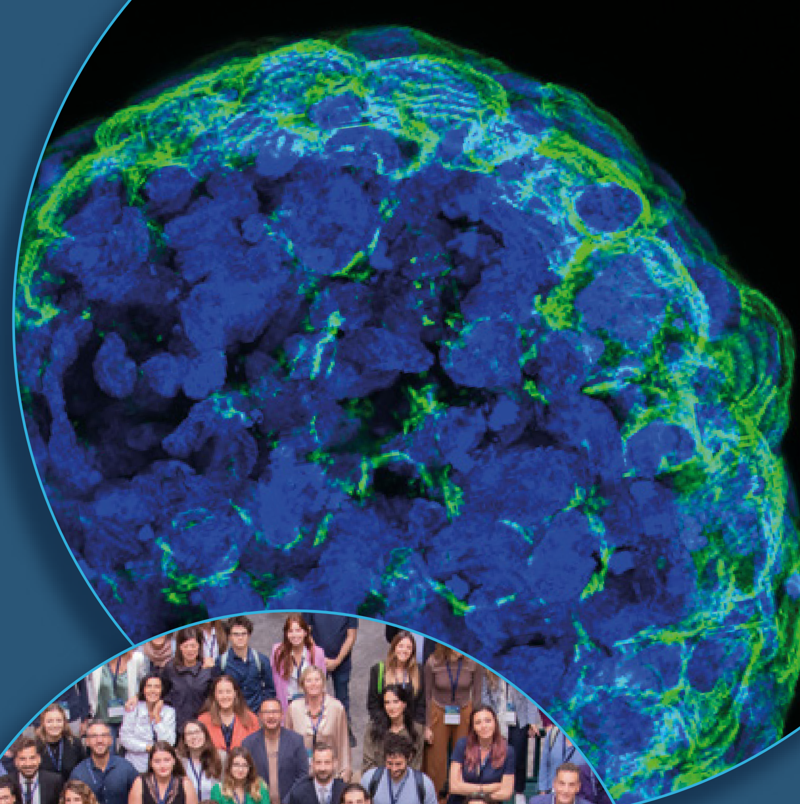
Fondazione
Ri.MED



ANNUAL REPORT 2024

Fondazione Ri.MED

FOUNDING PARTNERS

Presidenza del Consiglio dei Ministri

Regione Siciliana

Consiglio Nazionale delle Ricerche

University of Pittsburgh

UPMC
LIFE CHANGING MEDICINE

PARTNER

UPMC | IRCCS ISMETT
Palermo

Paolo Aquilanti
PRESIDENT AND CEO

I am proud to share the significant progress we have achieved across multiple fronts: from research, training, and scientific outreach, to the continued advancement of the construction of our new
Research Center. These accomplishments have been made possible thanks to the steadfast support of our founding partners: the Presidency of the Italian Council of Ministers, the Region of Sicily, the Italian National Research Council (CNR), the University of Pittsburgh (UP), and the University of Pittsburgh Medical Center (UPMC).

Ri.MED continues to grow steadily. New professionals have joined us, reinforcing our research teams, technology platforms, and project development capacity. In 2024 alone, the Foundation hosted 24 research fellows, 31 PhD students, and 27 trainees.
Our strong commitment to human capital development is also reflected in the implementation of the Gender Equality Plan, a key instrument to foster equal opportunities, support work-life balance, and eliminate all forms of discrimination. Investing in talent and advanced training is central to our mission and contributes to enhancing regional competitiveness.

Our 2024 International Symposium on "Nutrition, Microbiome and Metabolism" was a major success, drawing participants from 11 countries and receiving highly positive feedback.
This edition introduced new features such as a poster session, offering researchers a platform to present and discuss their work.

The public panel "Food, Health, and Society" further highlighted the strong links between human and environmental health, reaffirming nutrition as a critical pillar of future research at the upcoming Ri.MED Center in Carini.

Our outreach efforts have expanded as well. In January, Ri.MED signed a strategic agreement with the Regional School Office for Sicily and the Regional Department of Education and Professional Training. This collaboration supported for a wide-reaching program of educational activities, acknowledging the growing importance of biotechnology and Ri.MED's pivotal role in promoting scientific culture throughout Sicilian schools.

Our research network is becoming increasingly competitive. In 2024, nine new agreements were signed, bringing the total number of active collaborations to 55, spanning leading institutions in Europe and the United States.

Thanks to the outstanding work of our researchers and the Grants Office, Ri.MED secured €3,152,671 in funding from national and international grants this year, and substantial effort has been invested in preparing further applications for future opportunities.

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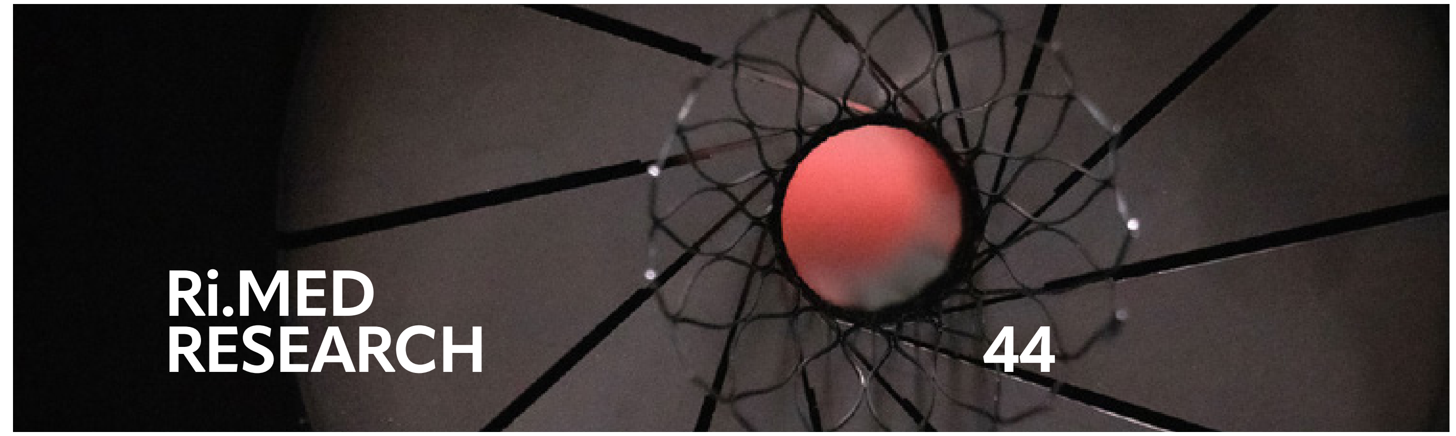

