polygalacturonase-PGIP.

STAFF | COLLABORATORS

Sarah Giulietti, *Post-doc (Sapienza)*
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Benedetta Mattei,
Full Professor (Università dell'Aquila)
Alice Y. Cheung, *Full Professor (University of Massachusetts, USA)*
Carlos Labate, *Full Professor (University of Saõ Paulo, Brazil)*

GRANTS

SiGaW: Plant tissue damage: SIgnalling Gunshots And Waves for Immunity (PRIN2022). PI: Prof. Giulia De Lorenzo

RESEARCH ACTIVITY

Plants activate immunity when challenged by microbes or mechanical damage, primarily through the perception of microbe associated molecular patterns (MAMPs) and damage associated molecular patterns (DAMPs). Mounting this defense often exacts a cost on growth. Many potent DAMPs are cell wall derived oligosaccharides released during pathogen attack—for example oligogalacturonides (OGs) from homogalacturonan and cellodextrins (CDs) from cellulose. Our work focuses on maintaining homeostatic levels of these cell wall DAMPs to avoid chronic immune activation.

We study two FAD dependent oxidases—oligogalacturonide oxidase (OGOX) and cellodextrin oxidase (CELLOX)—members of the berberine bridge enzyme like (BBEl) family. By oxidizing OGs and CDs, these enzymes simultaneously attenuate elicitor activity and generate hydrogen peroxide (H_2O_2), thereby fine tuning immune signaling. We dissect the molecular pathways by which OGs and CDs mediate the growth defense trade off, aiming to identify key signaling components and downstream effectors. To elucidate OG perception, we investigate MAPKKKs of the ANP subfamily and the plasma membrane H_2O_2 sensor HPCA1. To probe OG action in planta, we engineered transgenic "OG machine" lines that inducibly release OGs, enabling direct assessment of their impact on growth and cellular functions. Crossing these lines with hormone signaling or immunity mutants allows us to decouple defense activation from growth inhibition, offering routes to disease resistance without a growth penalty.

OGs act as pleiotropic signals whose outcomes depend on concentration, oligomer length, tissue context, and timing. They trigger pattern triggered immunity (PTI) in a size dependent fashion and antagonize auxin mediated development. We explore how receptor specificity is integrated via the FERONIA–RALF–LLG1 receptor complex and how plasma membrane dynamics and endocytosis modulate DAMP signaling. We also study H_2O_2 generated by OG oxidation as a mobile signal that primes distal tissues, focusing on long distance communication by reactive oxygen species.

Finally, we examine polygalacturonase inhibiting proteins (PGIPs) that bind pathogen secreted polygalacturonases (PGs). The resulting PGIP–PG complex not only curbs virulence but divert PG activity toward producing long, immunostimulatory OGs at the expense of short, immunosuppressive fragments. During infection, this interaction forms a unique dimeric enzyme that favors defense active DAMPs; whether a similar complex arises during development remains unknown. Understanding this mechanism offers avenues to engineer PGIPs with expanded specificity, converting pathogen tools into defense assets.

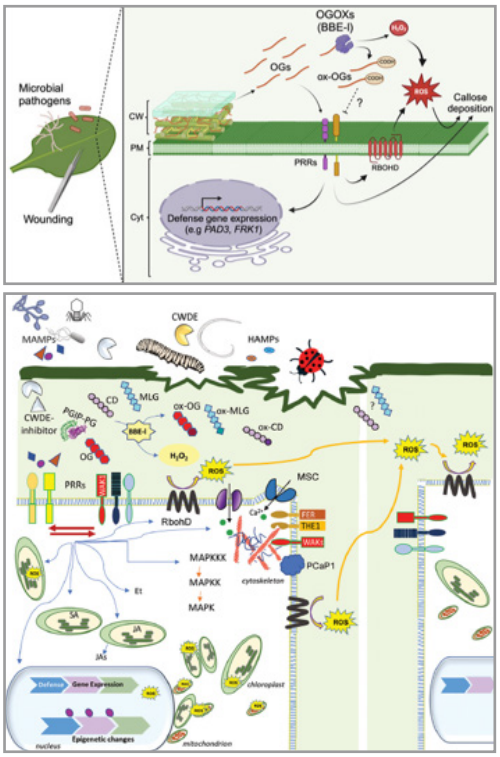

Figure. Upper panel: Model of OGOX action on local response following wounding or pathogen attack (Salvati et al, 2025. Plant J, 122: e70150) Lower panel: Cell wall-derived DAMPs: mediators of local and systemic immunity (modified from De Lorenzo & Cervone, 2022 Essays Biochem; 66(5): 459–469).

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Raffaele
Dello Ioio
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ORCID

RESEARCH LINES

- Formative Divisions
- Evolution and Development
- Plant Science and Bioengineering
- Stem cells

STAFF | COLLABORATORS

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GRANTS

HORIZON-CL6-2023-ZEROPOLLUTION-01 (Clean environment and zero pollution), unit coordinator. Monitoring and detection of biotic and abiotic pollutants by electronic, plants and microorganisms based sensors.
MOON-RICE. Cereal crop production for future planetary bases AGREEMENT SAPIENZA-ASI (Italian Space Agency), Prime, Scientific Coordinator.
MAECI-ASI. Green Recycling of Wastewaters through Cuttingedge Microalgae and Plant Cultivation Systems in Extreme Environments -Co-PI.
PRIN 2022. Root cortical variability among plants: the route to interspecific patterning diversity.

RESEARCH ACTIVITY

Our general interest lies in uncovering the molecular mechanisms underlying anatomical diversity among plant species. A classic example of this diversity is the variation in the number of root cortical layers, which can range from one to several, depending on the species. The cortex is one of the key root tissues contributing to the plant's adaptive potential.
For instance, in species adapted to waterlogged soils, such as rice, secondary cortical growth gives rise to aerenchyma—a tissue that regulates the air-to-water ratio. Conversely, in plants growing under harsh environmental conditions, like turnip, the cortex develops into storage parenchyma, a tissue specialized in carbohydrate storage, particularly starch.
Understanding the molecular and genetic basis of cortical layer number variation has both conceptual and biotechnological implications. Conceptually, this system provides an excellent model for studying the genetic mechanisms responsible for the emergence of functional, morphological, and anatomical traits. From a biotechnological perspective, manipulating the number of cortical layers may enhance crop performance in adverse environments.
To investigate these mechanisms, our group adopts a comparative developmental approach focused on root development in Arabidopsis thaliana—a model organism with a single cortical layer—and its close relative Cardamine hirsuta, which develops two cortical layers. Since cortical layers arise from asymmetric cell divisions in a subset of root stem cells, our research focuses heavily on the spatial and temporal in vivo tracking of molecular regulators that coordinate the cell cycle and specify cell fate.
We are also extending our studies to phylogenetically distant species that develop multiple cortical layers, such as turnip, rice, and tobacco, with the aim of identifying conserved or divergent molecular pathways. This work has the long-term goal of engineering crops with enhanced resilience to environmental stressors, including drought and water excess.

Figure: Confocal image of a Cardamine hirsuta embryo harbouring a CO3::NLS-3xVENUS construct. In green VENUS signal, in grey SCRI-RENAISSANCE 2000 staining.

Beyond fundamental research, our group addresses agricultural challenges related to climate change, anthropogenic contamination, and intensive farming practices.
These studies have led to collaborations with biotechnology companies and have contributed to expanding research networks focused on soil preservation and plant adaptability.
Recently, we have also initiated a new line of research investigating the use of plant-derived macromolecules, such as microRNAs, as anti-inflammatory agents in animals.

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3. Shtin M, Polverari L, Svolacchia N, Bertolotti G, Unterholzner SJ, Di Mambro R, Costantino P, Sabatini S, Dello Ioio R (2023)The Mutual Inhibition between PLETHORAs and ARABIDOPSIS RESPONSE REGULATORs Controls Root Zonation. Plant Cell Physiol. 15;64(3):317-324.

Paola
Del Porto
Associate Professor

ORCID

RESEARCH LINES

- Study of the interplay between host immune response and viral infections (HCV, SARS-CoV2)
- Impact of dysfunctional CFTR on the innate immune cells in Cystic Fibrosis
- Role of miR-146a in the inflammatory response of human macrophages

STAFF | COLLABORATORS

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Alberto Sinibaldi,
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RESEARCH ACTIVITY

Interplay between host immune response and viral infections.
My research activity is focused on the study of the interaction between the host immune response and microbial infections. In particular, in the past, I investigated the mechanisms employed by the hepatitis C virus to escape the host adaptive immune response demonstrating that the chronic evolution of the disease is associated with the emergence of escape mutations in cytotoxic T cell epitopes. More recently I'm involved in a collaborative study aimed to characterize the infecting virus and the host immune response during the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in individuals with different disease outcomes to establish their association with clinical severity.

Impact of dysfunctional CFTR on the innate immune cells in Cystic Fibrosis.
An additional scientific interest has been to investigate the expression and the role of the cystic fibrosis transmembrane conductance regulator (CFTR) in human monocyte/macrophages. In this context we demonstrated that human macrophages express CFTR and that dysfunctional CFTR is associated with defective bactericidal activity in such cells.
To determine whether miRNA dysregulation underlies the functional abnormalities of macrophages carrying dysfunctional CFTR we performed miRNA profiling in macrophages from cystic fibrosis (CF) individuals demonstrating that CF macrophages display increased miR-146a and that inhibition of miR-146a significantly increases IL-6 protein and mRNA levels in CF macrophages compared to controls. More recently, we have undertaken the study of the effect of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) modulators on the function of CF monocytes demonstrating that the modulator therapy significantly improves the antimicrobial activity of monocytes against P. aeruginosa. The effect of the therapy on the expression and function of CFTR in monocytes is under study.

Role of miR-146a in the inflammatory response of human macrophages.
The previous observation that dysregulation of miR-146a modulates the production of IL-6 in response to lipopolysaccharide stimulation of cystic fibrosis macrophages, led us to assess the role of miR-146a in the inflammatory response of human macrophages. To this aim, we are evaluating the effect of miR-146a inhibition on the secretion of pro- and anti-inflammatory cytokines production and on the expression of predicted miR-146a targets.

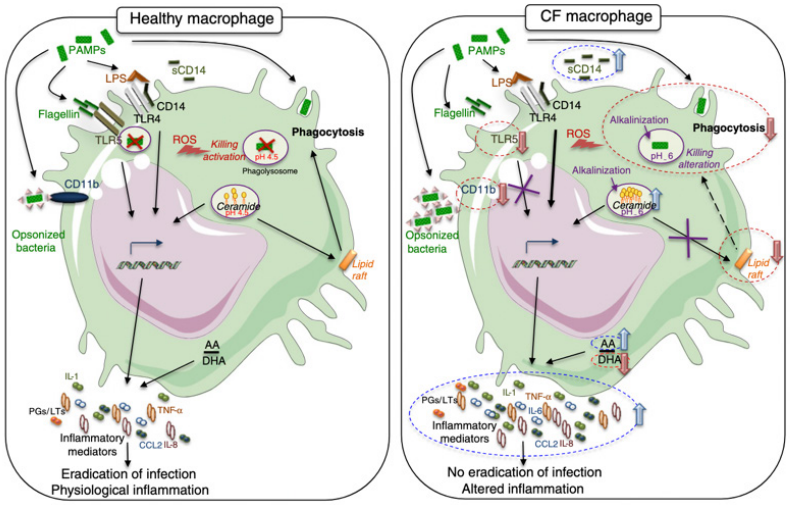

Figure. Impaired CF macrophage functions against P. aeruginosa. The figure illustrates the altered molecules and pathways causing an exaggerated inflammatory response and reduced P. aeruginosa elimination in CF macrophages, from M. Lévêque et al. Journal of Cystic Fibrosis, 2017.

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Patrizio
Dimitri
Full Professor

ORCID

RESEARCH LINES

- Elucidating the moonlighting roles of epigenetic factors in mitosis and cytokinesis, using Drosophila melanogaster and human cell lines as model systems.
- Deepening the genetic basis of the rare genetic syndrome Floating-Harbor.
- Studying the regulation of gene expression in pericentromeric heterochromatin.

STAFF | COLLABORATORS

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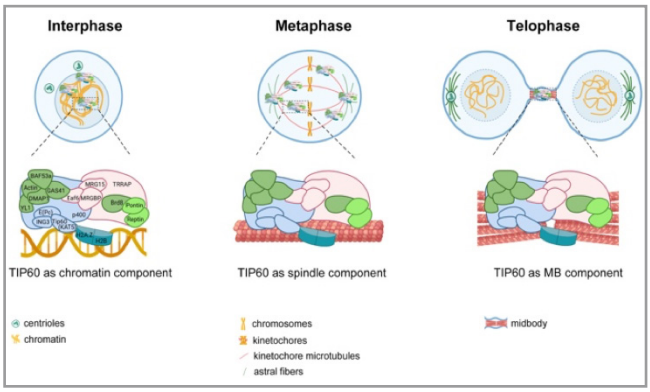
GRANTS

PRIN 2022 2022T59RWR:
Integrating genetic models to mechanistically dissect cytokinesis failure in neurodevelopmental disorders.

RESEARCH ACTIVITY

An early focus of my group was to study the genetic functions of constitutive heterochromatin at a time when it was mainly considered "junk" DNA. This pioneering work helped to shift the perception of heterochromatin, which is now recognized as being crucial to genome function, with roles in cell differentiation, disease, and cancer.
More recently, we proposed a functional reinterpretation of constitutive heterochromatin (Marsano et al., Trends in Genetics, 2019). Our current research projects focus on the non-canonical roles of epigenetic factors in ensuring accurate mitosis and cytokinesis, emphasizing their moonlighting functions in preserving genomic stability (Prozzillo et al., Cellular and Molecular Life Sciences, 2023). We hypothesize that lncRNAs, beyond their well-established roles in epigenetic regulation, may also function as essential architectural scaffolds in the assembly and activity of the midbody, a mitotic organelle crucial for cytokinesis that defines the site of daughter cell separation. To test this, we adopt an interdisciplinary approach that integrates advanced cutting-edge methodologies to study lncRNAs in the context of cytokinesis. By testing the architectural role of lncRNAs in midbody assembly during cytokinesis, our work aims to uncover a still hidden layer in cell biology, revealing new mechanisms that control the proper completion of cell division and how their dysfunction contributes to genomic instability and disease.



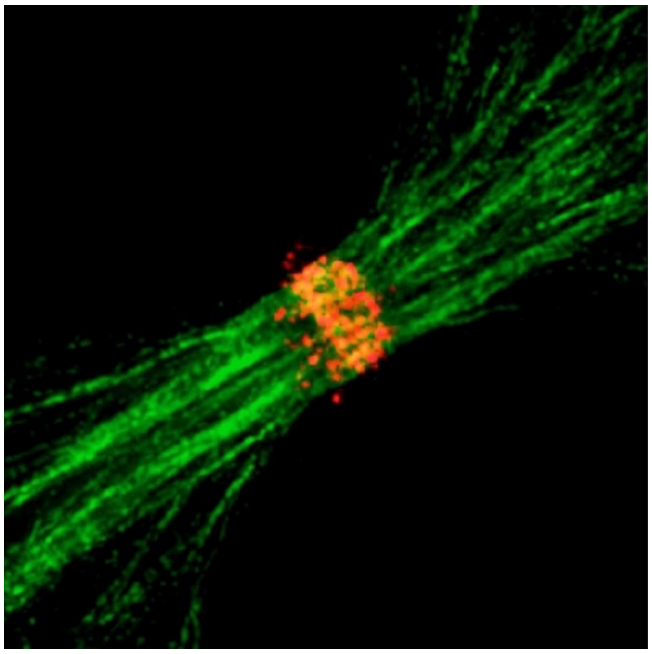


*Figure. **Upper panel:** The mitotic trip of human TIP60 complex subunits. The cartoon schematically shows the relocation of TIP60-C subunits to the cell division apparatus during different stages of cell division. **Lower panel:** The figure shows an example of the recruitment of TIP60 HAT (orange red) subunit to the midbody in human RPE-1 cells using Expansion Microscopy (Image by Maria Virginia Santopietro, at the Advanced Imaging Core Facility (AICF) in Trento, Italy (From Santopietro et al., Epigenetics & chromatin. 2025 doi: 10.1186/s13072-025-00603-8.).*

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Simone
Ferrari
Full Professor

ORCID

RESEARCH LINES

- Regulation of elicitor-induced defense responses in plants.
- Role of the cell wall in modulating plant growth and defense plant growth and defense.
- Biotechnological solutions for sustainable agriculture and cultivation of microalgae.

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Francesco Della Rocca,
(Bayer Crop Science, Italy)

GRANTS

PNRR – MISSIONE 4 COMPONENTE 2, INVESTIMENTO 1.4 – D.D. 1032 17/06/2022. PI: Carlo Giuseppe Rizzello; Co-PI: Simone Ferrari. Project "Sistemi produttivi agroalimentari multifunzionali, innovativi e sostenibili per lo sviluppo delle aree marginali", bando Centro Nazionale di Ricerca - Agritech (EU Next-GenerationEU.

RESEARCH ACTIVITY

Plants can detect invading microbes by perceiving elicitors, called Pathogen- and Damage-Associated Molecular Patterns (PAMPs and DAMPs), that trigger PAMP-Triggered Immunity (PTI). Examples of PAMPs and DAMPs are chitin in fungal cell walls and oligogalacturonides (OGs), pectin fragments released from the plant cell wall by fungal polygalacturonases (PGs), respectively. Activation of PTI is costly and, in the absence of pathogen pressure, might reduce fitness. On the other hand, plants treated with elicitors acquire a "primed" status and respond more efficiently to subsequent infections. Current research aims to characterize the mechanisms underlying this phenomenon, with a focus on the modulation of special metabolism. Moreover, we are investigating how cell wall damage modulate growth and defense responses in plants. Plant cell walls are indeed the first line of defense against pathogen attack and regulate growth under physiological and stress conditions. Cell wall integrity is constantly monitored to adjust growth and modulate defenses. We have shown that plants with altered cell walls constitutively express defense responses and are more resistant to infections but are severely impaired in growth. This growth defect is dependent on apoplastic peroxidases that cause the accumulation of reactive oxygen species (ROS). More recently, we found that altered cell walls also affect apical hook formation in etiolated seedlings by repressing gibberellin acid signalling. Current research focuses on the elucidation of the signalling pathways linking perception of cell wall damage and activation of defense responses against pathogens.
Besides our interest in plant biology, our group also aims at developing novel solutions to increase the sustainability of agriculture and food production. We are investigating methods to convert agricultural residues and food industry waste biomasses into "green" products for crop protection. A more recent line of research also deals with the use of agri-food by-products as carbon sources for the cultivation of microalgae.

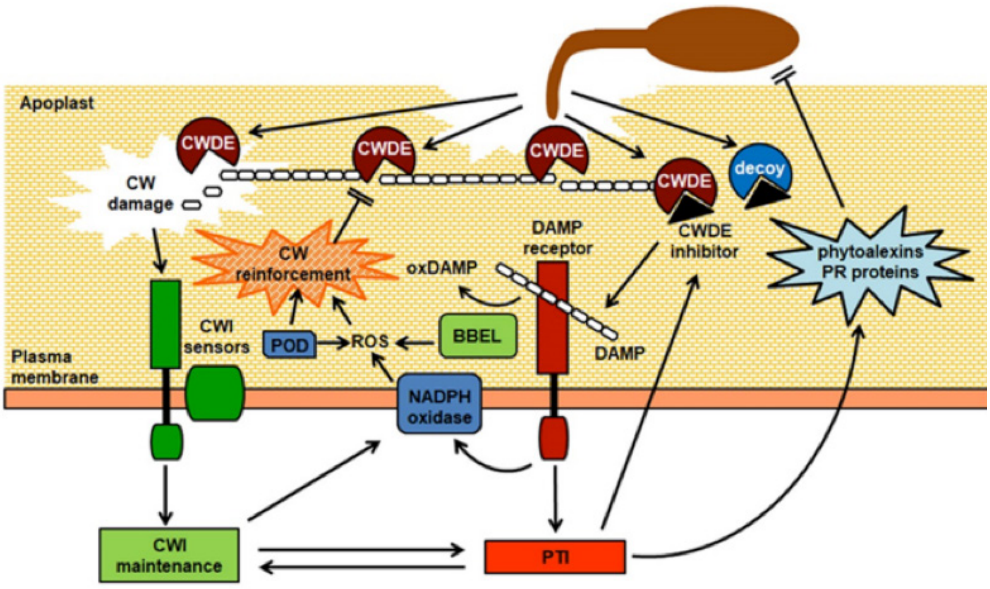

Figure. Overview of responses induced by cell wall damage during pathogen infection. CW, cell wall; CWDE, cell wall-degrading enzyme; CWI, cell wall integrity; PTI, pattern-triggered immunity; DAMP, Damage-Associated Molecular Pattern; BBEL, berberine bridge enzyme-like protein; oxDAMP, oxidized DAMP; POD, peroxidase; ROS, reactive oxygen species. (from Lorrai & Ferrari 2021 "Host Cell Wall Damage during Pathogen Infection: Mechanisms of Perception and Role in Plant-Pathogen Interactions" Plants, 10(2), 399).

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Maria Teresa
Fiorillo
Associate Professor

ORCID

RESEARCH LINES

- Molecular and cellular mechanisms of autoimmune disorders
- Role of HLA-B*27 alleles in Spondyloarthritis
- CD8+ T cell biology in immune-mediated diseases
- Crosstalk between T cell immunosenescence and chronic inflammation in autoimmune diseases

STAFF | COLLABORATORS

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Valerio Licursi,
Researcher (IBPM, CNR, Rome

GRANTS

2023. "Dissecting the role of HLA-B*27 and T lymphocytes in Ankylosing Spondylitis", Ceschina Foundation Grant,
€ 250.000 PI: Fiorillo M.T.

RESEARCH ACTIVITY

The molecular and cellular mechanisms underlying autoimmune diseases remain largely unknown. Hence, the growing need to improve our knowledge to identify appropriate therapeutic targets and personalize treatment options. In this context, my research project focused on the study of predisposing genetic factors associated with a group of chronic inflammatory rheumatic diseases called Spondyloarthritis (SpA) of which Ankylosing Spondylitis (AS) is the prototype.
Much of our effort was devoted to analysing the pathogenetic role of HLA-B*27, which represents the gene most strongly associated with this group of autoimmune diseases. Since the discovery of an allelic variant of HLA-B*27, found in Sardinia and not predisposing to autoimmunity, we conducted our analysis through a comparative approach between risk and non-risk HLA-B*27 alleles. Several studies combining T-cell antigen-presenting functions, HLA-B*27 peptidome characterization, biophysical and computational analysis have revealed a greater flexibility of the disease-associated HLA-B*27 allele. This confers the ability to bind and present a broader peptide repertoire, including atypical viral antigens and self-peptides, allowing autoreactive and virus-specific CD8+ T-cell responses that can be found in patients.
We are currently investigating how HLA-B*27 antigen-presenting functions may be influenced by the allelic variant of the aminopeptidases ERAP1 and ERAP2, which are other important risk factors for AS and related SpA.
Genome-wide association studies (GWAS) have identified over 100 genes that contribute to susceptibility to SpA, and many of them are involved in the development, differentiation, function and count of CD8+ T cells, justifying a specific interest in this lymphocyte subset in SpA. Consequently, we are now conducting studies to understand the correlation between CD8+ T cell immunosenescence, their migratory properties and the ability to sustain chronic inflammation in SpA patients compared to healthy controls and patients with other immune-mediated diseases.

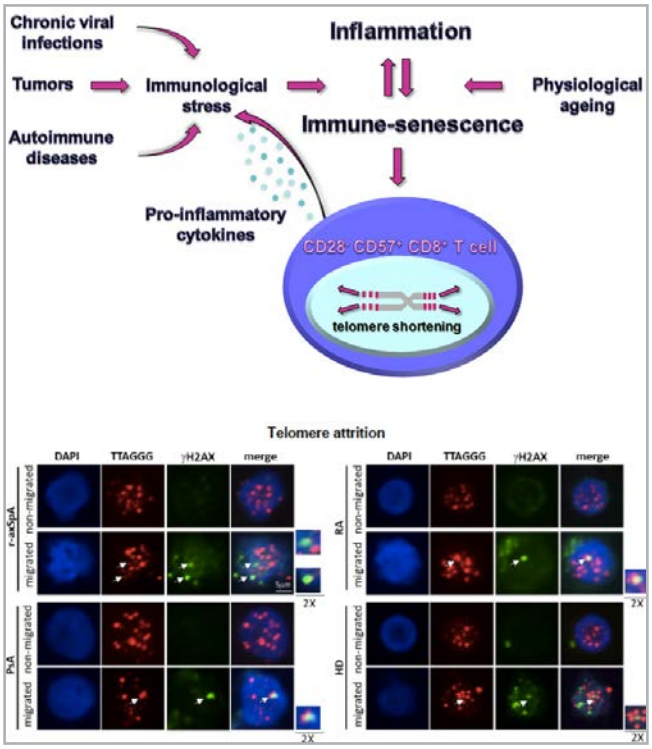

Figure. Upper panel: cartoon illustrating the interplay between autoimmune diseases, inflammation and CD8+ T cell immunosenescence (from Tedeschi et al., Int J Mol Sci. 2022; 23:3374). Lower panel: Confocal images showing telomere's dysfunction in CD8+ T cells from SpA patients versus controls: dysfunctional telomeres are identified by the colocalization of telomeric DNA sequences (red) and γ-H2AX, a DDR marker (green) (from Paldino et al., Arthritis Rheumatol. 2025; doi: 10.1002/art.43109).

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3. Tedeschi V, Paldino G, Kunkl M, Paroli M, Sorrentino R, Tuosto L, Fiorillo MT (2022) CD8+ T Cell Senescence: Lights and Shadows in Viral Infections, Autoimmune Disorders and Cancer. Int J Mol Sci. 23:3374. doi: 10.3390/ijms23063374.

Vincenzo
Lionetti
Associate Professor

ORCID

RESEARCH LINES

- Plant Cell Wall and Pectin Integrity in Plant Immunity and Disease Resistance
- Development of Vaccines for Plants from Agro-Industrial By-Products

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Giulia Caminada, *PhD student (Sapienza)*
Hugo Melida, *(Univ. of Leon, Spain)*
Henk Schols, *Professor (Wageningen Univ., Netherlands)*
Birgit Wasserman, *Post-doc (Graz Univ. of Technology, Austria)*

GRANTS

OLinWASTE. Smart sustainable biorefining of olive mill waste into biocompounds for plant and soil health, bioplastics, and bioenergy. HORIZON EUROPE. PI
XYWALL. Cell Wall in plant resistance to Xylella. PRIN 2022. PI research unit.
ROME TECHNOPOLE. Decarbonization and digitalization in research on new green energy sources. Next-Gen EU. Critical Mass
REACH-XY. Research actions to reduce the impact of the plant-harmful pathogen Xylella. MUR/MEF. Task leader

RESEARCH ACTIVITY

Throughout my scientific career, I have focused on the role of the plant cell wall in plant–microbe interactions. My research has contributed to understanding how plants perceive cell wall (CW) damage during pathogen attacks and regulate CW remodeling enzymes and their inhibitors to preserve wall integrity and activate defense responses.

A central part of my work concerns pectin methylesterases (PMEs) and their inhibitors (PMEIs), which control the degree of pectin methylesterification—a key factor affecting the degradability of the CW by microbial enzymes. I have demonstrated that modulating PME and PMEI expression and activity allows control over pectin structure, microbial accessibility, and plant resistance to biotic stresses.

Building on these findings, I have developed biotechnological strategies to improve the saccharification efficiency of lignocellulosic biomass for biofuel and bioproduct production, enhance the technological and nutritional quality of plant-derived foods, and optimize protoplast isolation for plant biotechnology.

More recently, I have extended my expertise to the sustainable valorization of agro-industrial by-products for the development of vaccines for plants and other high-value bioproducts, supporting the advancement of circular bioeconomy and green biotechnology.

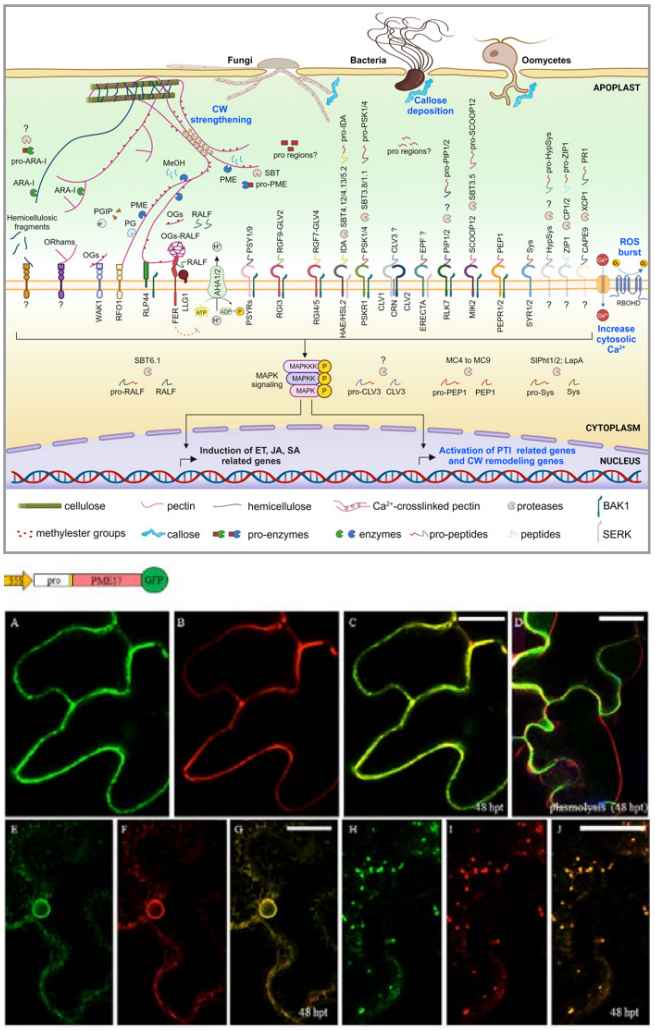

Figure. Upper panel. Overview of apoplastic protein precursor and their maturation, perception, and function in plant immunity (from Del Corpo et al., Plant Communication 2024, 5, 100931. Lower panel: Confocal images showing Pro-PME17 delivery in the apoplast through a conventional secretion pathway (from Coculo et al., Plant Physiology and Biochemistry 2023 201, 107865).

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Riccardo
Lorrai
Researcher Tenure Track

ORCID

RESEARCH LINES

- Plant Cell Wall Integrity and Its Role in Immunity and Development
- Biotechnological Strategies for Sustainable Crop Protection

STAFF | COLLABORATORS

Simone Ferrari,
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Shu-Hsing Wu,
Distinguished Research Fellow (Academia Sinica, Taiwan)

RESEARCH ACTIVITY

My research focuses on the complex interplay between plant development, environmental cues, and cell wall integrity, with a particular emphasis on how these factors shape stress responses and growth regulation. I investigate how the plant cell wall (CW) serves not only as a structural barrier but also as a dynamic interface for detecting microbial threats. Pathogens secrete CW-degrading enzymes (CWDEs), which plants counteract using specific inhibitors that limit damage and generate damage-associated molecular patterns (DAMPs), triggering immune responses. These DAMPs contribute to a broader cell wall integrity (CWI) surveillance system, which interacts with innate immunity to coordinate defense while maintaining growth.

To reduce reliance on synthetic pesticides in agriculture, I also explore the use of natural elicitors to trigger plant immunity. In this context, we developed a fermentation-based protocol using the white rot fungi grown on agrifood wastes. This extract induces resistance against Botrytis cinerea in Arabidopsis thaliana and various Solanaceae crops, with minimal impact on yield.

In parallel, I explore how environmental and metabolic signals regulate developmental transitions, especially during seedling emergence and light responses. A key focus is understanding how photosynthates like sucrose influence de-etiolation and whether sugar signaling alone can reprogram protein synthesis. I also investigate apical hook formation in etiolated seedlings, focusing on how altered cell wall properties affect hormone signaling and mechanical feedback.

Overall, my research integrates molecular biology, plant physiology, and biotechnology to understand how developmental and stress-related processes converge, with the long-term goal of improving crop resilience in sustainable agriculture.

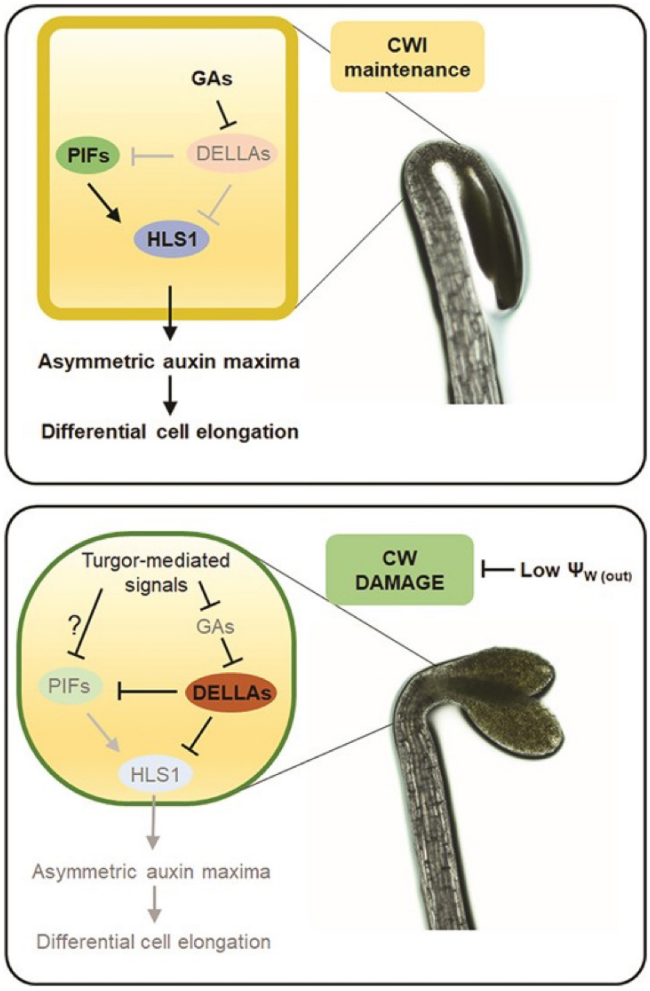

Figure. Proposed model of the effects of loss of CWI on apical hook formation. Perturbation of CWI, activates turgor-dependent responses that repress accumulation of active GAs, leading to stabilization of DELLA proteins and reduction of PIF4 and possibly other PIF protein levels. Increased DELLAs and reduced PIFs result in impaired HLS1 expression, impairing proper formation of auxin response maxima and differential cell elongation and ultimately inhibiting apical hook development. Ψw, water potential; PIFs, PHYTOCHROME INTERACTING FACTORs; HLS1, HOOKLESS1; DELLAs, DELLA proteins; GAs, gibberellins; CW, cell wall; CWI, cell wall integrity.

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Giulia
Matusali
Researcher Tenure Track

ORCID

RESEARCH LINES

- Mechanisms of sexual transmission of viruses and genital tract tropism
- Emerging and re-emerging viruses' interaction with the human host
- Immune response to emerging viruses' infection and vaccination

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Fabrizio Maggi, *Associate Professor (INMI, Univ. Insubria)*
Giovanni Chillemi, *Associate Prof. (Univ. Tor Vergata, INMI)*
Nathalie Dejucq-Rainsford, *Research Director (INSERM, Univ. Rennes)*

GRANTS

Project ID: S1.P0002 (INF-ACT, PNRR). GENESIS: Unraveling the molecular and immunologic mechanisms of intrahost persistence in emerging and reemerging arboviral infections. F Maggi/G Matusali
(5x1000) G Matusali.Meccanismi di trasmissione sessuale di virus emergenti: costruzione di un modello colturale tridimensionale del tratto genitale femminile per lo studio dell'interazione ospite patogeno e dell'azione di composti antivirali.