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Ri.MED OVERVIEW 2024

Networking

7 active agreements for labs management

55 active scientific collaborations and technology transfer agreements

9 new agreements signed in 2024

Training & employment

HUMAN RESOURCE in 2024

79 employees

62%

38%

24 fellows

31 Ph.D. students

27 trainees

Scientific knowledge dissemination

123 hours of training in schools

5 Ri.MED events

75 scientific papers

Fundings for Research

3,152,671 € awarded through national and international GRANTS in 2024

Intellectual property

32 patents portfolio up to 31.12.2024

Building the Research Center

600 planned occupancy opportunities

17,070 sq m of laboratories

220,000,000€ value of the investment

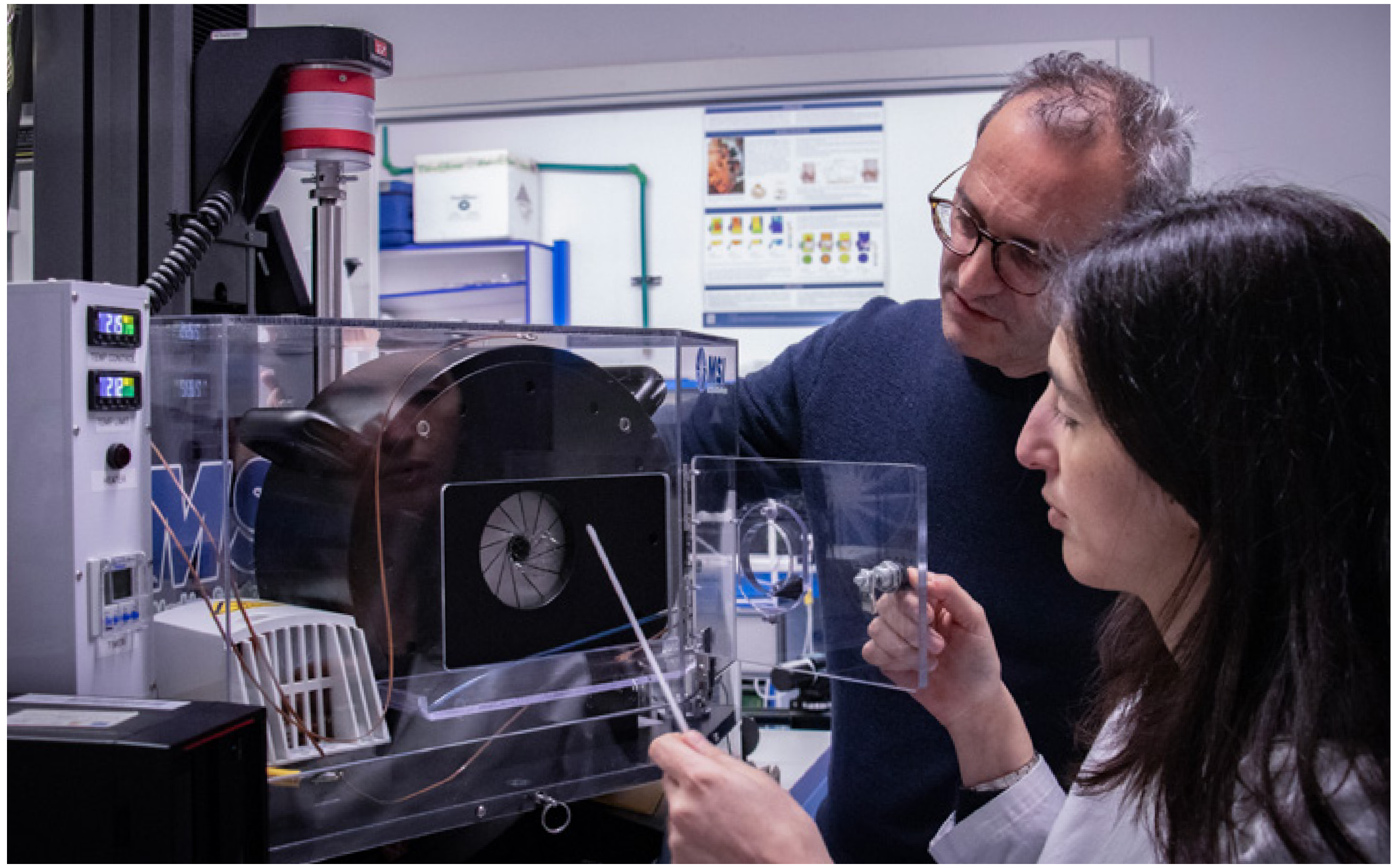
HUMAN RESOURCES

NURTURING NEW TALENTS

Ri.MED is committed to training highly qualified professionals, recognizing their crucial role in driving scientific excellence and fostering the competitiveness and growth of the region. To support this mission, the Foundation offers a range of training programs, some in partnership with the University of Pittsburgh, while others are funded through EU programs, ministerial grants, and regional initiatives.

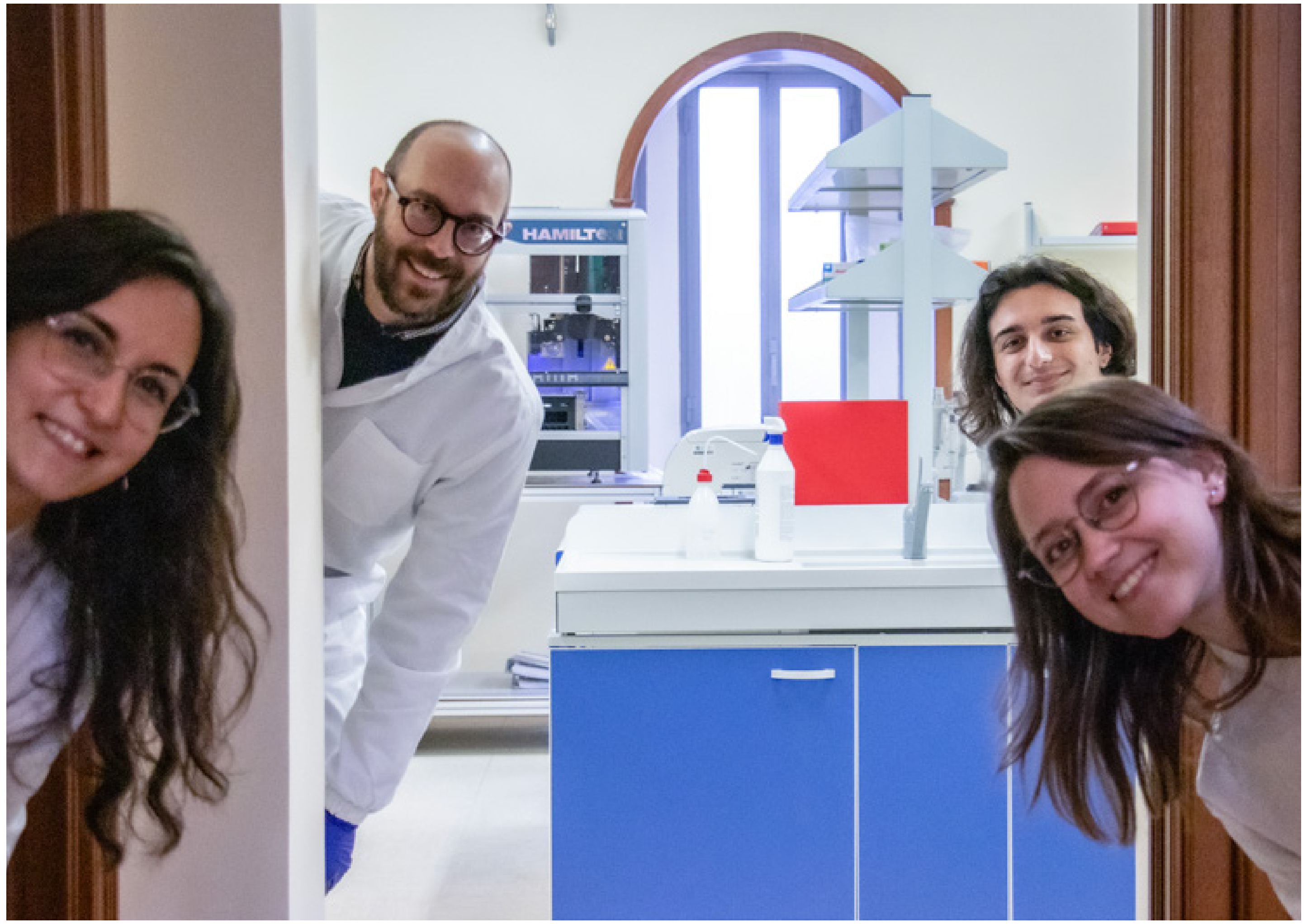
In 2024, interest in Ri.MED's training opportunities surged, reflected in a rise in PhD and internship applications. Over the year, the Foundation activated 24 scholarships, hosted 31 PhD students and offered 27 internships. These programs provide young professionals with valuable hands-on experience and skill development. Additionally, fellowships and research grants support researchers at all career stages, enabling them to advance their professional paths at Ri.MED.