RESEARCH ACTIVITY

My research focuses on the intricate interactions between emerging viruses and the human host, with particular attention to mucosal epithelia and the genital tract as sites of viral replication, persistence, and transmission. Since my postdoctoral fellowship at INSERM and afterwards, I have explored how viruses such as HIV-1, SIV, Zika (ZIKV), Dengue (DENV), monkeypox (MPXV), and Toscana virus (TOSV) interact with male and female reproductive tissues, investigating their potential for sexual transmission and long- term presence in genital fluids. In previous studies, I have demonstrated that arboviruses such as ZIKV, TOSV, and DENV can persist in semen even for months and may associate with seminal fractions, with evidence of ZIKV replicating in the testes. More recently, I have demonstrated that MPXV can infect vaginal and ectocervical epithelial cells, disrupting tissue homeostasis with potential implications for reproductive health.
In the context of SARS-CoV-2, my research has contributed to the understanding of host-pathogen interactions and tissue- specific responses, including the interplay between infected bronchial epithelium and immune cells, and the modulation of antiviral responses, inflammation, senescence, and fibrotic pathways in mesothelial and endothelial tissues.
Through the application of human-based 2D and 3D models, current investigations focus on the role of genetic, hormonal,
and microbial factors in shaping host susceptibility and responses to emerging viruses.
Since the COVID-19 pandemic and the re-emergence of MPXV, a significant part of my work has also focused on the immune response to infection and vaccination. I have studied humoral responses to SARS-CoV-2 and MPXV, including the dynamics of antibody production, the impact of hybrid immunity, and the immunogenicity of vaccines against emerging variants. My current aim is to investigate more deeply the role of host, viral, and microbial factors in determining and predicting the strength and durability of immune responses following infection or vaccination against emerging viruses. The ultimate goal is to contribute to scientific knowledge that supports the development and implementation of effective preventive and therapeutic strategies

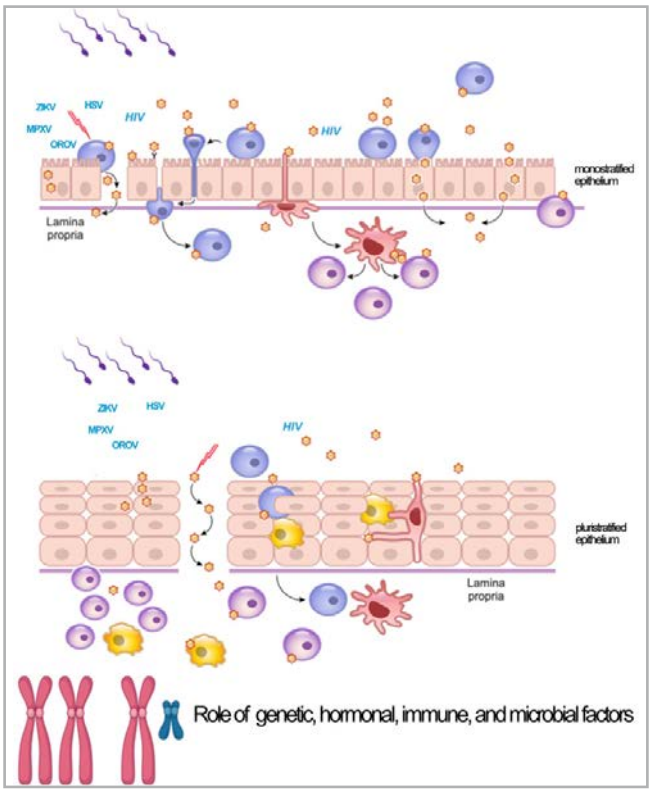

Figure. Mechanisms for sexual transmission of viruses through the mucosal epithelia. Viruses in genital secretions can be transmitted through the mono- (endo-cervix, colon, urethra) or pluristratified (vagina, ecto-cervix, foreskin, glans) mucosa (modified from Le Tortorec Matusali et al). The role of genetic, hormonal, and microbial factors in the acquisition of viral infections can be investigated through 3D-human-based models.

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Rodolfo
Negri
Full Professor

ORCID

RESEARCH LINES

- Role of histone demethylases in transcription and genome integrity
- Transcriptional response of eukaryotic cells to genotoxic damage
- Transcriptional response of mammalian cells to radiation and gravity alteration

STAFF | COLLABORATORS

Elena Di Nisio, *Post-doc (Sapienza);*
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PhD student (Sapienza)
Valeria Manzini, *PhD student (Sapienza)*
Valerio Licursi, *Researcher (IBPM, CNR)*
Virginia De Cesare, *Post-doctoral Researcher (University of Dundee, UK)*
Michela Clerici, *Associate Professor (University of Milano)*

GRANTS

PRIN 2023-2025 - Research unit PI: Chromatin landscape around DNA double-strand breaks: exploring the H3/H4 histone post-translational modifications and their influence on DNA repair pathway choice and efficiency - Prot. 2022MHRCC4 – National PI: Prof. Michela Clerici, University of Milano. € 93480.
PNRR-PE15-Spoke 9 Attività spaziali_2022. Coordinator: prof. Mariano Bizzarri. € 73000.

RESEARCH ACTIVITY

The main focus of the research work in the lab is on the influence of chromatin structure on transcription regulation. In the last years we analyzed the effects of the mammalian histone demethylases of class 5 (KDM5, targeting H3K4me3) on chromatin structure and gene regulation in human cancer cells. In particular, we characterized a catalytic inactive isoform of KDM5B which accumulates in breast cancer cells, due to its remarkable protein stability and analyzed its regulatory effects (Di Nisio et al., 2023; Di Nisio et al., 2024). We also studied the regulatory effects of the yeast orthologue JHD2 on transcription regulation (Di Nisio et al.2023b).
We previously set up an in vivo screening system for searching H3K4 histone demethylase inhibitors in yeast and mammalian cells (Mannironi et al., 2014). We then characterized the regulation of KDM5B by specific miRNAs in human breast cancer cell lines.
Using constructs overproducing these miRNAs and chemical inhibitors of the catalysis, we could show that KDM5 histone demethylases are deeply involved in the response of breast cancer cells to genotoxic damage (Mocavini et al., 2019; Pippa et al., 2019; Di Nisio et al., 2021). We are now studying more deeply the post-transcriptional regulation of KDM5B abundance in breast cancer cells by the ubiquitine-proteasome system.
Finally, an independent line of research in the lab is traditionally devoted to the study of the transcriptional response of human cells and of organized tissues to irradiation and altered gravity conditions. In particular, we are currently studying the effects of simulated microgravity on the expression of miRNAs in mammalian myocytes.

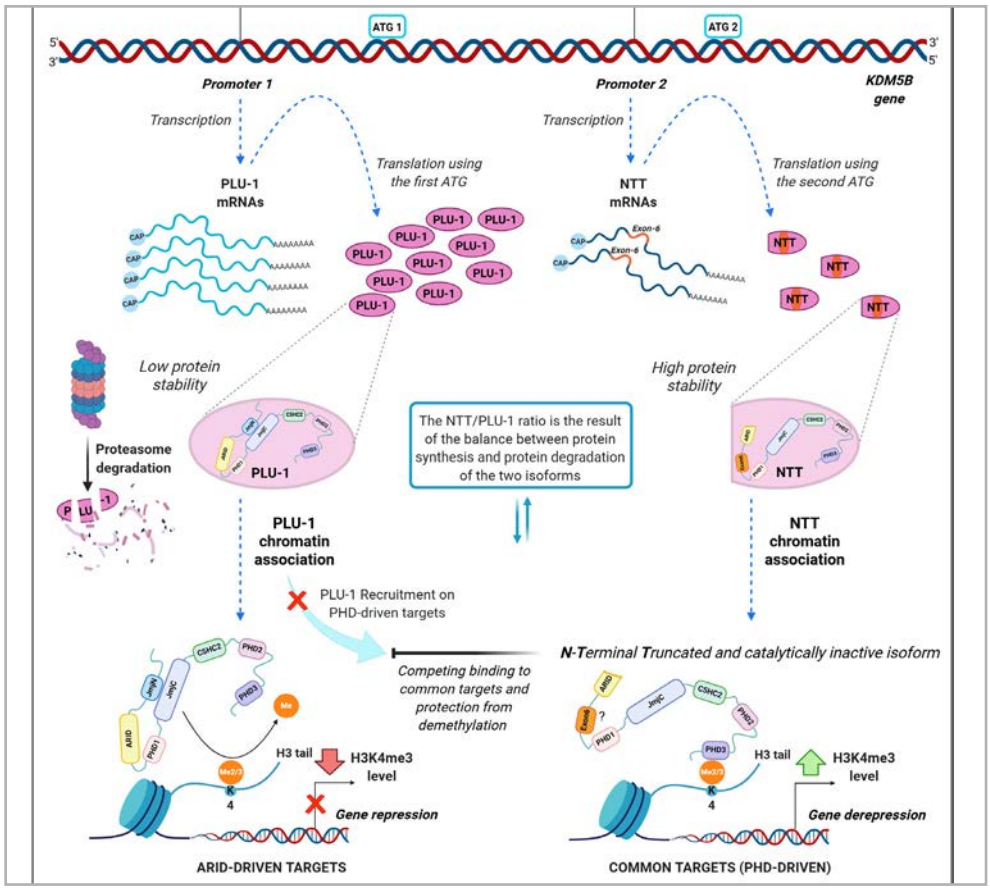

Figure. Proposed model for the regulation mode of the canonical isoform PLU 1 of the KDM5B histone demethylase and the truncated and catalytically inactive isoform NTT (from ref. 1).

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Martina
Pasqua
Researcher Tenure Track

ORCID

RESEARCH LINES

- Role of the MDR efflux pump AcrAB-TolC in enteropathogenic Escherichia coli
- Two-Component Signal Transduction Systems as key modulators of Shigella virulence
- Decoding the role of polyamines in host-pathogen dialogue

STAFF | COLLABORATORS

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Full Professor (Sapienza)
Daniela Scribano,
Researcher (Sapienza)
Jean François Collet, *Full Professor (de Duve Institute, UCLouvain)*
Ryutaro Utsumi, *Full Professor (Osaka University)*
Cecilia Ambrosi, *Associate Professor (San Raffaele University Rome)*

RESEARCH ACTIVITY

Role of the MDR efflux pump AcrAB-TolC in enteropathogenic Escherichia coli. AcrAB-TolC is the primary multidrug resistance efflux pump (EP) of the resistance-nodulation-division (RND) superfamily in Enterobacteriaceae. Beyond its well-characterized role in antibiotic resistance, AcrAB plays a pivotal role in the pathogenesis and virulence of several bacterial pathogens. In our lab, we investigate the contribution of AcrAB to the infectious processes of three major enteropathogenic E. coli pathotypes: Shigella flexneri, a causative agent of bacillary dysentery; Adherent-Invasive E. coli (AIEC), capable of colonizing the ileal mucosa of patients with Crohn's disease; and Enteroaggregative E. coli (EAEC), known for its strong epithelial adherence and biofilm-forming capabilities. Our findings will advance our understanding of the molecular mechanisms underlying E. coli pathogenesis and highlight AcrAB as a promising target for novel anti-virulence strategies.

Roles of Two-Component Signal Transduction Systems in Shigella virulence. In our group, we study two-component signal transduction systems (TCSs), which are key molecular mechanisms that allow bacteria to sense and respond to environmental changes. Our research focuses on how TCSs regulate virulence in Shigella, an intracellular pathogen responsible for severe intestinal disease. We investigate the role of specific TCSs — including PhoQ/PhoP, EvgS/EvgA, QseC/QseB and RcsC/RcsB — in linking environmental signals to the expression of virulence and fitness genes during host infection. Given their central role in pathogenesis, we are also exploring TCSs as potential targets for anti-virulence therapies.

Decoding the role of polyamines in host-pathogen dialogue. Polyamines are a class of small polycationic molecules present in all cells. Their fortune in the world of eukaryotes and prokaryotes is due to the multitude of biological functions they perform, including translation, gene regulation, stress resistance, cell proliferation and differentiation, making them essential molecules for life. In bacteria they are clearly emerging as crucial players in pathogenic process.

The question of the importance of polyamines has also been raised by our research group in Shigella flexneri, where the evolutionary pathway to pathogenicity involved the remodelling of the content and regulation of polyamines to optimize the bacterial fitness in the host. How does the rearrangement of polyamine metabolism affect the Shigella intracellular lifestyle? We aim to address this question by investigating the intramacrophage step of the complex invasion program of S. flexneri.

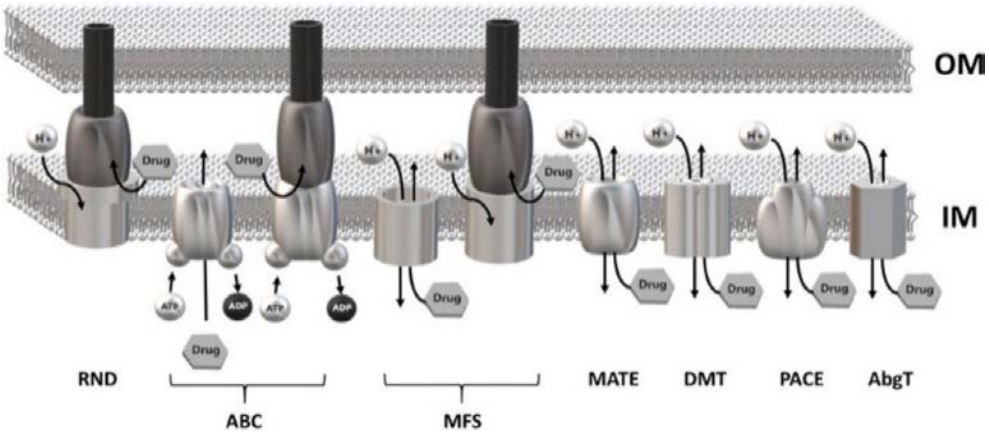

Figure. Schematic overview of the major families of multidrug efflux pumps.
Members of the RND (Resistance-Nodulation-Division) family form tripartite efflux pumps composed of an inner membrane transporter, a periplasmic adaptor protein, and an outer membrane factor. AcrAB-TolC, one of the best-characterized RND efflux systems, belongs to this family.

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Livia
Perfetto
Associate Professor

ORCID

RESEARCH LINES

- SIGNOR, curation and maintenance
- Multi-omics data integration and mechanistic modelling
- Graph-based strategies development

STAFF | COLLABORATORS

Veronica Venafra, *Post-doc*
Prisca Lo Surdo, *fellow student*
Veronica Lombardi, *PhD student*
Eleonora Meo, *fellow student*
Francesco Spallotta,
Associate Professor (Sapienza)
Francesca Sacco,
(Università di Tor Vergata, Rome)

GRANTS

Istituto Pasteur Italia, Fondazione Cenci Bolognetti: *Building SigMod, a web Resource for PTM browsing and functional visualization.*
PI: Livia Perfetto.
My First AIRC (MFAG): Modelling cell communication in Pancreatic Cancer: A Systems Biology Approach to Personalized Treatments.PI: Livia Perfetto.
PRIN PNRR 2022 NextGenerationEU): A systems-based approach toward personalised therapeutic strategies in Pancreatic ductal adenocarcinoma. PI: Livia Perfetto.

RESEARCH ACTIVITY

Antigen presentation is a crucial step in mounting the immune responses against foreign antiFrom the beginning of my research I have focused on Biological Networks and on the functional insights we can gain from the analysis of physical and causal relationships between proteins. I have contributed to this general goal by looking at it from several angles. Indeed at the center of my research interests are networks of causal interactions which can provide the structure to integrate multi-omics datasets by building context-specific models that are mechanistic (can provide understanding) or predictive (can generate novel hypotheses).
I am the coordinator of the SIGNOR database (Lo Surdo et al., 2023), a key resource for curated causal relationships in signaling. My current research focuses on the development of bioinformatics strategies for the interpretation of genomic data, leveraging protein interaction networks stored in SIGNOR to understand the effects of genetic variants and mutations on cellular signaling pathways, and ultimately, their phenotypic consequences.

A major part of my work involves designing computational approaches for integrating multi-omics data—including genomics, proteomics, phosphoproteomics, and transcriptomics—with causal networks from SIGNOR. These integrative models support patient-specific analyses to better understand the molecular mechanisms underlying complex diseases.

Over the years, I have demonstrated that SIGNOR data can be effectively used to elucidate disease mechanisms and develop tools for patient stratification and diagnosis in the context of personalized medicine. I supervised the development of key tools such as SignalingProfiler and PatientProfiler (Venafra et al, 2024), which integrate MS-based phosphoproteomic and transcriptomic data with causal networks to generate context-specific models of pancreatic and breast cancer signaling and drug response. Additionally, I developed ProxPath, a network-based method designed to identify phenotypes that are significantly proximate to a given protein hit list (Iannuccelli et al, 2023).

In summary, my work aims to explore the mechanistic links between genes and phenotypes, using network biology as a powerful framework for biomedical discovery.

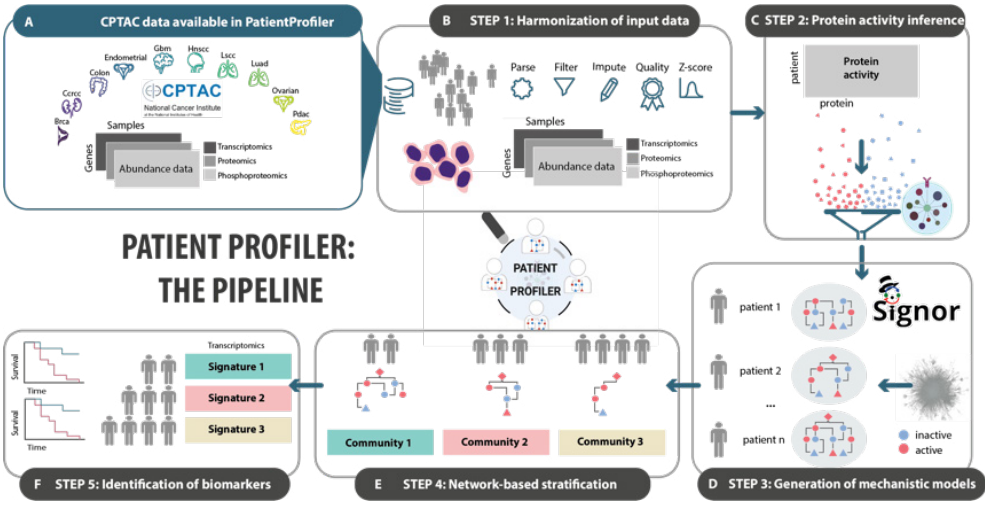

Figure. PatientProfiler, leverages causal interaction data to address how the molecular background of individual patients drives a malignancy. PatientProfiler integrates SignalingProfiler and ProxPath and allows multi-omic data analysis, generation of patient-specific mechanistic models, and extraction of network-based biomarkers.

References

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2: Iannuccelli M, Vitriolo A, Licata L, Lo Surdo P, Contino S, Cheroni C, Capocefalo D, Castagnoli L, Testa G, Cesareni G, Perfetto L*. Curation of causal interactions mediated by genes associated with autism accelerates the understanding of gene-phenotype relationships underlying neurodevelopmental disorders. Mol Psychiatry. 2024 doi: 10.1038/s41380-024-02432-9.
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Daniela
Pontiggia
Associate Professor

ORCID

RESEARCH LINES

- Perception and Modulation of Immune Responses Triggered by CW-DAMPs
- Role of CW-DAMPs in Root–Soil Fungi Interactions
- Valorization of Waste-Derived CW-DAMPs for Sustainable Agricultural Practices

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Benedetta Mattei, *Full Professor (Università dell'Aquila)*
Adele Di Matteo, *Research scientist (CNR – I.B.P.M., Rome)*
Alessandra Cona, *Assoc. Professor (Roma3 University, Rome)*

RESEARCH ACTIVITY

In response to pathogen attack, plants activate their innate immune system also through recognition of endogenous molecules called Damage-Associated Molecular Patterns (DAMPs). Key plant-derived DAMPs include oligogalacturonides (OGs), cellodextrins (CDs), and mixed-linked β-1→3/β-1→4-glucans (MLGs), which derive from the degradation of pectin, cellulose, and hemicelluloses, respectively. These fragments are released upon mechanical damage or infection and act as danger signals capable of triggering defense responses.
However, excessive accumulation of CW-DAMPs can impair plant growth, highlighting the need for a balance between development and immunity. To fine-tune immune activation and avoid harmful effects, plants use an enzymatic oxidation system based on FAD-dependent oxidases, such as OGOXs and CELLOXs, belonging to the berberine bridge enzyme-like (BBEl) family. These enzymes reduce the elicitor activity of OGs, CDs, and MLGs via H_2O_2-mediated oxidation, thus modulating the immune response. Our research focuses on dissecting the functional role of CW-DAMPs in plant defense, growth, and health, using biochemical approaches, carbohydrate mass spectrometry, and proteomics. We investigate OGOX enzymatic activity and its involvement in regulating OG-induced systemic immune responses, such as stomatal closure, hormone signaling, and defense gene expression, mediated by calcium waves. We also explore how the degree of polymerization of OGs shapes both immune responses and perception, particularly within receptor complexes formed by FERONIA and Rapid Alkalinization Factor (RALF) peptides.
Another area of interest is the role of CW-DAMPs in plant–soil fungal interactions. Fungi may be beneficial, neutral, or pathogenic, and a key challenge is understanding how CW-DAMPs help plants differentiate among them. This knowledge is crucial to improve sustainable management of plant–microbe relationships. Given their roles throughout the plant life cycle, CW-DAMPs are important targets for applied research. One goal is to valorize agro-industrial by-products rich in bioactive oligosaccharides. Within a circular economy framework, these molecules are being tested for their ability to boost disease resistance, enhance plant health, and improve crop quality, contributing to more sustainable agricultural practices.

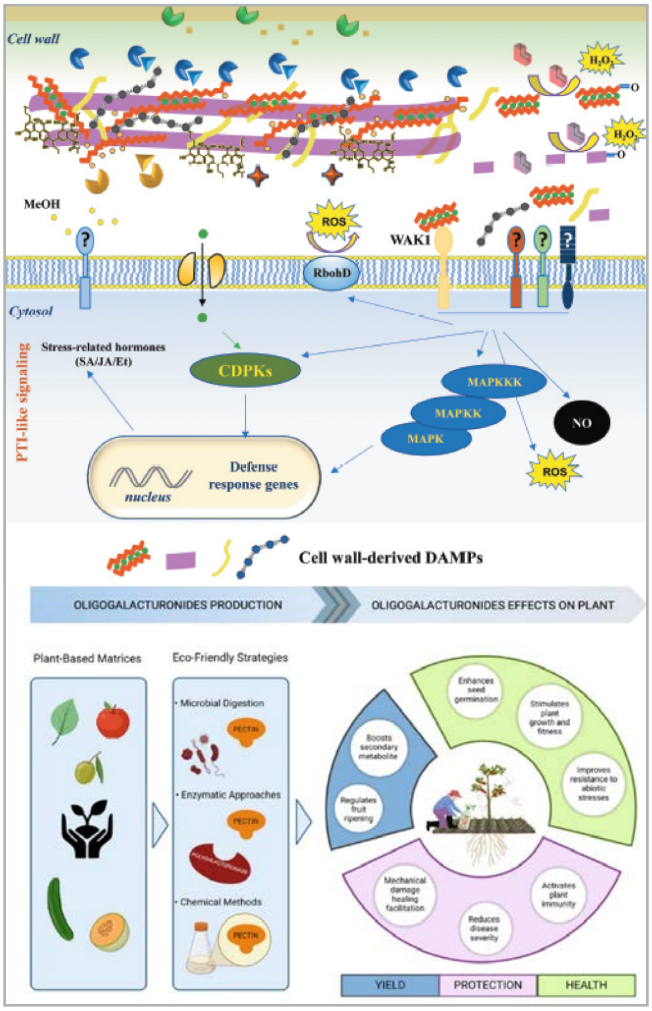

Figure. Upper panel: Plant cell wall structure with rupture-induced release of DAMPs, such as oligogalacturonides (OGs), activating the CW-DAMPs signaling pathway (Pontiggia et al., 2023). Lower panel: OGs as tools for sustainable crop protection (Degli Esposti et al., 2025).

References

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Carlo
Presutti
Associate Professor

ORCID

RESEARCH LINES

- Role of ncRNAs in Melanome
- ncRNAs in Central Nervous System
- miRNAs as biomarkers for ASD
- Plant small RNAs as anti-inflammatory molecules

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Vito Antonio Amico,
Post-doc (Sapienza)
Lucrezia De Santis,
Phd student (Sapienza)
Claudia Franco,
Phd student (Sapienza)

GRANTS

Horizon 23-25: salivary miRNAs as biomarkers for early ASD diagnosis - PI: € 270.000
PNRR2023/2026 -CN3 RNATherapy: ncRNAs as target and therapy molecules in Neurodevelopmental Disorders. PI: € 290.000

RESEARCH ACTIVITY

Prof. Carlo Presutti, has been working on regulation of RNA stability since 1986 at the Department of Genetics and Molecular Biology of University of Rome “La Sapienza”.
Current research lines are focalized on the role of ncRNAs in regulation of gene expression in different cells and tissues, in normal and pathological condition.
Both basic and translational research are carried out in the lab and recent advances leaded to a relevant patenting activity.
More specifically, role of lncRNAs involved in the development of resistance of melanoma tumours is currently under investigation (fig.1 and 2.)
Role of ncRNAs in Central Nervous System with a specific interest for ASD (Autism Spectrum Disorders) is another focus of the lab.

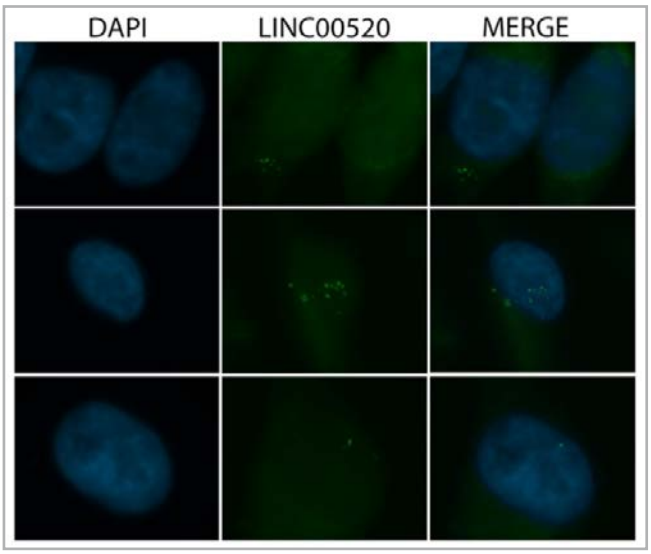

Figure.1. RNA fluorescence in situ hybridization (FISH) for LINC00520 using biotinylated probes against the lncRNA in 501mel cell line. LINC00520 (in green) were stained with Streptavidin Alexa Fluor 488

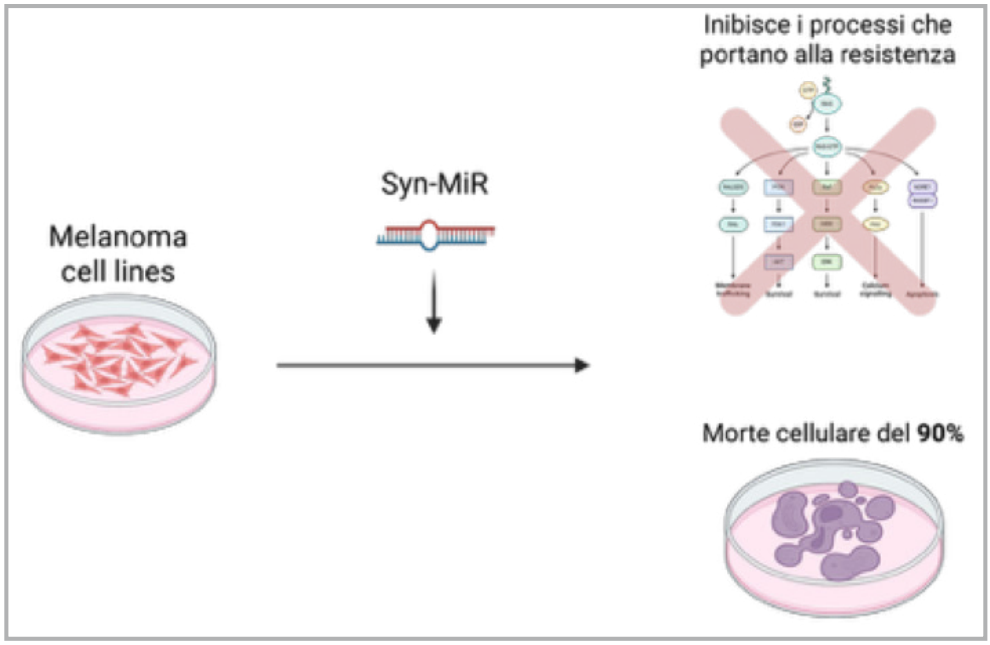

Figure 2. Effect of our synthetic miRs on tumour cells resistant to conventional therapy

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2. Gioiosa Silvia, Gasparini Silvia, Presutti Carlo, Rinaldi Arianna, Castrignanò Tiziana, Mannironi Cecilia. Scientific Reports, 2025 - Integrated gene expression and alternative splicing analysis in human and mouse models of Rett syndrome.
3. De Santis Alessandro, De Santis Lucrezia, Rossi Francesca, Gasparini Silvia, Licursi Valerio, Amico Vito Antonio, Capone Imerio, Fragale Alessandra, D’Atri Stefania, Gabriele Lucia, Presutti Carlo. Cancer Medicine - 2025 “NSD2 and miRNAs as Key Regulators of Melanoma Response to Romidepsin and Interferon-α2b Treatment”- Cancer Medicine

Gianni
Prosseda
Associate Professor

ORCID

RESEARCH LINES

- Study of the regulation of the main activator in the Shigella virulence system
- Investigating the main transcriptional activators of the AraC-XylS family in bacterial pathogens
- Influences of the intestinal metabolites on the virulence of enteropatogens.

STAFF | COLLABORATORS

Bianca Colonna,
Full Professor (Sapienza)
Rita Trirocco, *Post-doc (Sapienza)*
Tommaso Tacchetti,
PhD student (Sapienza)
Frederic Barras, *Research Director, (Institut Pasteur, Paris, FR)*
De Luca Michele,
Full Professor (Unimore)
Eguchi Yoko, *Associate Professor (Kindai University, Japan)*

GRANTS

PI unit 3, PTR 619-23 project: "ShigeFeS": "Iron-Sulfur Clusters Biogenesis Polymorphism and Virulence in Shigella"; 01/01/2024 - 31/12/2025 (75k)
2021-2025. PI Sapienza's Team (partnership with Università di Modena) for the ERC Advanced Grant Holo-GT (PI Prof. De Luca). (219k)

RESEARCH ACTIVITY

Study of the regulation of the main activator in the Shigella virulence system. *Shigella* spp. are highly adapted human pathogens that cause bacillary dysentery (Shigellosis). The sophisticated infectious strategy of Shigella is supported by a coordinated expression of several genes located on the chromosome as well as on a virulence plasmid (pINV) organised in a cascade manner. At the top of this regulatory structure is the VirF protein, responsible for the activation of the virulence system in *Shigella*.
This role implies a complex and multifactorial regulation that has been unveiled by our studies at the transcriptional and post-transcriptional. This research line focuses on the characterisation of inhibitory binding of the VirF protein with fatty acids (Figure). The identification of compounds able to mimic the FA binding may lead to new therapeutic approaches for the treatment of Shigellosis.

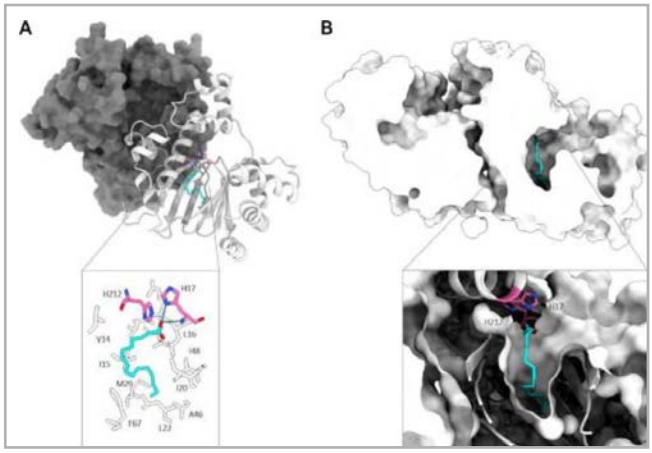

Figure. Structure of VirF in complex with a fatty acid. (A) The dimeric model of VirF is shown, with one monomer represented as a gray surface and the other one as a white cartoon. Palmitoleic acid is represented as cyan sticks. The residues interacting with the ligand are represented in the panel. (B) Representation of the cavities of VirF and the cavity accommodating the ligand are represented in the panel (Trirocco et al., 2013a).

Investigating the main transcriptional activators of the AraC-XylS family in bacterial pathogens.
The transcription factors belonging to this family control many virulence systems in Gram-negative bacterial pathogens. These proteins contain a domain that binds to specific molecules, thereby inhibiting their activity. In addition to VirFF of *Shigella*, we are characterising other regulators of this class, including AggR of enteroaggregative E. coli, YbtA of invasive adherent E. coli, and VirFA of *Acinetobacter baumannii*. We aim to identify common inhibitory ligands that could also inhibit the activity of other characterised regulators in this class, including ToxT from Vibrio cholerae and Rns from enterotoxigenic *E. coli.*

Influences of the intestinal metabolites on the virulence of enteropathogens. Human gut microbiota contributes to the physiology, function and development of the immune, nervous and digestive systems. It is also involved in the defence of the host from allogeneic microorganisms. This protective action is carried out by direct competition for nutrient sources as well as by the production of molecules by the microbiota or intestinal mucosa. However, enteropathogenic bacteria have learned to harness a panel of these molecules to modulate their virulent potential. This line of research is dedicated to the identification of these compounds and to the study of the mechanisms they use to program the virulence of enteropathogens.

References

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3. Carev, Ivana et al. "Centaurea triumfetii essential oil chemical composition, comparative analysis, and antimicrobial activity of selected compounds." Scientific reports vol. 13,1 7475. 8 May. 2023,

Sabrina
Sabatini
Full Professor

ORCID

RESEARCH LINES

- Role of mechanical forces during organogenesis
- Molecular mechanisms that balance cell division with cell differentiation
- Developmental boundary specification

STAFF | COLLABORATORS

Federico Vinciarelli, *Post-doc (Sapienza)*
Michela De Nittis, *PhD (Sapienza)*
Francesca Cazzaniga, *PhD (Sapienza)*
Krzysztof Wabnik, *Group leader (University of Madrid)*
Riccardo di Mambro, *University of Pisa*
Malcom Bennet, *University of Nottingam*

GRANTS

PRIN 2022-2024 - Coordinator: 2022NZ7M3W. Modelling root developmental plasticity in response to high salinity in Arabidopsis and rice. Budget: 89.500 €
PNRR-Spoke 7 Agritec CN2. Coordinator: Carlo Rizzello. Budget 85.000 €.

RESEARCH ACTIVITY

Sabrina Sabatini's research focuses on uncovering the fundamental principles that regulate organ growth, pattern formation, and developmental stability. Using the root of Arabidopsis thaliana as a model system, her work integrates molecular genetics, live imaging, and computational modeling to study how cells coordinate their behavior in space and time to generate organized and functional structures.
A central goal of her research is to understand how stem cell activity and cell fate decisions give rise to spatially distinct domains of cell division and differentiation. Her team has elucidated the mechanisms that maintain the transition zone—the developmental boundary separating dividing and differentiating cells—highlighting how graded molecular signals provide positional cues for developmental transitions. In particular, her group demonstrated that the antagonistic interaction between auxin and cytokinin creates an auxin minimum that positions the transition zone.
Dividing cells sensing this minimum exit the cell cycle and begin to differentiate. In addition to biochemical signals, they also showed that cell size and volume changes act as key mechanical triggers for differentiation, underscoring the role of physical constraints in development.
More recently, her research has uncovered a self-organizing regulatory network involving auxin, PLETHORA transcription factors (PLTs), and ARR-type cytokinin response regulators (ARRs), which controls the expansion and stabilization of proliferative and differentiating zones. This work provides a broader framework for understanding how molecular and mechanical signals are integrated to achieve robust organ growth and spatial organization—principles that extend beyond plant systems to multicellular development in general.

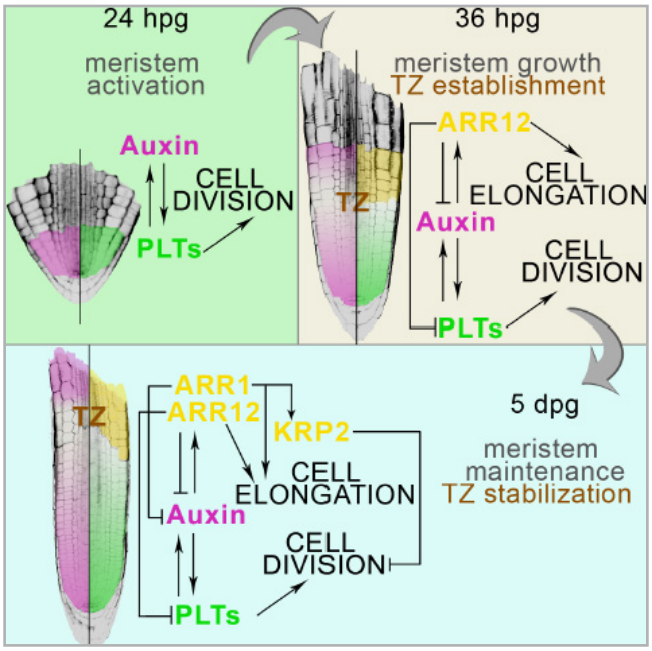

Figure. Self-organizing regulatory mechanisms controlling root meristem patterning and size stabilization. Upon germination, proliferative activity leads to the formation of a PLETHORA (PLT) gradient, with a local drop marking the position of the transition zone (TZ). A mutual antagonism between PLTs and the cytokinin response regulator ARR12 limits early root meristem expansion. ARR1 contributes to meristem size stabilization by repressing cell division through activation of the CDK inhibitor KRP2. Together, auxin, PLTs, and ARRs form an integrated regulatory network that drives the self-organization of root zonation and growth dynamics.image).