By attracting talented young scientists, Ri.MED continues to establish itself as a leading center of scientific excellence, nurturing the next generation of biomedical innovators.



HUMAN RESOURCES

GROWING TOGETHER



In 2024, the Ri.MED Foundation successfully completed 27 recruitment procedures, 25 dedicated to research. Over the year, the Foundation's team reached 161 members, including employees and fellows, with 122 researchers at its core.

Ri.MED is not only fostering local talent but also attracting global expertise. 20% of its researchers are Sicilians who returned home for the professional opportunities the Foundation provides, while 13% come from other parts of the world, reinforcing Ri.MED's growing international reputation.

In 2022 Ri.MED was recognized as an authorized research institutions issued by the Italian Ministry of University and Research (MUR) to host researchers from nonEU countries. International vision has always been the strategy of Ri.MED, also thanks to the partnership with the University of Pittsburgh and UPMC, to offer researchers rotations in top scientific institutions, in line with the EU recommendations on mobility of scientific research as a means of developing research networks and consolidating the role of European research at a global level.

With the upcoming opening of Ri.MED's new research center in Carini, near Palermo, and the support of new research funds, the Foundation is set for further expansion. In the coming years, Ri.MED will continue to grow its research teams and solidify its role as a premier international host institution.

Ri.MED OVERVIEW

HUMAN RESOURCES

WOMEN IN SCIENCE & GENDER EQUALITY PLAN

2024 was the second year of the Gender Equality Plan (GEP) at Ri.MED, a key initiative aimed at strengthening the gender perspective in the design, review and implementation of internal policies, training contents and research activities.
At the beginning of the year, a Memorandum of Understanding for the fight against discrimination, sexual harassment and mobbing was signed with a local association (Co.Tu.Le Vi.), offering specialized staff and a dedicated telephone line h24, inaugurating an independent tool available for all Ri.MED workers.

To achieve gender awareness raising objectives, from April to October 2024, all Ri.MED staff participated in 18 hours of training on targeted gender topics, such as: gender stereotypes and biases, the gender pay gap, strategies to promote equality and work-life balance, the use of gender-neutral language, and violence in the workplace.
Furthermore, recurrent monitoring activities have been executed, as the biannual data collection on workforce composition, salaries, and employee's role.

In 2024, Ri.MED also hosted the event "Valuing Gender Diversity in R&D to Enhance Scientific Impact", featuring an outstanding talk by Vera Regitz-Zagrosek: "Gender Medicine: A Prerequisite for Precision Medicine". This event highlighted the importance of the gender dimension in all scientific research projects to achieve more robust results able to incorporate any possible difference between men and women, to finally further the goal of personalized and precision medicine.

A good-balanced gender workforce in Ri.MED was recorded also in 2024, with an equal gender distribution in both research and administrative area, represented by around 62% of women and 38% of male. A promising data given the underrepresentation of women STEM researchers within Europe.
We take pride in our brilliant and skilled women!

DISSEMINATION OF SCIENTIFIC KNOWLEDGE

Ri.MED SYMPOSIUM

As part of its mission, the Ri.MED Foundation actively engages in scientific dissemination and the sharing of research outcomes. The 2024 Ri.MED Scientific Symposium was "NUTRITION, MICROBIOME AND METABOLISM – A science based multidisciplinary Symposium to explore cutting-edge research and nutritional health" – was held on October 17th and 18th, 2024 in Palermo.

This meeting brought together a panel of internationally recognized researchers for a two-day meeting to address the future of health through food. The event was chaired by Giulio Superti-Furga, Scientific Director of the Ri.MED Foundation and Director of CeMM (Austria); Maria Rescigno, Full Professor and Deputy Rector at Humanitas University; Benoit Chassaing, Group Leader at Institut Pasteur; Massimo Pinzani, Scientific Director of IRCCS ISMETT and Professor of Medicine at University College London; and Timothy R. Billiar, Chief Scientific Officer at UPMC.

The 2024 edition introduced new features aimed at enhancing scientific exchange and networking opportunities. A poster session was included, allowing researchers to showcase their work and engage in discussions with peers. Additionally, the social event "Sharing Culture Through Food," held at the historic Palazzo Asmundo, offered a new and fascinating perspective on food as a vehicle for cultural sharing, with the contribution of the food writer Saghar Setareh.

The symposium attracted participants from eleven different countries and received highly positive feedback. Its visibility was further strengthened by a media partnership with MicrobiomePost.com.
The Foundation's press office contributed in disseminating key research findings to a broader audience, ensuring that scientific advancements reached both the academic community and the general public. These efforts align with Ri.MED's commitment to fostering knowledge exchange, strengthening international collaborations, and promoting awareness of scientific progress

DISSEMINATION OF SCIENTIFIC KNOWLEDGE

PUBLIC ENGAGEMENT

Engaging and inspiring a diverse audience remains one of Ri.MED's top priorities. Through a comprehensive public engagement program, developed in collaboration with local institutions, Ri.MED aims to reach people of all ages. In 2024, Ri.MED organized a series of events designed to inspire and entertain a broad audience while fostering interest in scientific culture. Through these initiatives, Ri.MED continues to shape the territory's identity as a reference point in the life sciences sector. One notable example was the panel discussion "**Food, Health, and Society**", held in the lead-up to the annual scientific symposium. This discussion highlighted the deep connection between human health and environmental health, emphasizing the critical role of nutrition. These themes will be central to the research conducted at the upcoming Ri.MED research center in Carini.

Our Scientific Director, Giulio Superti-Furga, was interviewed at the **Innovation Island** panel discussion at Teatro Massimo. His contribution to the field of science and innovation was later recognized with the "Innovator of the Year" award, proclaimed during the annual event dedicated to entrepreneurs, investors and startuppers and promoted by the Department of Productive Activities of the Sicilian Region.

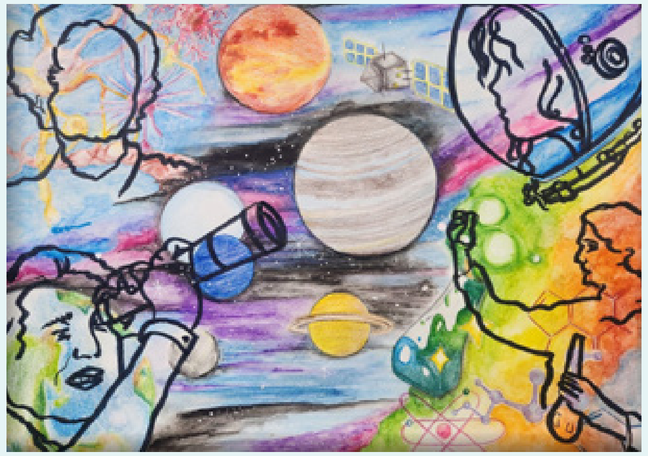
The Ri.MED Foundation also received the award in the "Innovation" category during the **Sicilian edition of Motore Italia 2024** for the creation of the Carini Research Center.

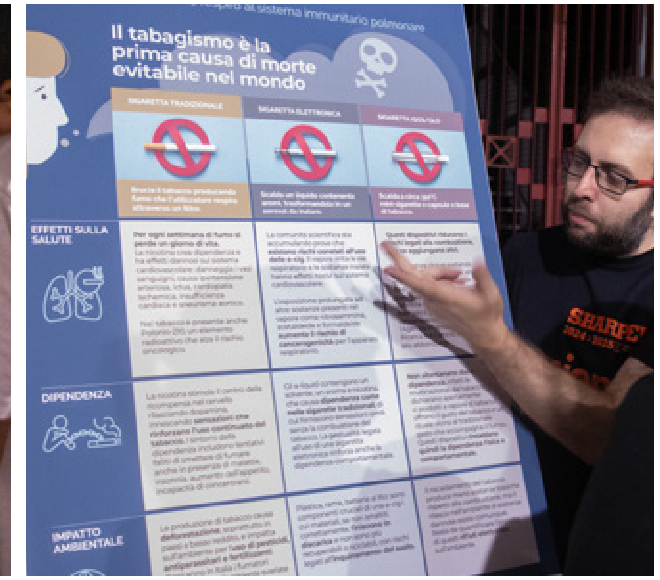
As part of our commitment to public engagement, Ri.MED also carried out several outreach activities in Carini, where the new research center is being built. Two workshops for children were organized, including "**Read My DNA" at the Park Art Fest**.

In this hands-on workshop, children created a complete copy of a DNA segment, transcribed it, and then translated it using the universal genetic code to understand how small genetic variations can lead to diseases.

Furthering our collaboration with the local community, Ri.MED participated in a **journalism competition organized by Il Carinese** for students in Carini. Over 100 students wrote articles on the theme "What the Territory Offers to Make Dreams Come True," with nearly half choosing the Ri.MED research center as their subject. In recognition of this enthusiasm, the winner received an additional prize: a guided tour of the research center's construction site, accompanied by their teacher.

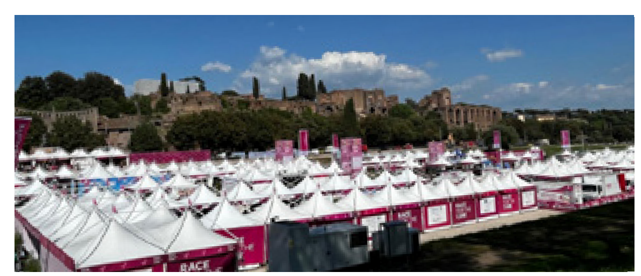
Ri.MED also co-organized the competition "**Science as a Tool for Equality**", targeting schools in the Province of Palermo. During the final award ceremony, students showcased their outstanding work, including videos, interactive slides, paintings, science articles, and even comics! Using diverse forms of expression, they explored themes of diversity and the historical (and present) gender gap in STEM disciplines. From Rita Levi-Montalcini to Margherita Hack, and from Alice Ball to Rosalind Franklin and Jocelyn Bell, the students skillfully narrated the stories of many pioneering women in science.





As in previous years, Ri.MED participated in **Sharper – The European Researchers' Night**, a major European Union initiative dedicated to scientific dissemination and interactive learning. Held on the last Friday of September, this event spans over 300 cities in more than 30 European countries. Ri.MED and ISMETT jointly organized the initiative "A Pieni Polmoni" (Full Lungs), where researchers educated participants about the effects of smoking on lung cells and ongoing research aimed at improving treatments for those affected by smoking-related damage. Using a memory game, interactive scoreboards, and a microscope, visitors were able to observe firsthand the impact of scientific advancements on pulmonary health.

Lastly, in 2024, the Ri.MED Foundation participated in **Race for the Cure in Rome**, one of the largest global initiatives in the fight against breast cancer, organized by Komen Italia. This event provided a vital opportunity to raise awareness about the importance of prevention and early detection in the battle against breast cancer.



Ri.MED OVERVIEW

DISSEMINATION OF SCIENTIFIC KNOWLEDGE

SCHOOLS

The year 2024 represented a turning point as regard Ri.MED commitment towards the activities addressed to scientific knowledge diffusion in local schools, also as a direct effect of the entry into force of the Memorandum of Understanding signed at the end of 2023 with the Sicilian Regional Department of Education and Professional Training and the Regional School Office. Indeed, during the second term of the school year 2023/2024, Ri.MED received numerous applications from local High schools asking for hosting teaching sessions hold by Ri.MED researchers. Ri.MED training sessions were delivered to eight different School Institutes, for a total of 123 hours taught, involving more than 250 students. Teaching modules offered by Ri.MED covered several topics, from Structural Biology to Molecular Informatics, and also Pharmaceutical Chemistry and Advanced Therapies.

Not only scientific topics, but also more technical ones, as the modules on project management processes for the biotechnology sector, enriched with a focus on Intellectual Properties rights.

A very interesting and rich "educational program", tailored according to students' expectations and entrance skills, and framed in collaboration with school teachers. Ri.MED is confident that through theoretical lessons, practice exercises and lab visits, this experience positively impacts the way students intend the link between what they learn at school and the practical application in real life (in particular, at work), keeping them more motivated, curious and self-confident towards STEM paths.

Ri.MED will continue to invest in young people education, as a worthy opportunity to foster the professional, social and personal growth of young people, valuing all students, regardless of gender identity and backgrounds, and nurturing their interest in STEM by countering stereotypes, also in an effort to reduce drop-out rates.