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2. Salvi E., Rutten JP., Di Mambro R., Polverari L., Licursi V., Negri R., Dello Ioio R., Sabatini S., Ten Tusscher K. "A Self-Organized PLT/Auxin/ARR-B Network Controls the Dynamics of Root Zonation Development in Arabidopsis thaliana." Developmental Cell, 53(4):431–443 (2020)
3. Di Mambro R, Svolacchia N, Dello Ioio R, Pierdonati E, Salvi E, Pedrazzini E, Vitale A, Perilli S, Sozzani R, Benfey PN, Busch W, Costantino P, Sabatini S. The Lateral Root Cap Acts as an Auxin Sink that Controls Meristem Size. Curr Biol. 2019;29:1199-1205

Francesco
Spallotta
Associate Professor

ORCID

RESEARCH LINES

- Association between metabolic syndrome and cancer onset and progression
- To investigate the metabolic-epigenetic link in cancer
- To unveil the role of cancer associated fibroblasts (CAFs) within tumor microenvironment in pancreatic cancer

STAFF | COLLABORATORS

Silvia Malatesta, *Post-doc (Sapienza)*
Claudia Camplone, *PhD student (Sapienza)*
Virginia Vigiano Benedetti, *PhD student (Univ. Cattolica - Rome)*
Chiara Cencioni, *PhD student (CNR-IASI - Rome)*
Carmine Carbone *PhD student, (Fondazione Policlinico Gemelli, IRCCS - Rome)*
Mattia Mori, *Professor (University of Siena)*

GRANTS

My First AIRC grant (MFAG #23099) "Metabolic regulation of the DNA demethylation enzymatic machinery in pancreatic cancer". PI: F. Spallotta.
PRIN 2022 PNRR (P2022E3BTH) "Exploiting metabolic vulnerabilities to overcome resistance to targeted therapies in colorectal cancer". PI Unit: F. Spallotta
PRIN 2022 (20229JKZR4) "Insight into the role of brain cell-derived exosomes as mediators of insulin resistance-associated epigenetic alteration affecting cognitive function". PI: F. Spallotta

RESEARCH ACTIVITY

From the beginning of my research, I worked in the field of epigenetics pointing out novel molecular mechanisms underpinning onset and progression of different human diseases. Recently, my lab explored the alteration of the link between metabolism and epigenetics, with a specific focus in relation to the presence of dysmetabolic chronic disease (i.e. type 2 diabetes, obesity) during cancer development.

Specifically, my lab team is investigating the link between pancreatic ductal adenocarcinoma (PDAC) and type 2 diabetes and obesity, two well-known PDAC risk factors, to identify novel vulnerabilities of this highly aggressive cancer. In our studies we took advantage of both in vivo and ex vivo models where we applied integrative OMICS analysis deriving data from DNA methylome-seq, ChIP-seq, RNA-seq and metabolome analysis. Drug screening and repositioning are two additional big tasks of our activities aimed at identification of novel targets to restore normal phenotype in vitro and in vivo.

Recently we demonstrated how the collagen deposition is enhanced by dysmetabolism in CAFs and how the GLP1R agonists reduces collagen deposition allowing T lymphocyte infiltration in PDAC slowing down its growth. Furthermore, we are investigating the role α-ketoglutarate/succinate ratio imbalance supporting PDAC tumorigenesis.

The lab conducts research projects also on breast and colorectal cancer to identify novel strategies able to stratify tumor and to point out unprecedented vulnerabilities for novel combinatorial therapeutic approaches.

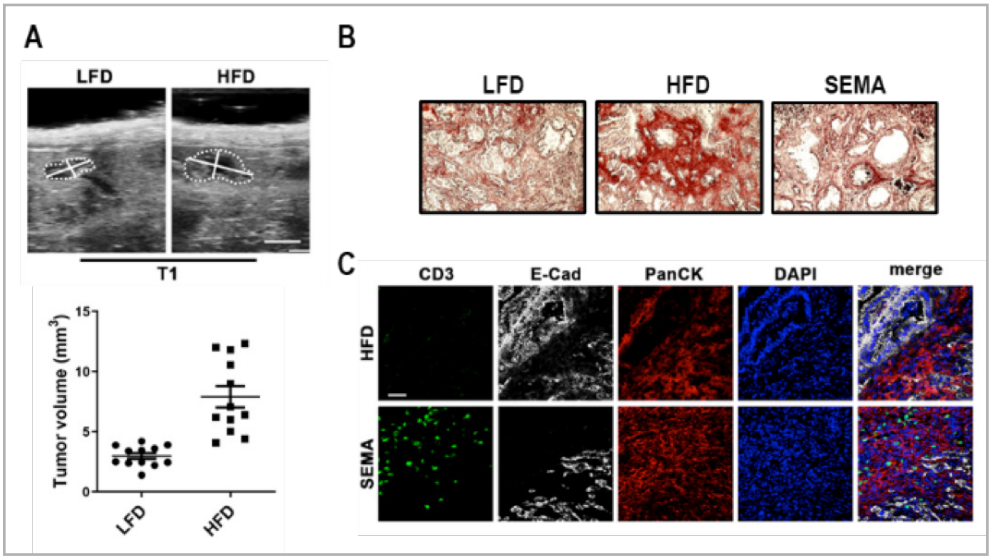

Figure. (A) Upper panel: Representative endoscopic ultrasound images of LFD and HFD mice at T1 (30 days) from KPC organoid injection. T1 original scale bar, 1.5 mm; Lower panel: Tumor size measurement at time point T1. (B) Representative picrosirius red staining images of pancreatic lesions at time point T2 (90 days) in LFD (left panel), HFD (middle panel) and HFD+SEMA (right panel) mice bearing pre-neoplastic lesions. (C) Representative confocal microscopy images depicting HFD and HFD+SEMA mouse cryosections at time point T2 probed by an anti-CD3 antibody (green), an anti-E-Cadherin (white), and an anti-pan cytokeratin (red). Nuclei were counterstained with DAPI (blue). Merged pictures were depicted on the right. Original scale bar, 50 μm.

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2. Crecca E, Di Giuseppe G, Camplone C, Vigiano Benedetti V, Melaiu O, Mezza T, Cencioni C, Spallotta F. The multifaceted role of agents counteracting metabolic syndrome: A new hope for gastrointestinal cancer therapy. Pharmacol Ther. 2025 Jun:270:108847.
3. Carbone C, Piro G, Agostini A, Delfino P, De Sanctis F, Nasca V, Spallotta F, Sette C, Martini M, Ugel S, Corbo V, Cappello P, Bria E, Scarpa A, Tortora G. Intratumoral injection of TLR9 agonist promotes an immunopermissive microenvironment transition and causes cooperative antitumor activity in combination with anti-PD1 in pancreatic cancer. J Immunother Cancer. 2021 Sep;9(9):e002876.

Loretta
Tuosto
Full Professor

ORCID

RESEARCH LINES

- The role of CD28 in T cell inflammatory responses to bacterial superantigens and their pathological effects.
- Immunotherapeutic efficacy of bispecific antibodies targeting CD28 and tumour-associated antigens in ovarian cancer.

STAFF | COLLABORATORS

Martina Kunkl, *Post-doc (Sapienza)*
Alessandro Paiardini, *Associate Professor (Sapienza)*
Laura Rosanò, *Laboratory Director (IBPM, CNR, Rome)*
Emanuele Mauri, *Researcher (Politecnico di Milano)*
Manolo Sambucci, *Researcher (Fondazione Santa Lucia, Rome)*

GRANTS

PRIN 2022 PNRR (P2022Z7TEC)
"Improving ovarian cancer immunotherapy".
PI: Loretta Tuosto
PRIN 2022 (2022JFRWCA)
"Dissecting how microenvironment facilitate ovarian cancer metastasis".
PI: Loretta Tuosto
ISTITUTO PASTEUR ITALIA - Fondazione Cenci Bolognetti,
"Anna Tramontano" Project 2024.
"Bispecific antibodies targeting CD28 and MUC1 for improving cancer immunotherapy." PI: Loretta Tuosto

RESEARCH ACTIVITY

Our research activity is aimed at characterising the mechanisms that regulate pro-inflammatory functions of T lymphocytes in response to the CD28 costimulatory molecule and bacterial superantigens. We were among the first to demonstrate that staphylococcal enterotoxins B (SEB) and A (SEA) act as superantigens by binding in a bivalent manner to both the T cell receptor (TCR) and the CD28 costimulatory molecule, thereby stimulating T cells to produce large quantities of inflammatory cytokines, which impair the integrity and function of the intestinal epithelial barrier.

In collaboration with Prof. Alessandro Paiardini, we also identified a SEB-mimetic peptide (pSEB116–132) that blocks the interaction between SEB and CD28, thereby dampening inflammation-mediated dysregulation of the intestinal epithelial barrier.
Within this framework, Staphylococcus aureus—detected in the oncobiome of the female reproductive tract—produces toxin superantigens, including SEA and SEB, which may stimulate T cells to secrete inflammatory cytokines that support metastatic progression in ovarian cancer. Indeed, we found that SEB-activated T cells could enhance epithelial-to-mesenchymal transition (EMT) in ovarian cancer cells, as indicated by upregulation of N-cadherin and downregulation of E-cadherin.

We are currently developing novel immunotherapeutic strategies based on the administration of bispecific antibodies (BsAbs) targeting CD28 and MUC1, in combination with an inhibitor of the collagen receptor DDR2, for the treatment of serous ovarian cancer (SOC). Using OVCA433 and OVCAR3 cell lines as models of SOC, we generated several tumour-specific T cell lines and demonstrated that inhibition of the DDR2/Col1 interaction sensitises SOC cells to CD28xMUC1 BsAb-mediated immunotherapy.

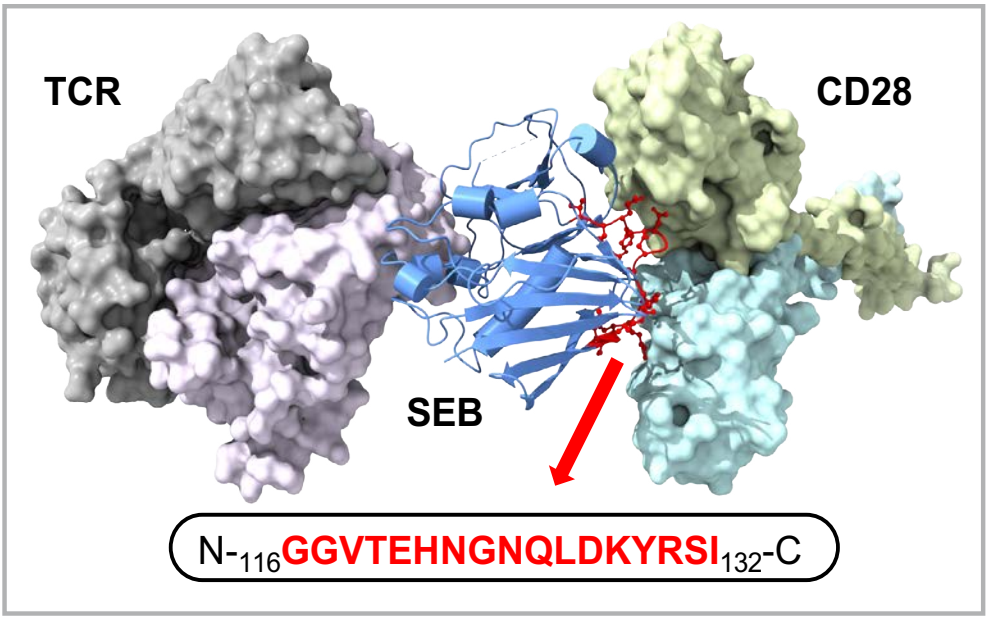

Figure. Structural model of the TCR–SEB–CD28 complex. The TCR (TCRVβ in light purple and TCRVα in grey) and CD28 dimers (light blue and yellow) are represented as solid surface, SEB in cartoon ribbons (blue). The sequence of pSEB116-132 mimetic peptide targeting the region of SEB interacting with the homodimer interface of CD28 is shown in red ball-and-sticks models.

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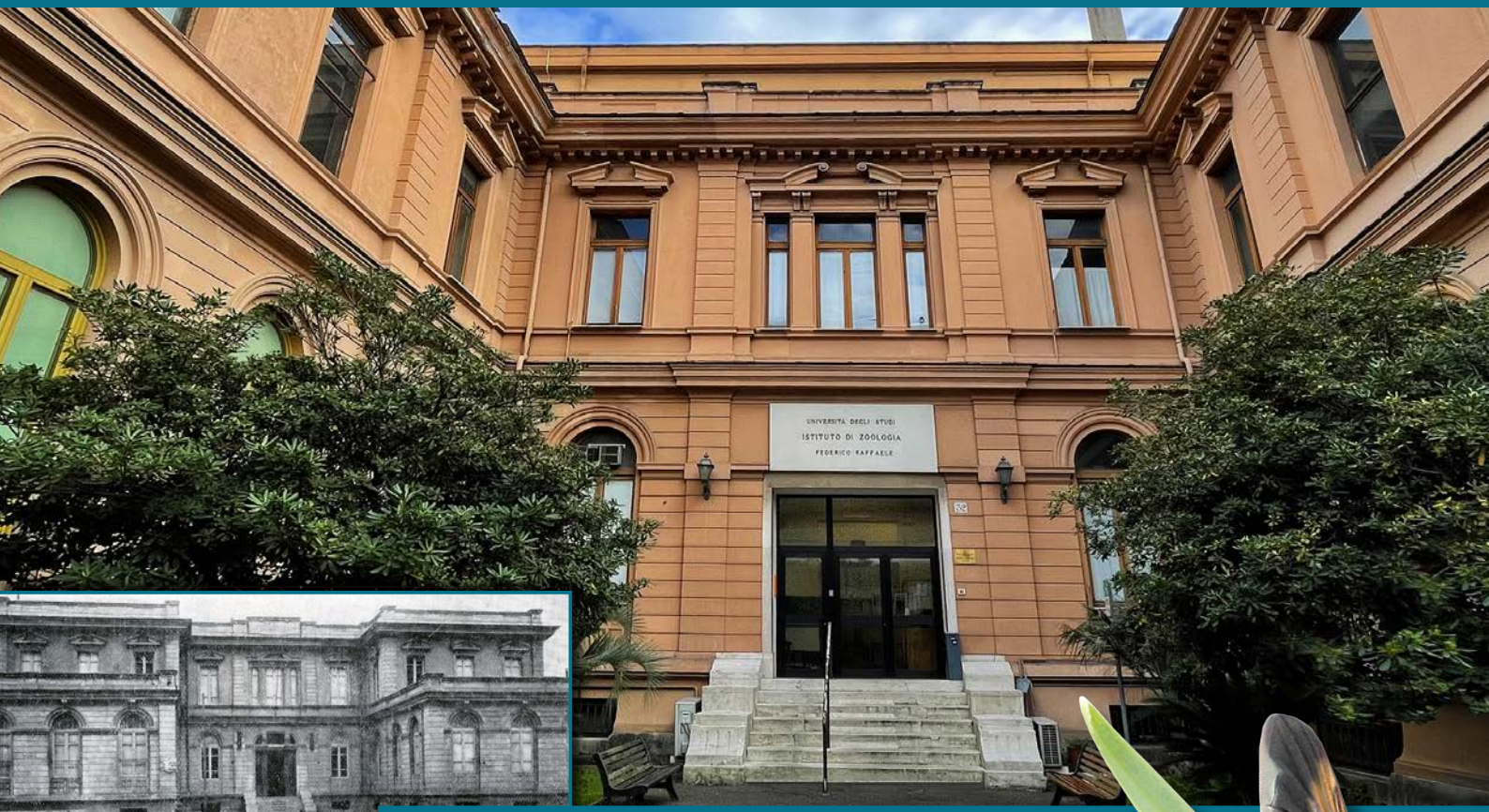
3. Kunkl M, Amormino C, Spallotta F, Caristi S, Fiorillo MT, Paiardini A, Kaempfer R, Tuosto L. Bivalent binding of staphylococcal superantigens to the TCR and CD28 triggers inflammatory signals independently of antigen presenting cells. Front Immunol. 2023 May 3;14:1170821.

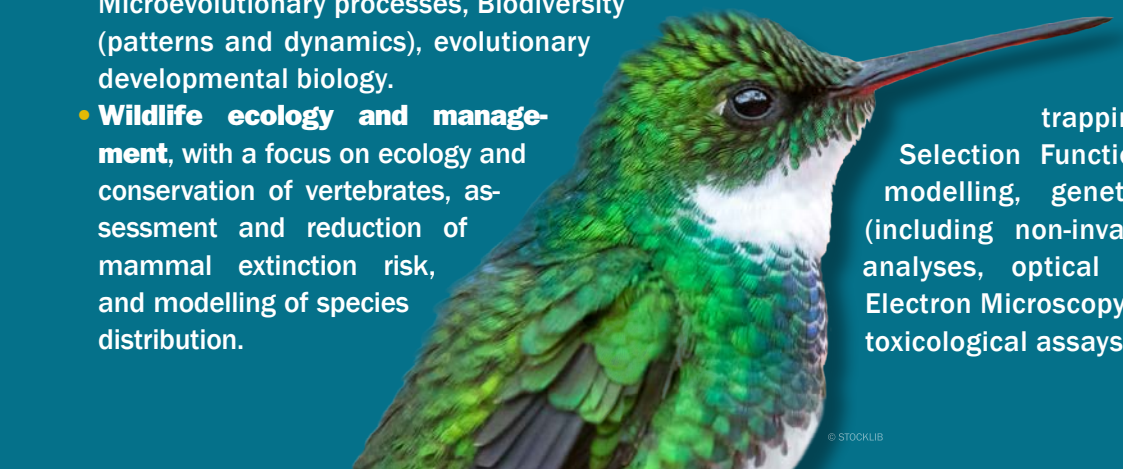


“ ZOOLOGY ”

During the ‘70s of the XX century, the zoologists of Sapienza moved to their current location, a beautiful Liberty-style building on the campus edge. The diversity of expertise spans several taxonomic groups and a variety of methodological and theoretical approaches, carried out at the main location and at the ***Museum of Zoology***.

The research lines can be summarised under the following headings:

- **Evolutionary Biology** of insects (Coleoptera and Diptera), molluscs, and vertebrates, with a focus on: Integrative Taxonomy, Phylogeny, Biogeography, Population genetics/genomics (spatial patterns of variation, divergence rates), Molecular evolution (biochemical and ecological drivers of evolution), Microevolutionary processes, Biodiversity (patterns and dynamics), evolutionary developmental biology.
- **Wildlife ecology and management**, with a focus on ecology and conservation of vertebrates, assessment and reduction of mammal extinction risk, and modelling of species distribution.



Ecotoxicology. Global change and biodiversity from species, to communities, to wilderness areas, including forecast of scenarios of global change for both native and invasive vertebrates.

Applications of zoological research include: bioprospecting, development of monitoring methods, conservation planning, conflict mitigation, integration of biodiversity conservation with other societal goals (food production, climate change mitigation, improved human well-being).

Methods employed include: field observations and sampling in terrestrial and aquatic (marine and freshwater) habitats, VHF- and GPS-telemetry, camera-trapping, scat-analysis, Resource Selection Functions, population and habitat modelling, genetic and genomic analyses (including non-invasive genetics), phylogenetic analyses, optical stereomicroscopy, Scanning Electron Microscopy, histological techniques, ecotoxicological assays.