Ri.MED OVERVIEW

DISSEMINATION OF SCIENTIFIC KNOWLEDGE

PRESS


healthcare policy

BIOTECH
La sfida dell'Italia

RICERCA E BIOMEDICINA — prospettive, direzione e impatto

Nell'era della biotecnologia e della biomedicina il rapporto tra esseri umani, salute e ambiente subirà cambiamenti epocali. L'intelligenza artificiale, in sinergia con la bioingegneria, aprirà le porte a questa nuova fase ricca di innovazioni. Dobbiamo prepararci, come società, a questa rivoluzione biotecnologica, gestendone direzione e impatto e affrontare consapevolmente le questioni riguardanti il futuro biologico dell'umanità

GIULIO SUPERTI-FURGA


Dossier PALERMOTODAY

Il campus abbracciato dalla montagna che si affaccia sul mare


MF MILANO FINANZA

CONSEGNATI I PREMI DEDICATI ALLE NUOVE IMPRESE E ALLE IDEE NUOVE

Un'isola di innovazione

Sette premi per le diverse categorie della strategia regionale dell'assessorato regionale alle attività produttive. Un riconoscimento anche a Giulio Superti Furga direttore scientifico della fondazione Rimed per la sua visione di ricerca


INNOVATION ISLAND

Superti-Furga: "Bisogna superare la paura per liberare il coraggio di innovare"


QdS.it

L'Austria premia l'attività scientifica del prof. Giulio Superti-Furga


LA SICILIA

Superti-Furga (Ri.Med): "Con nuovo centro Sicilia sarà faro internazionale ricerca"

"Attireremo talenti da tutto il mondo, sarà strutturato attorno allo studio di organi specifici come cervello e fegato"


PALERMOTODAY

Uomo, salute e ambiente: un accordo d'impresa per lo sviluppo delle tre anime di Rimed


GIORNALE DI SICILIA

Accordo Rimed, Ismett e Gonzaga Campus

Gli studi del futuro passano da Carini


MF MILANO FINANZA

Energia e turismo, ma non solo. I premi di Motore Italia Sicilia


INNOVATION ISLAND

Da Palermo la ricerca d'avanguardia sul microbioma

Giulio Superti-Furga
Direttore Scientifico Ri.MED


TRMWeb.it

Palermo – Tra poco più di un anno l'inaugurazione del centro di ricerca Ri.Med a Carini

Paolo Aquilanti Presidente Fondazione Ri.Med


>> Italpress
Agenzia di Stampa

Simposio Ri.MED a Palermo, la salute e l'umore passano dalla "pancia"


GIORNALE DI SICILIA

Professioni del futuro: a Palermo accordo fra scuola, Regione e Fondazione Ri.Med

Protocollo d'intesa firmato al liceo scientifico Galileo Galilei di Palermo


24OreSalute

La piattaforma del Sole 24 Ore dedicata alla sanità, alla medicina e alle cure innovative

Il microbiota intestinale: un super-organismo che regola il benessere fisico e mentale


LA SICILIA

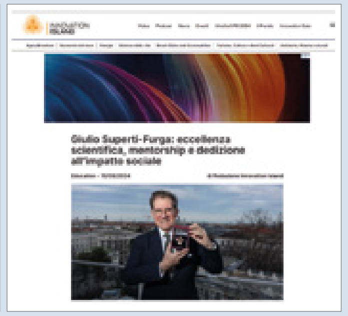
IL PREMIO INNOVAZIONE AL DIRETTORE SCIENTIFICO DELLA FONDAZIONE RIMED

Innovation Island: la Sicilia culla di creatori di tecnologie


la Repubblica

Il Rimed apre le porte agli studenti delle scuole. Via ai corsi: dall'informatica molecolare alle biotecnologie alimentari

Protocollo d'intesa tra Ufficio scolastico regionale, assessorato regionale all'Istruzione e Fondazione Rimed


INNOVATION ISLAND

Giulio Superti-Furga: eccellenza scientifica, mentorship e dedizione all'impatto sociale


iO DONNA

Donne Stem (italiane), storia di una scienziata che ha trovato l'America in Sicilia


L'ORA

Ri.MED, ISMETT- UPMC e Gonzaga Campus insieme per la scuola del futuro: scuola internazionale e liceo scientifico STEAM

PALERMO - Per una scuola del futuro, sempre più aperta e multidisciplinare, nel cuore del Mediterraneo.


PALERMOTODAY

Viabilità nell'area del Rimed, una nuova stazione ferroviaria e più collegamenti con Carini