Paolo
Audisio
Full Professor

ORCID

RESEARCH LINES

- Taxonomy and biogeography of beetles
- Phylogeny and molecular evolution of insects
- Population and conservation genetics
- Conservation Biology of insects
- Molecular evolution of phytophagous insects
- Ecology and evolution of aquatic beetles
- Applied entomology

STAFF | COLLABORATORS

Alessio De Biase,
Associate Professor (Sapienza)
Emiliano Mancini,
Associate Professor (Sapienza)
Simone Sabatelli,
Temporary Research Fellow (Sapienza)
Min Huang, *Associate Professor (N&W University, Yangling, China)*
Meike Liu, *Associate Professor (Yangtze University, CHINA)*
Andrea Di Giulio,
Full Professor (Roma Tre)

GRANTS

Circeo N.P. Project "Monitoraggio presenza e consistenza artropodi di interesse comunitario Parco Nazionale Circeo". PI: P Audisio
Insugherata R.N. "RomaNatura" Project Conoscenza, tutela e valorizzazione della Riserva Naturale dell'Insugherata come hotspot di biodiversità. CSM: P Audisio

RESEARCH ACTIVITY

My research activities are carried out through field collections, study of Museum collections, morphological and cladistic investigations (including SEM), ecological investigations, genetics/genomics methods, and fauna monitoring techniques. These activities are all framed in the vast fields of the evolutionary biology, biodiversity, ecology, and conservation biology of insects. My main research lines aim to: 1) outline the phylogeny, taxonomy and biogeography of insects(fossil included, mostly Coleoptera), by integrating morphology, ecological information, DNA barcoding and conservation genetics, even by creating interactive keys to identification, 2) unravel the biological factors favoring and maintaining over time the interactions among phytophagous insects and their host plants by taking into account their parallel evolution, their ecological shifts, and their microbiome component, 3) unravel the biological factors involved in the interactions among aquatic beetles and their habitats, with particular emphasis on running waters and terrestrial salt waters, 3) improve our knowledge on European saproxylic forest beetle communities, with particular emphasis on Conservation Biology of flagship species listed in the in EU Habitat Directive and in IUCN European Red Lists, and on new tools for monitoring the biological quality of forest habitats, based on beetle biodiversity.Other research activities pertain to applied evolutionary entomology and aim to: 1) outline the evolutionary relationships of the phytophagous insects associated with alien and invasive weeds, potentially able to be used as biological control agents, 2) outline the evolutionary relationships of some beetle species associated with beehives, with particular emphasis on the alien invasive small hive beetle (SHB) Aethina tumida (Coleoptera, Nitidulidae).

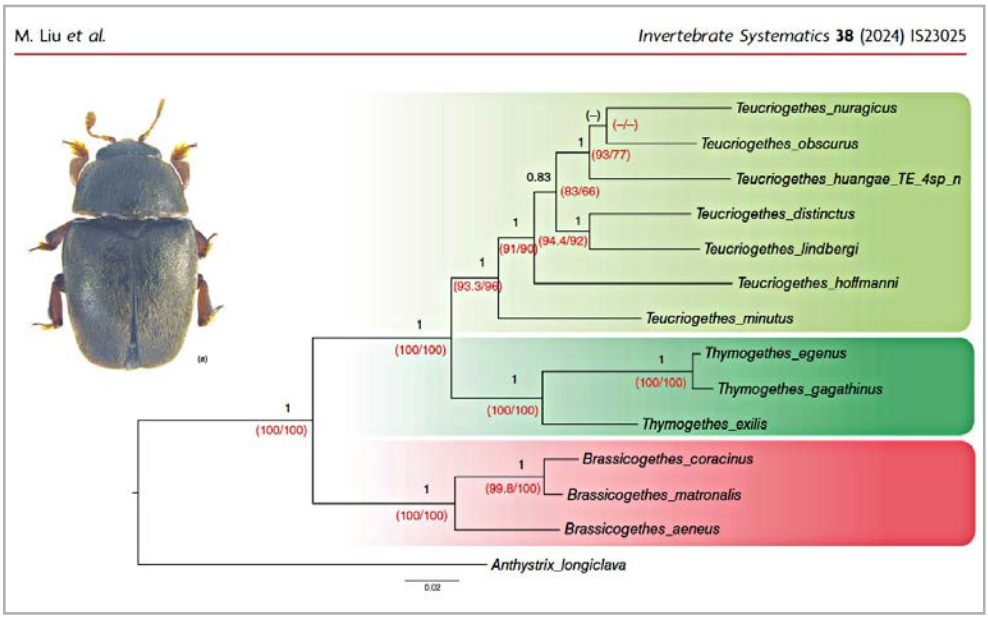


Figure. Phylogenetic interrelationships of representative members of Teucriogethes and selected outgroups based on the concatenated molecular dataset (COI, 16S, CAD, 28S) using Bayesian inference (BI) performed by MrBayes, and maximum likelihood (ML) analyses performed by IQ-TREE. The final molecular data matrix includes 15 terminals and 1904 aligned characters. See Supplementary Table S2, for details on the examined specimens. Only BI posterior probability (black) values and ML bootstrap (red) values exceeding 70% are shown.

References

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Pierfilippo
Cerretti
Associate Professor

ORCID

RESEARCH LINES

- Systematics and phylogeny
- Parasitoid community structure and diversity
- Insect diversity inventories, catalogues, checklists
- Museology, zoological collections, type material, curatorial activities

STAFF | COLLABORATORS

Aleida Ascenzi,
Post-doc (Università della Tuscia)
Andrea Cristiano,
Post-doc (Sapienza)
Michela Gabrieli,
PhD student (Sapienza)
Maurizio Mei,
Technician (Sapienza)
Dario Nania, *Post-doc (Sapienza)*
Francesco Paone,
PhD student (Sapienza)
Edoardo Pulvirenti, *MSc student and research fellow (Sapienza)*

GRANTS

PRIN PNRR2022
Improving FORest insect BIOsecurity in the era of globalization (FORBIO)
PRIN 2022
Identification of priority sites for the conservation of terrestrial animal and plant diversity to meet European and CBD 2030 targets
LIFE GOPROFOR MED

RESEARCH ACTIVITY

Since 2001 I have focused my research on the systematics, phylogeny, and evolution of Diptera, with particular emphasis on the Oestroidea (blow flies, flesh flies, and relatives). My ongoing work aims to elucidate the phylogenetic relationships and key character evolution within this clade, using both morphological and molecular approaches. A robust reconstruction of its evolutionary history is essential to develop a stable, predictive classification applicable worldwide, and to understand the evolution of diverse traits, such as reproductive strategies and host associations, in these economically important flies. In addition to these studies, I have also investigated the phylogeny and evolution of Mesozoic insects, focusing on their morphological diversity and the early evolutionary history of Holometabola.
I am deeply interested in documenting and understanding insect diversity, particularly in the face of biodiversity loss driven by the conversion of natural ecosystems into farmland and urban areas, which is a pressing concern in Europe. To this end, I have developed collaborative research lines with ecologists to study the effects of climate change, habitat loss, and fragmentation on higher trophic levels, especially insect predators and parasitoids.
Currently, I am engaged in large-scale studies on the integrative taxonomy of dark taxa, particularly Diptera and parasitic Hymenoptera, combining morphological, molecular, and ecological data to accelerate species discovery and description. In this context, I collaborate with colleagues at the Karlsruhe Institute of Technology and the Museum für Naturkunde (Leibniz Institute for Evolution and Biodiversity Science) on the development of robotic tools that implement AI-based methods for species identification, image segmentation, and biomass estimation from 2D images.

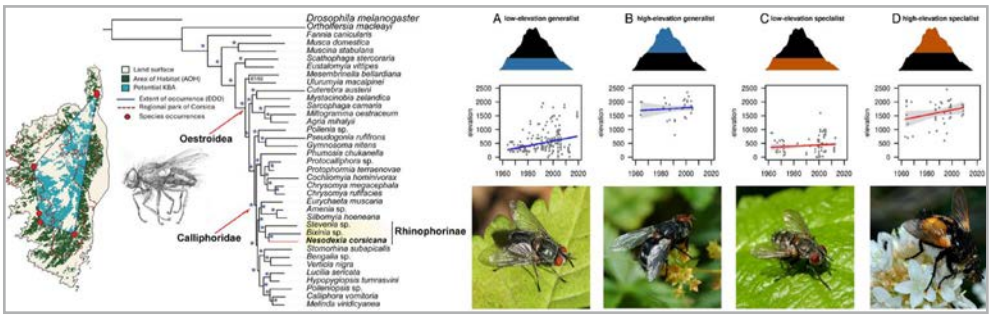

*Figure: Left. Maximum likelihoodtree of Oestroidea (Diptera) inferred using IQ-TREE version2.0.5, based on AA and NT12 matrices. Numbers at branches indicate ultrafast bootstrap support values from phylogenetic reconstructions using the AA/NT12 matrices; asterisks () indicate full support.**
Right. Temporal trend in the sampling elevation of four commonly collected bristle fly species.

Figure: Setting up a 6-meter Malaise trap at Rio Fiume (Santa Severa) during a field activity with students. Surrounding the central image are live photographs of tachinid flies.

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Claudio
Chimenti
Researcher

ORCID

RESEARCH LINES

- Diversity and new Dolichopoda species in Peloponnese
- Microclimate risk assessment in heritage quarantine spaces
- Microclimate risk assessment in heritage quarantine spaces

STAFF | COLLABORATORS

Claudio Di Russo,
Researcher (Sapienza)
Davide Tamagnini,
Researcher (Sapienza)
Domenico Davolos,
Researcher, (INAIL)

RESEARCH ACTIVITY

The three research lines emerging from our studies reflect multidisciplinary approaches to the understanding, documentation, and preservation of both biodiversity and cultural heritage.

The first line focuses on the diversity and discovery of new Dolichopoda species in the Peloponnese. Through morphological and molecular analyses, seven distinct lineages of these cave-dwelling orthopterans were identified, four of which have been described as new species. This work contributes not only to the taxonomy and biogeography of the region, but also to a deeper understanding of the evolutionary mechanisms driving diversification in subterranean environments.

The second research line centers on microclimate risk assessment in quarantine spaces for museum and library collections, with a case study in the DORA I bunker at the Norwegian University of Science and Technology. By monitoring temperature and relative humidity over a three-year period, a model was developed to evaluate chemical and biological risks affecting materials, supporting informed decisions on the safest times to introduce incoming objects into quarantine based on their composition and the selected isolation timeframe.

Finally, the third research line involves the development of protocols for 3D photogrammetry and morphological digitization of skulls, including complex specimens with tusks, antlers, or horns. This approach enables the creation of high-fidelity digital models and the extraction of geometric morphometric data for comparative analyses, opening new possibilities in the study of vertebrate functional morphology and evolution.

Together, these studies demonstrate how traditional tools and digital technologies can be effectively integrated to address issues ranging from taxonomy and preventive conservation to the digital documentation of natural and cultural heritage.

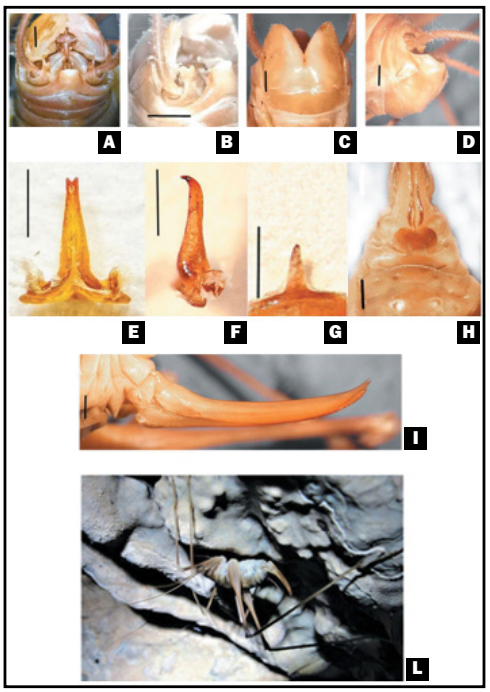

Figure 1. Dolichopoda kofinasi n. sp.: (A) male tenth tergum; (B) male subgenital plate (ventral view); (C) male subgenital plate (lateral view); (D) median process of epiphallus (dorsal view); (E) median process of epiphallus (lateral view); (F) plica dorsalis; (G) female subgenital plate; (H) ovipositor (lateral view). Scale bars: 1 mm.

Figure 2. (A) DORA I U-boat bunker with an indication of the location of the quarantine room within the building. (B) Incoming cellulose-based heritage objects stored within the quarantine room.

Figure 3. Example of single landmarking in Damaliscus lunatus (AN.CO.ac331) skull and Stratovan checkpoint main interface.

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Paolo
Ciucci
Associate Professor

ORCID

RESEARCH LINES

- Wildlife Ecology, Management, and Conservation
- Animal movement, space-use patterns, resource selection and feeding ecology
- Species-habitat relationship and species distribution models
- Sampling, assessment and monitoring of vertebrate populations

STAFF | COLLABORATORS

Aurora Donatelli
PhD student (Sapienza)
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Luigi Maiorano,
Associate Professor (Sapienza)
Nina Santostasi,
Post-doc (Sapienza)
Daniele Battilani, *Post-doc (Fondazione Edmind Mach)*

GRANTS

2022-25. EU Biodiversa+,
€ 1.354.377. PI: P. Ciucci.
2020-21. 2022-24. MUR/PRIN,
€ 264.765. PI Sapienza: P. Ciucci.
2020-21. Parco Nazionale d'Abruzzo Lazio e Molise,
€ 30.000. PI: P. Ciucci.

RESEARCH ACTIVITY

My main research interests center on wildlife ecology, including behavioral ecology and the estimation of biological and ecological parameters of wildlife populations, comprising the development and evaluation of field and estimation techniques. Although I worked with various mammal species, the main focus of my research is on the ecology of large carnivores and applied research for management and conservation, including mitigation of wildlife-human conflicts from a human dimension perspective. Research activities range from the estimation of free-ranging and feral dog populations, to the assessment of wolves and brown bears and their monitoring through time, to dietary and predation studies and investigation of species-habitat relationships to inform habitat modelling and assist conservation planning. Field and lab work entails a diversity of wildlife techniques (live-trapping, VHF- and GPS-telemetry, GPS-cluster checking, scat analysis, stable isotope analysis, non-invasive genetic sampling and hormonal essays, camera trapping, genome sequencing, 3D morphometry), and data are used to make inference at the demographic, ecological, taxonomic, genetic, and genomic domains.
Recent research has focused on the behavioral ecology of wolves and brown bears in different national parks. I am project leader of an international Biodiversa+ project on the genetic integrity of the wolf (Canis lupus) at the European scale, in light of on-going anthropogenic hybridization with dogs (project Wolfness), coordinating a consortium of 14 scientific institutions from 7 European countries. I'm also member of a PRIN project (2022), coordinated by CNR, whose main aim is to assess epigenomic and transcriptomic effects on the survival and evolutionary potential of the brown bears. Other investigations, recently conducted by my PhD students, regard the circadian activity of brown bears (A. Donatelli), the genomic legacies of recent bottlenecks in Italian wolves (D. Battilani), and modelling habitat permeability at the landscape scale for brown bears (D. Falcinelli). Research results have been translated into practical management implications, often entailing the production of guidelines and management action plans for local, regional and national administrations.

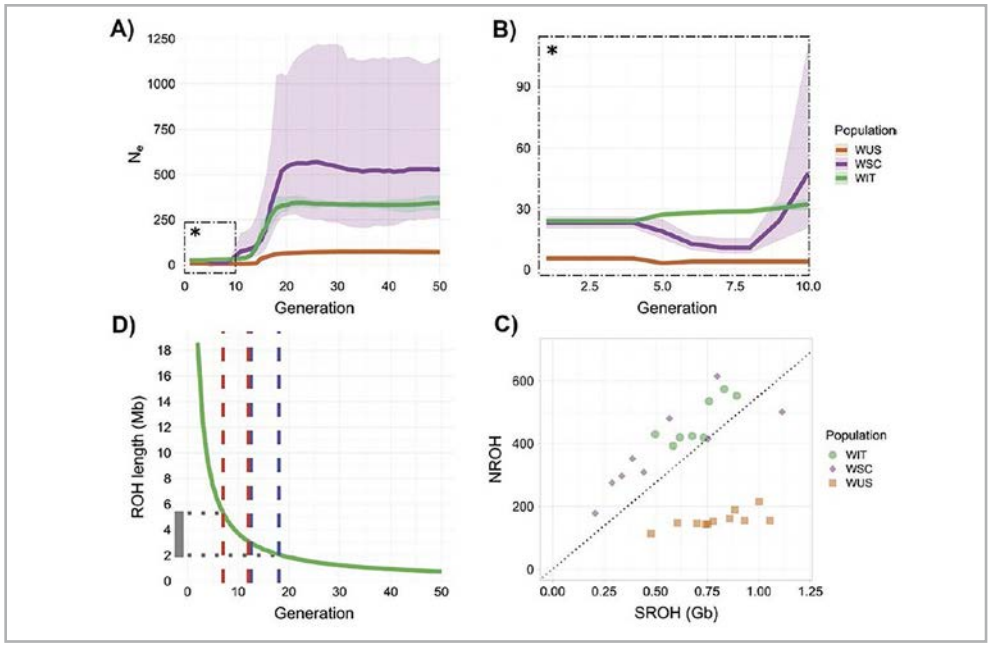

Figure. Two dimensional habitat model for brown bears in the central Apennines (Italy), developed by integrating an occurrence model (1399 bear occurrence points, 1999–2006) and a mortality risk model (37 human-caused bear fatalities, 1980–2007). A limited amount of source-like habitat appears highly fragmented by ecological traps (from Falcucci et al., J Appl Ecol 2009 46:600).

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Alessio
De Biase
Associate Professor

ORCID

RESEARCH LINES

- Investigation of patterns and driving factor of intraspecific genetic diversity in insects to better understand insect–plant interactions and support biodiversity conservation and biological control actions
- Molecular evolutionary systematics and zoogeography of Beetles

STAFF | COLLABORATORS

Serena Baini, *Post-doc (Sapienza)*
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Vincenzo Buono, *RTD-A (Sapienza)*
Carlo Rondinini,
Full Professor (Sapienza)
Matteo Montagna,
Associate Professor
(University of Naples, Federico II)
Matteo Brunetti, *Post-doc*
(University of Naples, Federico II)
Giulia Magoga, *Post-doc*
(University of Naples, Federico II)

GRANTS

2025. Project "ELIXIR x NextGenerationIT: consolidation of the Italian Infrastructure for Omics Data and Bioinformatics" Codice N° IR0000010 - Genome assembly of saproxylic beetles listed under the EU Habitats Directive and allied species of conservation interest. PI Alessio De Biase

RESEARCH ACTIVITY

I am interested in intraspecific diversity of insects, mainly phytophagous and saproxylic species, in both evolutionary contexts—concerning insect–plant relationships and the adaptive significance of genetic polymorphisms in certain groups of phytophagous beetles (Weevils; Curculionidae)—and in conservation-related issues, particularly in the prioritization of protected areas aimed at safeguarding insect species included in the Habitats Directive. I study the relationships between genetic variability and diet breadth (from monophagy to polyphagy) in certain species of Curculionidae and Chrysomelidae, also using a population genomics approach. Additionally, in the context of these studies, from 2002 to 2020 I was the principal investigator of a research project, in collaboration with the European Biological Control Laboratory (EBCL) of the USDA (United States Department of Agriculture) and the Biotechnology and Biological Control Agency (BBCA, Rome, Italy), focused on the biological control of invasive plants. We genetically characterized several natural populations of phytophagous insects to evaluate them as potential biological control agents against invasive weeds. These insect populations were biotypes associated with the target weeds and could potentially serve as sources for the release of biological control agents.
Therefore, the project was strongly based on the integration of genetic and ecological data to plan the release of these insects into the wild. Some results of this project initiated a research program aimed at understanding: a) the genetic divergence associated with the use of alternative host plants by closely related species of leaf beetles (Psylliodes spp.; Chrysomelidae) and weevils (Trichosirocalus spp.; Curculionidae), and b) possible hybridization events between host races of these beetles. Regarding the conservation aspects of insects listed in the Habitats Directive, I am working on estimating, based on both publicly available database records and newly generated data for certain saproxylic beetle species, their intraspecific genetic diversity to study its spatial distribution using geostatistical methods and to identify areas of greatest conservation interest.
I am also interested in the taxonomy and systematics of beetle groups, particularly within the families Curculionidae, Nitidulidae, Phalacridae, Scarabaeidae, Hydraenidae, and Endomychidae, from both the Palaearctic and Afrotropical regions. Resolving taxonomic and phylogenetic issues is a fundamental prerequisite for investigating these beetles from a biogeographic and evolutionary standpoint. To this end, I apply both morphological and molecular methodologies within a modern cladistic framework to infer phylogenetic relationships among the taxa under study. My biogeographic and phylogeographic work primarily focuses on analyzing beetle faunas from the Euro-Mediterranean and Afrotropical regions. Key objectives include reconstructing the palaeodynamics of colonization events and delineating biogeographically homogeneous areas, such as zoogeographic regions or districts.
I have published more than 90 scientific papers primarily on insects. I have participated and organized many trips to collect biological samples in European and African countries
Summary bibliometrics: (Scholar) 110 publications; 2647 citations; H-index 22; (Scopus): 47 publications; 879 citations; H-index: 17.

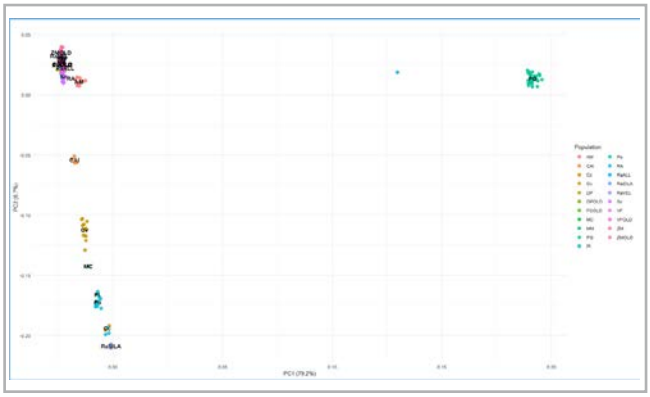

Figure: A PCA plot showing the geographical structure of the Italian population of the iconic beetle Rosalia alpina that follows the geographical distribution of beach forest inhabited by this species.

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Moreno
Di Marco
Associate Professor

ORCID

RESEARCH LINES

- Biodiversity Conservation
- Global Change Biology
- One Health

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Chiara Dragonetti, *Postdoc (Sapienza)*
Giordano Mancini, *Postdoc (Sapienza)*
Andrea Tonelli, *PhD student (Sapienza)*
Lara Marcolin, *PhD student (Sapienza)*
Michela Simeoni,
Lab manager (Sapienza)

GRANTS

2023-2026 MUR-PRIN, One Health PREPAREDness: an integrated framework to manage the risk of zoonotic disease emergence. PI, EUR 243,098
2023-2025 European Commission, Marie Skłodowska-Curie Action Postdoctoral Fellowship. Project "HUMAN-CONSERVATION". PI (Project Supervisor), EUR 172,750
2022-2026 Horizon Europe, project NaturaConnect. Local co-PI, EUR 661,683

www.biodiversitychange.com

RESEARCH ACTIVITY

I am a conservation biologist with a passion for addressing the challenges that global change poses to biodiversity. I am especially interested in developing quantitative techniques for addressing large-scale conservation problems and evaluate how the solution to these problems interact with the achievement of other societal goals (such as food production, climate change mitigation, improved human well-being). I received a PhD in Ecological Sciences in 2013, and have published >100 scientific articles since 2011, receiving >5 million EUR in research funds (>40% as PI) and collaborating with >400 researchers worldwide (source Scopus). Since 2009 I've worked for Universities, NGOs, and GOs across Europe and Australia. I am currently an Associate Prof at Sapienza University of Rome (Italy), and I serve in a number of additional roles, including the Editorial board of Conservation Biology, the Red List Scientific Committee of the International Union for Conservation of Nature, the Standards and Appeals committee of the Key Biodiversity Area programme, and many governmental research evaluation panels across Europe.
After completion of my PhD, I contributed to the definition of a new global Standard for the identification of Key Biodiversity Areas (KBA). I led a working group to demonstrate the value of complementing KBA identification with conservation planning techniques. KBAs are highly influential to inform protected area establishment and monitoring worldwide. I then moved to the University of Queensland and CSIRO (Australia) where I was part of the team unveiling the global distribution and decline of wilderness areas, and led a research project to demonstrate the importance of areas of high ecological integrity for biodiversity. My work resulted in a Nature article which informed the targets set under the UN Convention on Biological Diversity. Back in Sapienza I led or contributed to several projects aimed at understanding the environmental drivers of zoonotic disease risk. My contribution to zoonotic risk science led to several high-profile scientific articles that advanced both the thory of zoonotic disease risk and the methodologies for its prediction. I was involved in several panel discussing pandemic risk prevention strategies, eg I was Keynote Speaker at the G20 and I was involved in the Italian partnership for pandemic prevention (INF-ACT). At present, I am coordinating research on the impact of climate change on biodiversity and zoonotic risk in Europe (Fig. 1).

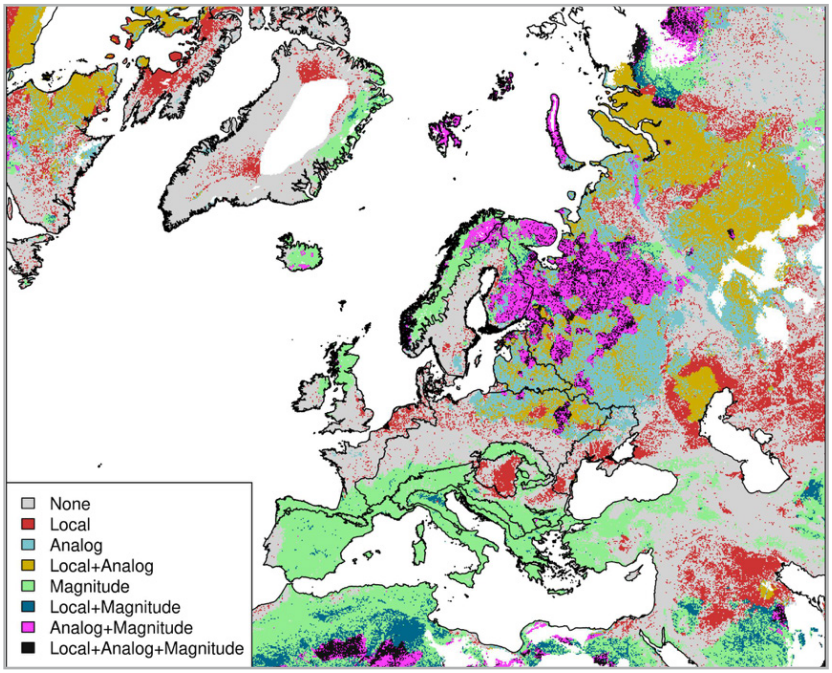

Figure 1. Overlay of high climate risk across Europe, looking at three different climate risk metrics: local velocity, analog velocity, relative magnitude. Source: Cimatti et al. (2025).

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2. Tonelli, A., M. Blagrove, M. Wardeh, M. Di Marco (2025) A framework to predict zoonotic hosts under data uncertainty: a case study on betacoronaviruses. Methods in Ecology and Evolution, 16(3): 611-624.
3. Di Marco, M., L. Santini, D. Corcos, H. Tschorsnig, and P. Cerretti (2023) Elevational homogenization of mountain parasitoids across six decades. PNAS, 120(46): e2308273120,

Luigi
Maiorano
Associate Professor

ORCID

RESEARCH LINES

- Macroecology
- Biogeography
- Global Change Biology
- Conservation Biology

STAFF | COLLABORATORS

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Assoc. Professor (Sapienza)
Moreno Di Marco,
Assoc. Professor (Sapienza)
Daniele Canestrelli,
Full Professor (University of Tuscia)
Wilfried Thuiller,
Researcher (CNRS, Zurich)

GRANTS

2022. PRIN INGEN: mapping and conserving INtraspecific GENetic diversity for endemic vertebrates in the Italian peninsula, € 280,586.
2021. LIFE21-NAT-IT-LIFE TURTLENEST - Project 101074584, €4,831,501.04
2022, NaturaConnect: building a resilient ecological network of conserved areas across Europe for nature and people. € 9,709,202.75.

RESEARCH ACTIVITY

My research aims at exploring the patterns and processes that shape species distribution in space and time, going from local to continental/global scales. I focus on various systems, considering both animals and plants, marine and terrestrial, but my main study system is focused on terrestrial vertebrates in the Mediterranean basin.

My research activities are in the field of macroecology, focusing particularly on assessing the impacts of past and future global changes on biodiversity. I'm also interested in conservation biology and wildlife management, always considering the spatial components of complex research problems. I'm currently involved in research projects spanning the macro-ecology of trophic interactions for terrestrial vertebrates in Europe, ecosystem services in the Atlantic Ocean, protected areas in Europe, and intraspecific genetic diversity in Italy. In the last few years I have been exploring the evolutionary component of terrestrial biodiversity, focusing on the contribution of macroecology to macroevolution as well as on the impact of climate change on species hybridization.

In particular, I'm working on the detection of evolutionary trends in mammalian carnivores and ungulates using 3D-morphometry of both existing and fossils species. On the other side I'm using hybridization to explore the paradox of the tyranny of the golden mean. In many areas of the life sciences differences between individuals, although ubiquitous in natural populations, are commonly summarized within descriptive statistics. This blurs the role played by non-average individuals, potentially biasing our appreciation of the process under study.

In a collaborative study, I will address this gap by focusing on the role of inter-individual differences in hybridization dynamics. Hybridization in a perfect window to study this paradox, since it is at the same time a fundamental step of major evolutionary processes, a consequence of global changes, and one of the main triggers of their outcomes.

Figure. Interspecific hybridisation between the common toad (Bufo bufo) and the green toad (Bufotes balearicus) in the wild. As a consequence of global changes, two species separated by 30 million years of evolution get in sympatry and form hybrid pairs. All tadpoles were heavily malformed, and none survived until metamorphosis. Photo: M. Zampiglia.

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Emiliano
Mancini
Associate Professor

ORCID

RESEARCH LINES

- Phylogeny and biogeography of insects
- Population and conservation genetics
- Molecular evolution
- Evolutionary parasitology

STAFF | COLLABORATORS

Paolo Audisio,
Full Professor (Sapienza)
Alessandra della Torre,
Full Professor (Sapienza)
Liliia Baikova,
PhD student (Sapienza)
Carlos D. Vecco Giove,
Entomologist *(UNSAM)*

GRANTS

Sapienza - Bando di Cooperazione 2022 (PVS) - "Progettare un futuro per la meliponicoltura e le api native del perù", € 25,000.
PROCIENCIA - Proyectos de Investigación Básica 2023, Peruvian Ministry of Education
"Modelo transdisciplinar para la comprensión de la diversidad clave de las abejas peruanas sin aguijón (Hymenoptera: Apidae: Meliponini) con fines de conservación y el desarrollo de una meliponicultura competitiva en la Amazonia", € 280,988 .

RESEARCH ACTIVITY

My research activities - carried out through field collections, fauna monitoring techniques, morphological/ecological investigations, genetics/genomics methods - deal with some of the main themes of evolutionary biology and are all framed in the field of entomology.

Current research lines aim to:
1) outline the phylogeny and biogeography of insects (coleoptera and hymenoptera) by integrating ecological monitoring, DNA barcoding and conservation genetics;
2) unravel the biological factors favouring - and maintaining over time - the interaction among phytophagous insects and their host plants by taking into account their parallel evolution and microbiome component;
3) understand - through chemical ecology and transcriptomics - the ecological role and metabolism of cantharidin, a defensive terpene of blister beetles owning a great potential in medicine and crop-protection.

Other research activities pertain to evolutionary parasitology and medical entomology and aim to:
1) outline the evolution of Anopheles mosquito genetic traits (in reproduction and immunity) mostly influencing the transmission of malaria in Sub-Saharan Africa;
2) detect the genetic/genomic consequences on malaria transmission of the hybridization process occurring in West Africa between the two main malaria mosquito vectors (A. gambiae and A. coluzzii);
3) examine the evolution of emerging insecticide resistance mechanisms in mosquito populations (Anopheles and Aedes) to tackle their possible consequences on the spread of vector-borne diseases.

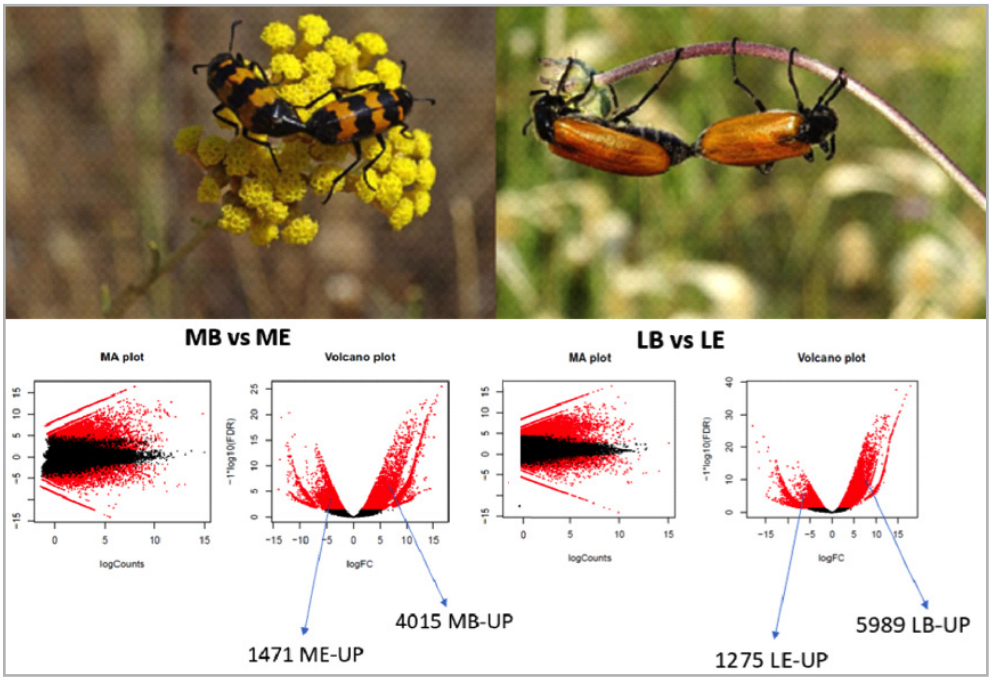

Figure. Upper panel: Mylabris variabilis (left) and Lydus trimaculatus (right) feeding and copulating on their host plants. Lower panel: "volcano plots" from transcriptomic analyses showing the number of differentially expressed genes in the exuded haemolymph containing the toxic terpene cantharidin in Mylabris variabilis (left, ME UP) and Lydus trimaculatus (right, LE UP).

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Marco
Oliverio
Full Professor

ORCID

RESEARCH LINES

- Taxonomy, systematics and biogeography of molluscs
- Population genetics/genomics
- Microevolutionary processes and larval ecology of marine invertebrates
- Animal associations
- Molecular Evolution

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GRANTS

COREBIOM (AICS)
Co-PI: Fabio Attorre (Sapienza),
€ 261,000.
TRADE (PRIN-PNRR)
Co-PI: MV Modica (SZN),
€ 66,000.

RESEARCH ACTIVITY

My whole research activity is bound by the fil-rouge of the evolutionary perspective. This results in a primary interest in the Evolutionary Biology of molluscs, with a focus on: Integrative Taxonomy, Phylogeny, Biogeography, Population genetics/genomics (spatial patterns of variation, divergence rates), Molecular evolution (biochemical drivers of evolution), Microevolutionary processes, Biodiversity (patterns and dynamics), evolutionary developmental biology.
I am currently focused on the evolutionary biology of Neogastropoda, with a special emphasis on the phylogeny of this group, on the Integrative Taxonomy of some families (Muricidae, Columbellidae, Raphitomidae, Colubrariidae, Mitridae), and on the diversification of the trophic specializations at the various levels (ecological, anatomical, biochemical). In particular, I am using transcriptomic comparative approaches to address the role of biochemical drivers in the evolution of haematophagous and corallivorous groups (Colubrariidae; Coralliophilinae), with remarkable bioprospecting outputs.
I am also interested in the role of the ecological associations between different species of animals (mutualistic and parasitic symbioses), in shaping the current patterns of biodiversity in the involved groups. I am currently studying gastropods parasitically associated to cnidarians (Calliostomatidae; Ovulidae; Epitoniidae; Coralliophilinae; Architectonicidae), echinoderms (Eulimidae), other molluscs (Capulidae), ascidians (Velutinidae).
Since genetic connectivity plays a crucial role in shaping the geographic structure of species, I am studying marine gastropods as excellent models for testing the influence of pelagic larval dispersal on genetic structure. In gastropods the developmental type (long v. short pelagic phase) can be inferred from the morphology of the embryonic and larval shells. I am contrasting closely related species with opposite larval development, in several families, to test the hypothesis that long lasting dispersal yields higher connectivity over long distances, and short dispersal produces isolation-by-distance patterns.
I have published over 180 scientific papers (mostly on molluscs, but also on insects and vertebrates). I have participated in and/or organized dozens of collecting expeditions at many distinct localities (from the SW Pacific to the Indian Ocean, from the Mediterranean Sea to the Antarctic) shore-based and onboard international research vessels, logging more than 2000 SCUBA dives.