QUOTIDIANO DI SICILIA

One health, accordo per la ricerca scientifica al Sud

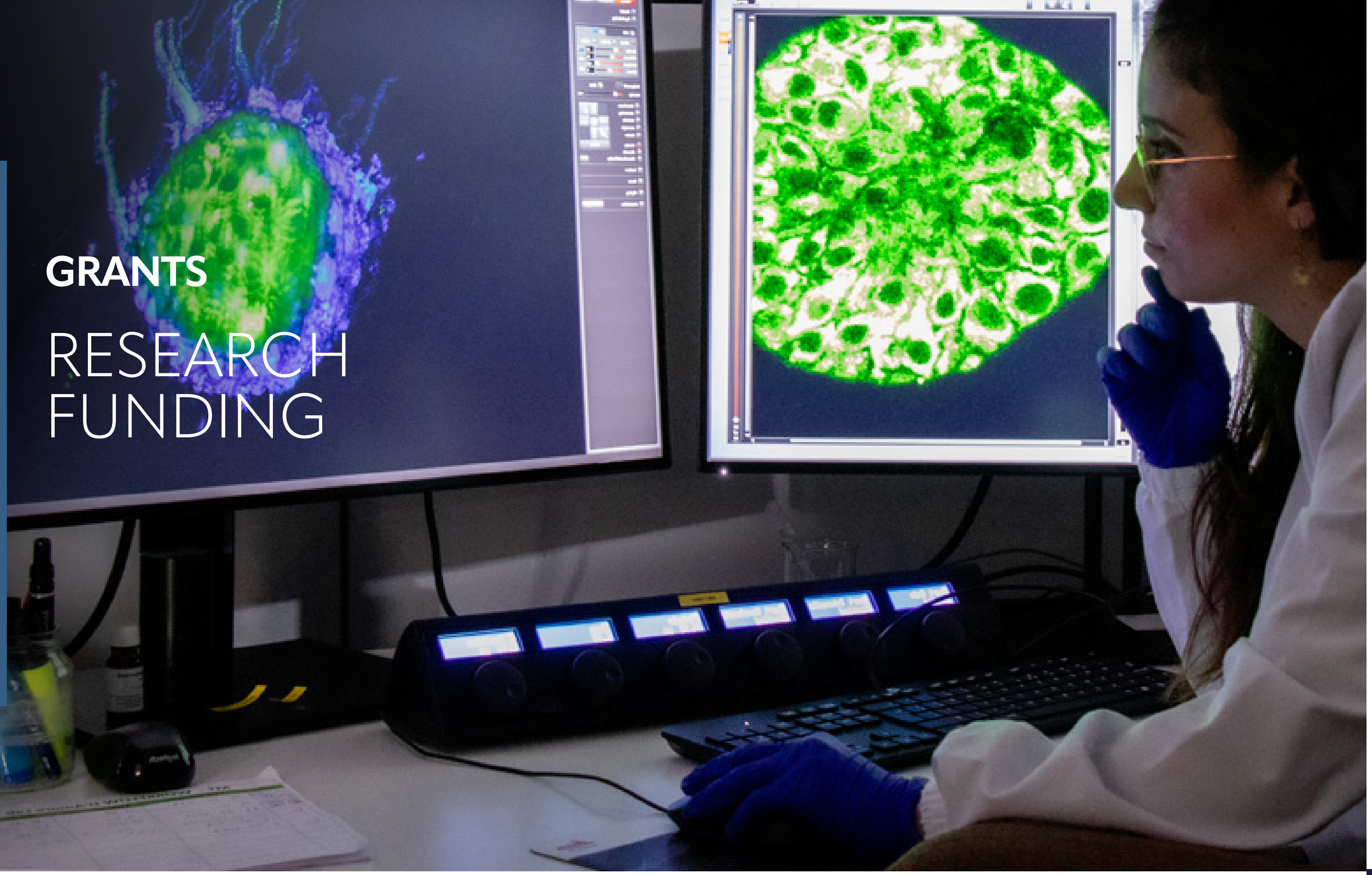
NETWORKING

PARTNERSHIPS & COLLABORATIONS

Collaborations aim to integrate complementary skills with joint translational research projects, maximizing critical mass and enhancing the prospects for success. Ri.MED prioritizes the continuous development of its network of scientific collaborations and scientific agreements with centers and institutions operating in its areas of interest: there are currently 55 agreements in place for the development of technological innovation, promotion of research activities, and sharing laboratories and resources with national and international institutions.
A total of 9 agreements were signed in 2024.

Ri.MED has 7 ongoing agreements for lab hosting, such as the management of the Regenerative Medicine and Immunology laboratories at **ISMETT**, which are of strategic importance for integrating basic and clinical research; the Experimental Lung Research lab at **CNR**; and the Preclinical In Vivo Research Group at the **Experimental Zooprophylactic and Zootechnical Institutes of Sicily**. Ri.MED also manages the Structural Biology and Biophysics labs, the Tissue Engineering Lab, the Bioengineering and Medical Devices Lab, the Medicinal Chemistry Lab and the Imaging and Radiomics Lab at various sites of the **University of Palermo**. Additionally, Ri.MED has leased suitable spaces to establish the Advanced Data Analysis and Molecular Informatics laboratories.

Ri.MED Foundation attended the 2024 BIO International Convention organized by the Italian Trade & Investment Agency, the governmental agency supporting business development of Italian companies abroad and promoting the attraction of foreign investments in Italy.



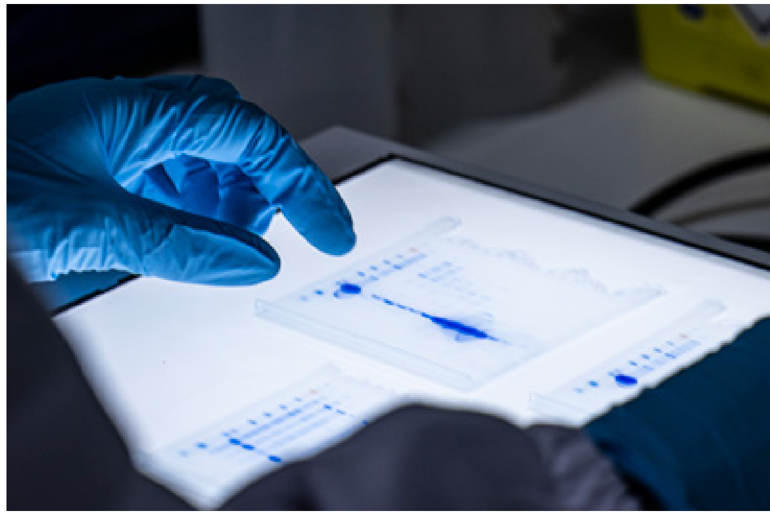
GRANTS

RESEARCH FUNDING

Finding and obtaining competitive grants, creating new partnerships, expanding existing networks, sharing know-how and results with abroad, making research and innovation sustainable... these are the most important objectives guiding the daily work of Ri.MED Grant Office. In 2024 too, the office worked in strict collaboration with all Ri.MED researchers, supporting them for participating in those calls of proposals best fitting their scientific priorities.

Numerous successes have been achieved, above all at National level, thanks to the opportunities offered by the National Recovery and Resilience Plan (NRRP), with a particular reference to the cascade calls, most of which launched this year.
A great recognition for Ri.MED researchers which won the 90% of the cascade calls to which participated in: from personalized medical smart devices for asthma monitoring, to the integration of artificial intelligence solutions to prevent and predict atrial fibrillation, continuing with the synthesis and radiobiological validation of natural-based polymeric nanoparticles and theranostic nanogel (NG) radiolabelled with Lutetium-177 in prostate cancer cell lines.
Also collaborations with the most important Italian health and pharma actors experienced a relevant growth this year, as demonstrated by two new projects funded by the Ministry of Health, through NRRP funds, and where Ri.MED researchers actively collaborate: one in the medical chemistry sector and aimed at validate the druggability of PCYOX1 for the future development of cardiovascular and anticancer drugs; and a second one, addressed to the development of a biohybrid medical device to prevent esophageal re-stenosis and induce constructive tissue remodeling. A third one, this time funded by Ministry of Enterprises and Made in Italy, aims at creating a diagnostic, prognostic and therapeutic network, through the synergic activities of Big Pharma, SMEs, IRCCS and Academia, for the deconvolution of the pathogenetic mechanisms underlying the etiogenesis of colorectal carcinoma.

Not only collaborative grants, but also individual and infrastructural strengthening ones. This is the examples of the the applications submitted according to the prestigious Italian AIRC Program, the EU Marie Skłodowska-Curie Actions, the Roche Foundation and the Orthoregeneration Network. While, as for the infrastructural upgrading, Ri.MED researchers obtained a relevant grant totally dedicated to strengthening the current Ri.MED genomics/transcriptomics laboratory with the necessary equipment for extracting genetic material from a single cell and install a dedicated server for processing and storing acquired data.



PHD COURSES ACTIVATED IN 2024 in partnership with Italian Universities (Academic Year 2024/2025 – Cycle XL°) and co-funded by public resources:

FUNDING AGENCY/PROGRAMME:
National Recovery and Resilience Plan (NRRP) – M4/C2/I3.3 (Ministry Decree n.630/2024), with Ri.MED Foundation participating as both fellowship co-financier and hosting institution of PhD students (for a period of 6-12 months):

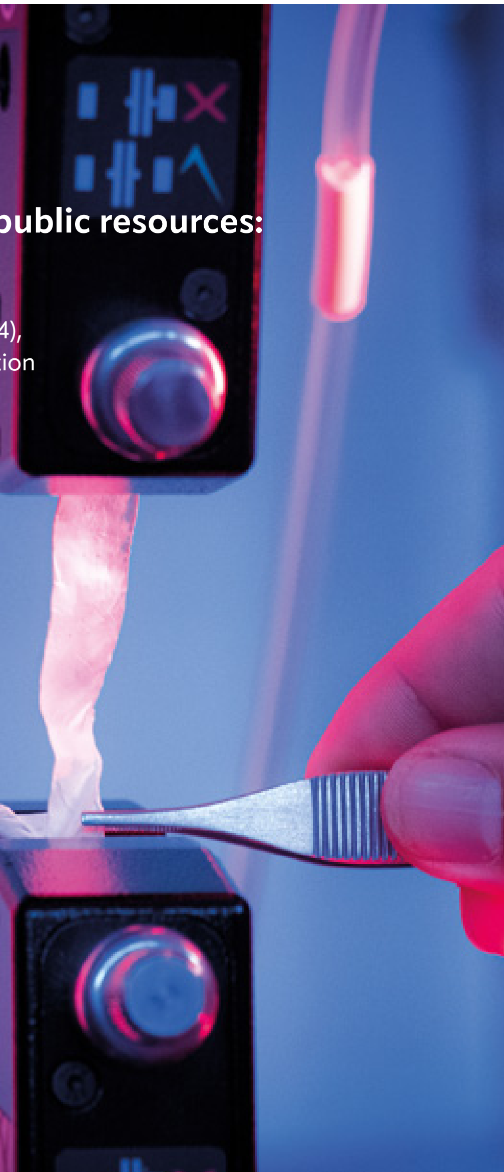
University of Palermo
- N. 1 PhD Fellowship in Chemical, Environmental, Biomedical, Hydraulic and Materials Engineering.
- N. 1 PhD Fellowship in Technologies and Sciences for Human Health.
- N. 1 PhD Fellowship in Biomedicine, neuroscience and advanced diagnostics.
- N. 1 PhD Fellowship in Molecular and Clinical Medicine.

FUNDING AGENCY/PROGRAMME:
Sicilian Region
Public Call n.15/2024, under the OP ESF 2021/2027:

University of Palermo
- N. 1 PhD Fellowship in Precision Medicine (National Doctoral Course).
- N. 1 PhD Fellowship in Molecular and Clinical Medicine.
- N. 1 PhD Fellowship in Biomedicine, neuroscience and advanced diagnostics.

FUNDING AGENCY/PROGRAMME:
Italian Space Agency (ASI). Resolution no. 67/2023 of 20.03. 2023:

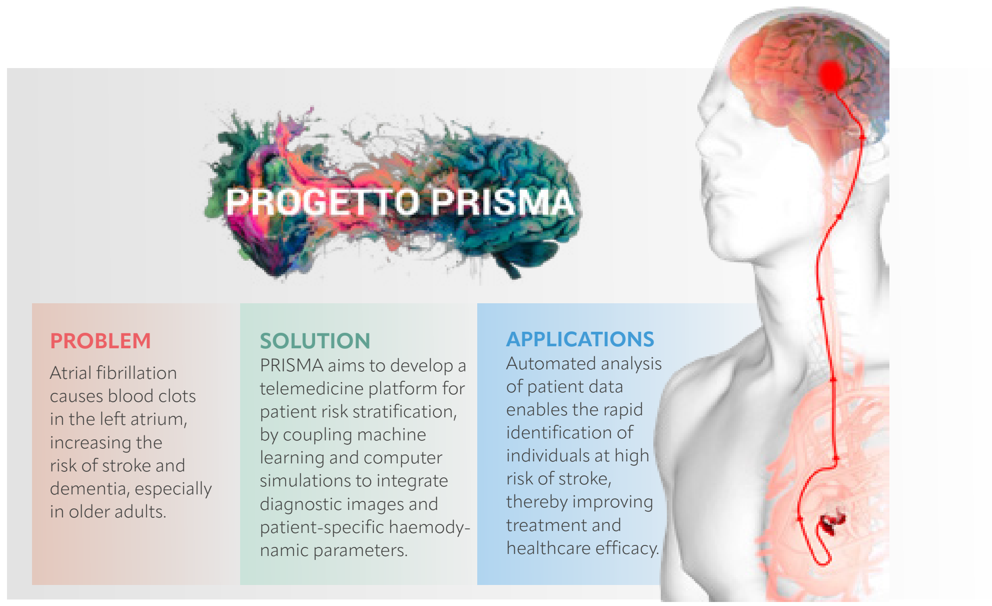
University of Cagliari.
- N. 1 PhD Fellowship in Sciences and Technologies for Innovation.



GRANTS

Focus on

When bioengineer meets the power of machine learning systems: a personalised medical approach to thromboembolic risk assessment



When bioengineer meets the power of machine learning systems: a personalised medical approach to thromboembolic risk assessment.

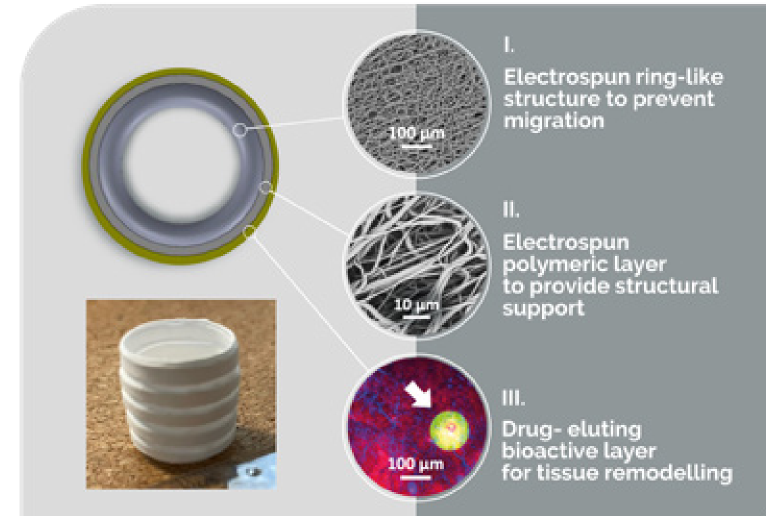
In recent years, bioengineering solutions for medical applications have been widely recognised as strategic tools for supporting clinicians in their daily work, as well as assisting health public authorities in better managing national healthcare expenditure. Acknowledging this, the Italian Ministry of University and Research, through the NRRP funds, has supported the creation of several Innovation Ecosystems, including the "Tuscany Health Ecosystem" (THE). This is the only ecosystem entirely dedicated to life sciences, with the goal of establishing Tuscany a "health region" by promoting research and its applications while collaborating with other regions to improve interoperability among regional healthcare systems. As part of this initiative, in 2024, THE funded **PRISMA (Prediction of the risk of ischemia in atrial fibrillation using machine learning)**, a project managed by the Ri.MED research group of Bioengineering & Medical Devices, led by **Gaetano Burriesci** and supported by the group of Advanced Data Analysis. Under the coordination of the PI, **Danila Vella** (Scientist in Informatics Bioengineering), PRISMA aims to bridge a critical gap in medical diagnosis and treatment of atrial fibrillation, a leading cause of ischemic stroke. Currently, risk estimation relies on numerical clinical scores such as CHA$_2$DS$_2$-VASc, which do not account for anatomo-physiological parameters. However, 90% of thrombi originate in the left atrial appendage (LAA), and recent studies suggest that the shape and contractility of this cardiac district significantly influence local hemodynamics, promoting thromboembolic risk. Based on this evidence, PRISMA aims to develop a telemedicine platform exploiting machine learning to integrate diagnostic images and patient specific haemodynamic parameters in the risk stratification. **The project is structured into three phases: 1) creation of a synthetic dataset of LAA models using statistical shape analysis (SSA) and data augmentation; 2) application of computational fluid-structure interaction (FSI) to simulate the interaction between blood flow and the LAA structure, allowing for a more precise ischemic risk prediction; 3) development a deep learning model for personalised thromboembolic risk assessment.** Thanks to a multidisciplinary scientific work, including cardiovascular engineering, bioinformatics and advanced data analysis expertise, PRISMA will offer a more accurate risk assessment, supporting clinicians in the selection of the most appropriate therapy — whether anticoagulation, surgical exclusion, or percutaneous occlusion of the LAA. This will contribute to advancing personalised treatment strategies and precision medicine.