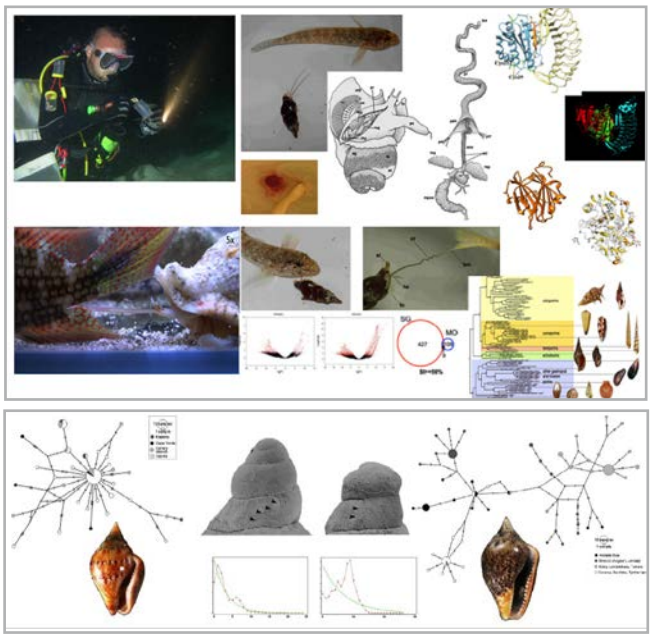

Figure. Upper panel. The vampire snail Cumia reticulata *and its biochemical weaponry. From sampling specimens, to the study of the molecules in its venomous cocktail, their evolution and physiological role. Lower panel. Genetic connectivity in two species with opposite larval development: left,* Columbella adansoni, *with long lasting pelagic larva; right,* C. rustica, *with short dispersing larva. Haplotypes (COI) networks and spatial PCA showed significant differences, with isolation-by-distance and a global structure in* C. rustica *vs high connectivity and no geographic structure in* C. adansoni.

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2. Fedosov A.E., Zaharias P., Lemarcis T., Modica M.V., Holford M., Oliverio M., Kantor Yu.I., Puillandre N. 2024. Phylogenomics of Neogastropoda: The Backbone Hidden in the Bush. Systematic Biology, 73(3): 521–531.
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Michela
Pacifici
Researcher Tenure Track

ORCID

RESEARCH LINES

- Impact of global changes on species
- Protected areas effectiveness
- Identification of Key Biodiversity Areas
- Species conservation targets

STAFF | COLLABORATORS

Marco Davoli, *Researcher (Sapienza)*
Andrea Cristiano,
Researcher (Sapienza)
Alessandra D'Alessio,
Researcher (Sapienza)
Piero Visconti, *Researcher (IIASA)*
Alessandro Chiarucci, *Full Professor (University of Bologna)*
James Watson, *Professor (University of Queensland)*

GRANTS

2022-2026 Horizon Europe "NaturaConnect - Italian PI: Michela Pacifici 661,683 €
2023-2026 Biodiversa+ "GaP: Guiding expansion of protection under the EU Biodiversity Strategy. Italian PI: Michela Pacifici 199,100 €
2024-2025 ISPRA "Attività di revisione di parametri ambientali, sulla base dell'aggiornamento dei metodi di monitoraggio marino costieri, a supporto dell'Integrated Monitoring and Assessment Programme (IMAP). 82,000 €

RESEARCH ACTIVITY

I am a conservation biologist whose research is deeply focused on unraveling the complex drivers behind biodiversity loss and developing innovative, science-based tools to support effective wildlife conservation. My work is distinguished by the integration of large-scale species distribution data with advanced spatial analyses and cutting-edge modelling techniques, which collectively enable a detailed and nuanced understanding of the multifaceted impacts of habitat loss, climate change, invasive species, and various human-induced pressures on terrestrial vertebrate fauna, with a particular emphasis on mammals.

I am also the chair of the Italian National Coordination Group for Key Biodiversity Areas (KBA), a critical initiative aimed at identifying and protecting the most biologically important sites across the country. Through this project I contribute to ensuring that decisions are informed by the best available science and that they align with both national and international biodiversity targets.

Furthermore, I led two projects on favourable reference values for biodiversity assessments at multiple scales, including both European and Italian levels. These benchmarks are crucial as they establish scientifically grounded standards for evaluating the status of biodiversity, enabling policymakers and conservation practitioners to measure progress and implement effective management strategies. By contributing to these foundational frameworks, I support the creation of robust, evidence-based conservation policies that can withstand scientific scrutiny and drive real-world positive outcomes for biodiversity.

Current research lines of my lab include the development of the first spatially explicit information on the areas most at risk due to illegal hunting globally, and the analysis of how threats distribute across mammalian taxonomic groups and how these correlate with functional rarity. Finally, I am exploring the impacts of renewable energy transition on biodiversity and the effects of the decommissioning of carbon plants on species habitat.

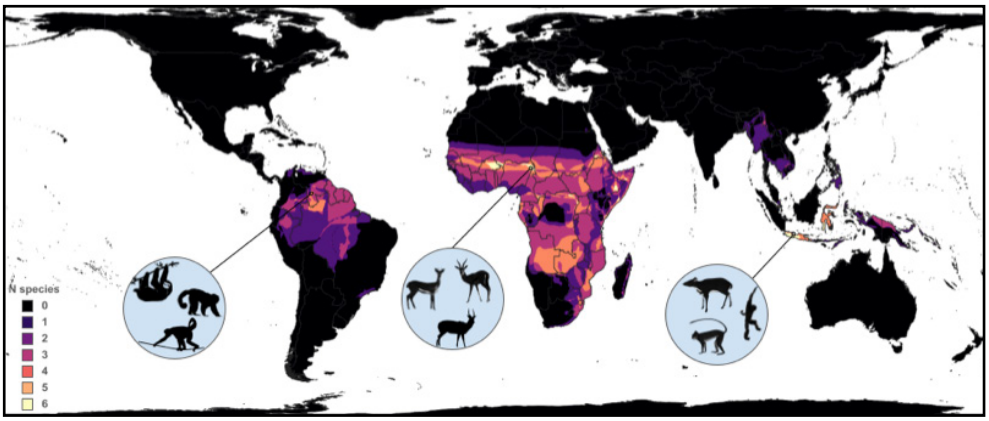

Figure. Emerging risk of bushmeat hunting. Number of new species that could become hunted for bushmeat in 2050 if socio-economic conditions change. Areas in yellow are hotspots of emerging risk.

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3. Pacifici, M., Rondinini, C., Rhodes, J. R., Burbidge, A. A., Cristiano, A., Watson, J. E., ... & Di Marco, M. (2020). Global correlates of range contractions and expansions in terrestrial mammals. Nature Communications, 11(1), 2840.

Carlo
Rondinini
Full Professor

ORCID

RESEARCH LINES

- Global species distributions
- Global species extinction risk
- Global biodiversity scenarios

STAFF | COLLABORATORS

Michela Pacifici, *RTT (Sapienza)*
Nina Luisa Santostasi, *RTDA (Sapienza)*
Noemi Spagnoletti, *Post Doc (Sapienza)*
Piero Visconti, *Research Group Leader at IIASA*
Henrique Pereira, *Head of Research Group, iDiv Speaker*
Franz Essl, *Professor (Univ.of Vienna)*

GRANTS

2022. Horizon NaturaConnect
€ 661,682.50 at Sapienza,
PI Michela Pacifici, Moreno Di Marco, Luigi Maiorano, Carlo Rondinini, Luca Santini
2022. MUR PNRR, € 328.217.375,39 (€ 9.801.918,34 at Sapienza, 2.901.917,34 at Spoke 4) Sapienza
PI Prof. Marco Oliverio,
Prof. Carlo Rondinini
2023. IUCN Knowledge-4-Nature: Provisioning the biodiversity data behind global goals for nature.
€ 49,850.00 at Sapienza,
PI Prof. Carlo Rondinini
2024. Enel Green Power S.p.A.
Collaborazione su tematiche di ricerca in ambito biodiversità.
€ 200,000.00, PI Prof. Carlo Rondinini

RESEARCH ACTIVITY

My research focuses on species distribution, extinction risk, conservation prioritization, biodiversity scenarios, invasive alien mammals, and protected area effectiveness. My lab models the distribution of terrestrial vertebrates — including mammals, amphibians, and birds — at regional to global scales using the concept of Area of Habitat (AOH), which represents the habitat available to a species within its geographic range (Brooks et al., 2019).
In partnership with the IUCN (International Union for Conservation of Nature), my Lab coordinates the global program monitoring the extinction risk of all mammal species. This involves collaboration with thousands of experts organized into 35 Specialist Groups, who assess extinction risk and publish the results on the IUCN Red List. These assessments provide policy-relevant indicators for multilateral environmental agreements, including the Convention on Biological Diversity (CBD) and the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES).
My lab assesses protected area effectiveness[1] and identifies priority conservation sites and actions based on spatial analyses of biodiversity distributions and threats. To support scenario-based conservation planning, the GMA Lab has developed the InSiGHTS modelling framework, which evaluates the impacts of socio-economic development pathways, policy interventions, land-use changes, and climate scenarios on biodiversity outcomes[2],[3].

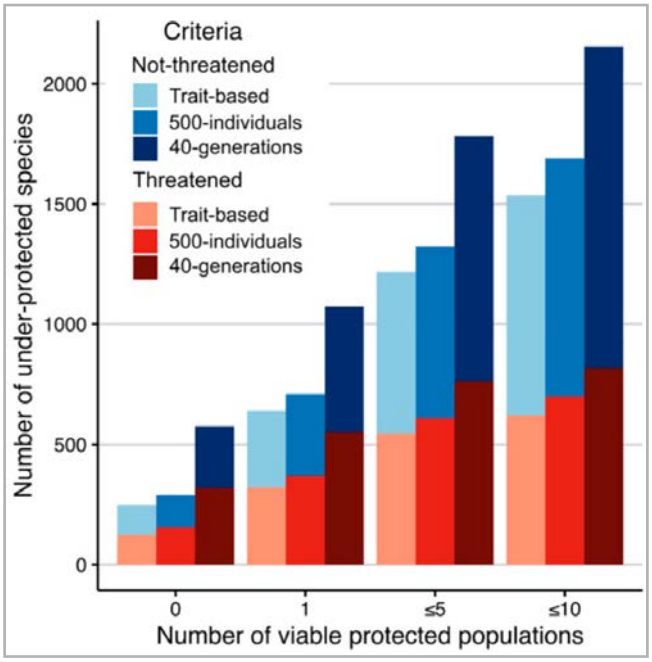

Figure. Based on connected Minimum Viable Area for terrestrial mammals inside the global protected area network, half of the mammals and most threatened mammals may be under-protected[3].

Current research integrates:
- Spatially explicit models of future AOH, based on land-use and climate change projections.
- Forecasts of species responses to global environmental change, including population trends and distribution shifts.
- Assessments of current and projected impacts of biological invasions on global biodiversity.
- Conservation prioritization, combining species distribution, threat mapping, and scenario modelling to inform effective conservation strategies.

Through these approaches, the GMA Lab provides critical scientific insights that support evidence-based conservation policies, global biodiversity monitoring, and the implementation of international conservation agreements.

References

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2. Pereira, H.M., Rondinini, C. et al., 2024. Global trends and scenarios for terrestrial biodiversity and ecosystem services from 1900 to 2050. Science, 384(6694), pp.458-465.
3. Williams, D.R., Rondinini, C. and Tilman, D., 2022. Global protected areas seem insufficient to safeguard half of the world's mammals from human-induced extinction. Proceedings of the National Academy of Sciences, 119(24), p.e2200118119.

Luca
Santini
Associate Professor

ORCID

RESEARCH LINES

- Macroecology
- Conservation biogeography
- Functional ecology
- Animal Ecology
- More on www.ecaslab.com

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Daniele Saracino, *PhD (Sapienza)*
Matteo Giuliani,
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GRANTS

2023-2025 – PRIN - PI
"UrBiS - Biogeography of urban green spaces: direct and indirect drivers of biodiversity and ecosystem services in Rome", € 231,462.

RESEARCH ACTIVITY

My research focuses on ecological patterns and processes acting at different spatial, temporal and taxonomic scales to derive general principles that explain how life on earth is distributed and structured. Scales span from urban areas up to global scales, from single species to community dynamics.. A recurrent theme in my research is unravelling how such patterns and processes have been altered by anthropogenic pressures, to estimate natural baselines and get a deeper insight on the ongoing reorganization of biotic systems. I'm particularly interested in macroecological patterns of abundance across vertebrate species, and processes underlying them. To this end, I have created the TetraDENSITY database, which includes tens of thousands of dated and georeferenced population density estimates from the literature. Important applicative sides of my research consist in the integration of macroecological and biogeographical principles into biodiversity and conservation assessments, with the ultimate goal of reducing our dependency on species-level information by focusing on general ecological principles and species functional differences. Specifically, by understanding biodiversity patterns and their causes, I attempt to use existing biodiversity knowledge to infer missing information on poorly known species and areas that are relevant for conservation assessments and planning. A practical example is the development of semi-automated approaches to assess species conservation status in a rapid and cost-efficient manner. A practical example is sRedList project which led to the development of the sRedList platform for extinction risk assessments (sredlist.org). I believe in the potential of big data to deepen our knowledge beyond the specifics of local case studies, and I rely on a variety of statistical, machine learning, and meta-analytical approaches, and to address both theoretical and applicative questions. I strongly support "predictive ecology", not only as an important tool for conservation biology, but also as a proof of concept of our understanding of ecological dynamics.
I also make a large use of ecological simulations in order to explore ecological mechanisms, test methodological approaches on virtual species, and assess possible outcomes of human actions. More recently I started exploring several novel approaches for biodiversity monitoring in the field, spanning from camera trapping to passive acustic recorders, and the use of AI to support data processing.

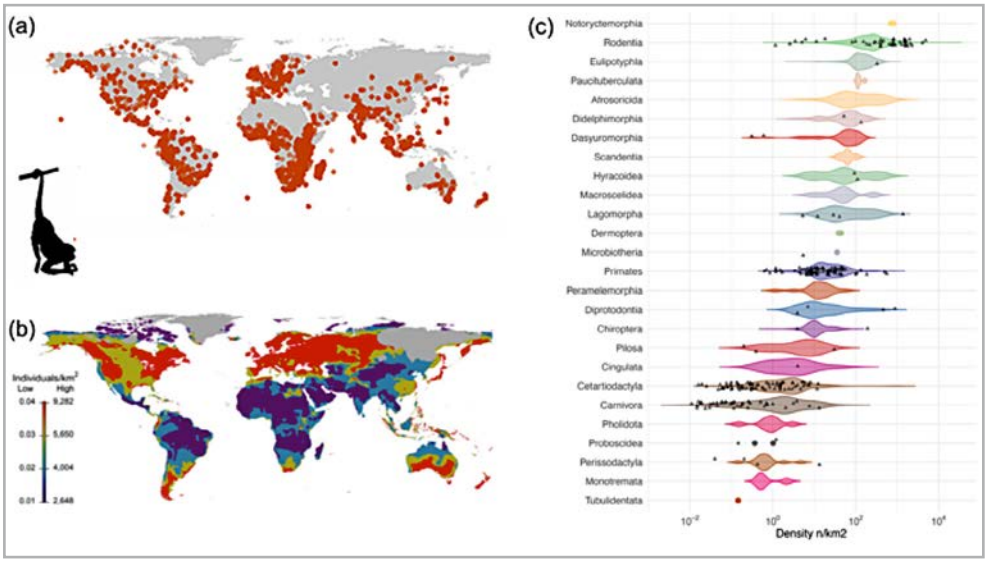

Figure. (a) Distribution of population density estimates for terrestrial mammals from the TetraDENSITY database (Santini et al. 2018a Glob Ecol Biogeog 10.1111/geb.12756); (b) Global prediction of how average population density in mammals scales with climatic conditions (Santini et al. 2018b Glob Ecol Biogeog 10.1111/geb.12758); (c) Distribution of population density predictions for all mammal orders (Santini et al. in prep).

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2. Cazalis V., [...], Santini L. 2024. Accelerating and standardising IUCN Red List assessments with sRedList. Biological Conservation 298: 110761
3. Santini L., Tobias J., Callaghan C., Gallego-Zamorano J., Benítez López A. 2023. Global patterns and predictors of avian population density. Global Ecology and Biogeography 32(7): 1189-1204

RESEARCHERS FIXED-TERM | RTDA

Adriano SETTI

PHISIOLOGY | SSD BIOS-08/A

ORCID

Project 1. RNA-RNA interactions.
Project 2. RNA subcellular localization.
Project 3. Phase-separation mechanisms in neurodegeneration.

Mattia LA TORRE

GENETICS | SSD BIOS-14/A

ORCID

Project 1. Aging and cancer.

Alessandra Maria BISSATTINI

ZOOLOGY | SSD BIOS-03/A

ORCID

Project 1. Gimme shelter: insights into the role of artificial aquatic sites for amphibian conservation and future directions of management.
Project 2. How you doing? Conservation status of amphibians under different protection measures.

Vincenzo BUONO

ZOOLOGY | SSD BIOS-03/A

ORCID

Project 1. Population and landscape genomics analysis for the conservation of threatened saproxylic beetles

RESEARCHERS FIXED-TERM | RTDA

Giulia FASSIO

ZOOLOGY | SSD BIOS-03/A

ORCID

Project 1. Evolutionary biology, molecular systematics, and integrative taxonomy of invertebrates, with a particular focus on marine molluscs

Simone SABATELLI

ZOOLOGY | SSD BIOS-03/A

ORCID

Project 1. COREBIOM. Conservation and Renovation for Biodiversity in Mozambique" AID 12042- Coordinator of Terrestrial Zoology Research.
Project 2. International Cooperation project (PVS 2023)- Support to Mozambican institutions in detection and monitoring of the agricultural invasive insect pests: training through an integrated surveillance approach- PI
Project 3. Roma Natura - Biodiversità Insugherata. SCM BBCD
Project 4. BioScan Europe -Biodiversity Genomics Europe. SCM BBCD

My research activities focus on evolutionary biology, systematics, taxonomy, biogeography, molecular ecology, population and conservation genetics applied to the study of invertebrates, particularly insects, using an integrated approach combining morphological, ecological, and genetic/genomic methods, field sampling, and faunistic monitoring techniques. Since 2016, I have been involved in the Italian Agency for Development Cooperation program (Projects AID10524, AID11096, AID012089, and AID12042) supporting environmental research, biodiversity conservation, and biotechnology in Mozambique.

Nina Luisa SANTOSTASI

ZOOLOGY | SSD BIOS-03/A

ORCID

Project. Systematic Conservation Planning to Support Italy's Protected Areas Network Expansion Under the EU 30x30 Target

Davide TAMAGNINI

ZOOLOGY | SSD BIOS-03/A

ORCID

Project. Eco-evolutionary perspectives and applications deriving from natural history museum digitization and open-access datasets.

EMERITUS PROFESSOR

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Luigi BOITANI — **ZOOLOGY** | SSD BIOS-03/A

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Full professor of Comparative Anatomy.

EMERITUS PROFESSOR

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