PRISMA exemplifies how biomedical engineering is reshaping healthcare, improving diagnosis, treatment and enhancing the quality of life of the patients population.

Focus on

Tissue engineering innovations to tackle unmet medical need in gastroenterology

Tissue engineered Esophageal graft
OUR STRATEGY



In august 2024, a new scientific project gets the endorsement of the Italian Ministry of Health. The reference is on the "**Benign and malignant esophageal stricture, an innovative approach to address an unmet clinical need: a biohybrid polymer – extracellular matrix, drug-eluting, esophageal prosthesis able to provide sustained mechanical support, actively prevent re-stenosis and induce constructive tissue remodelling**".

An excellent tangible result of the strict and multiannual collaboration between researchers and clinicians from Ri.MED and ISMETT, in this project we can see synergy, joint effort and know-how sharing, to effectively tackle an unmet medical need in gastroenterology. The focus is on the esophageal stenosis, a condition characterized by a reduction in the lumen diameter caused by cancer, chronic inflammation, or ulcerative processes. The project starting point is represented by those cases of non resolutive pharmacological treatments, which usually need to be tackled with surgery procedures for endoscopic dilation, which includes the endoscopic placement of various types of stents, including both covered and uncovered self-expanding metal stents (SEMS) and self-expanding plastic stents (SEPS). Although SEMS and SEPS allow for effective dilation of the stenotic area, their main disadvantage remains the migration rate (approximately 35%). Combining this unmet clinical need with tissue engineering represents an element of methodological innovation.

To overcome these limitations, a biohybrid medical device will be developed using advanced tissue engineering technologies. This graft will be compared to a Niti-S stent as it features characteristics such as silicone coating and flared ends with rounded edges designed to potentially reduce obstruction from tissue infiltration between the mesh and hyperplastic mucosal reaction at the ends.

In collaboration with clinicians and researchers belonging to ISMETT Endoscopy unit, **Antonio D'Amore** is coordinating the scientific work of **Laura Modica de Mohac** (expert in biofabrication and drug release) and **Federica Cosentino** (expert in fluid dynamic simulation and quantitative imaging analysis), of carrying out the design, characterization, and validation of a biohybrid esophageal graft without a stent in a clinically relevant animal model.

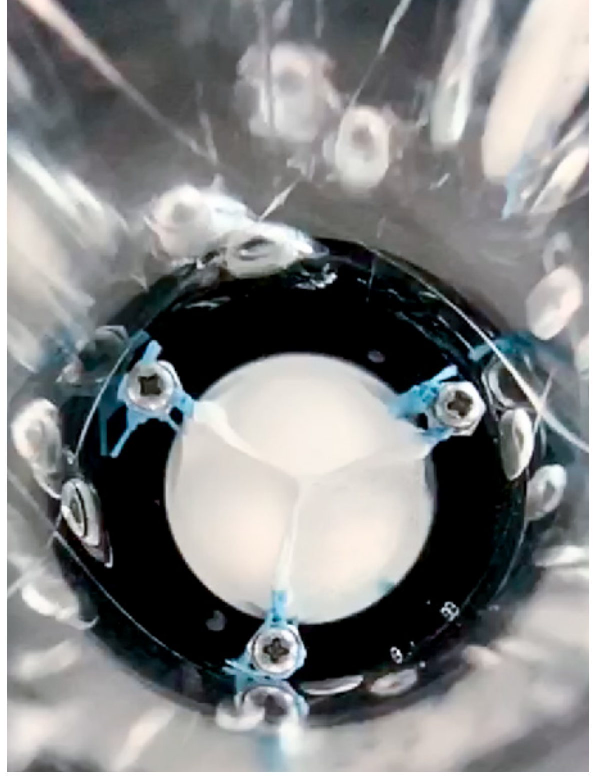
This graft is expected to provide sustained mechanical support, release active pharmaceutical ingredients, and deliver bioactive components derived from the extracellular matrix (ECM) to induce constructive tissue remodeling. Specifically, the biohybrid graft in question will be able of providing mechanical resistance to buckling and device migration. A such innovation will be of course protected by a dedicated patent so that the scientific group can go further, finally achieving the patient.

Ri.MED OVERVIEW

GRANTS

2024 ONGOING SCIENTIFIC PROJECTS

PROJECTS IN PARTNERSHIP WITH SCIENTIFIC AND/OR HEALTH CARE INSTITUTIONS AND SMEs/BIG ENTERPRISES



National Biodiversity Future Center

Funding Agency/Programme: Ministry of University and Research. National Recovery and Resilience Plan (NRRP) - Mission 4 (Education and Research), Component 2 - Investment 1.4.
Objective: promoting the sustainable management of Italian biodiversity in order to improve the planet's health and return beneficial effects, essential for all people. Specific objective in the health sector is the exploitation of natural products for therapeutic scopes.
Click here for more information

National Center for Gene Therapy and Drugs based on RNA Technology

Funding Agency/Programme: Ministry of University and Research. National Recovery and Resilience Plan (NRRP) –Mission 4 (Education and Research), Component 2 - Investment 1.4.
Objective: increasing the technological know-how necessary to design and deliver RNA-based and gene therapy medicinal products and identifying promising candidate drugs/genes in five major areas of human diseases (genetic diseases, cancer, metabolic/cardiovascular diseases, neurodegenerative disorders and inflammatory/infectious diseases).
Click here for more information

NABUCCO
New drugs and biomarkers for response and pharmacological resistance in colon cancer

Funding Agency/Programme: Innovation Agreement - Ministry of Enterprises and Made in Italy.
Objective: creating a diagnostic, prognostic and therapeutic network, through the synergic activities of Big Pharma, SMEs, IRCCS and Academia, for the deconvolution of the pathogenetic mechanisms underlying the etiogenesis of colorectal carcinoma (CCR). The final objective is the development of non-invasive tools for the identification of predisposed patients, in order to prevent CCR. New diagnostic and prognostic kits as well as new drugs will be produced.
Click here for more information

SmartSense
Smart testing device for personalized medicine based on nanostructured electrochemical biosensors

Funding Agency/Programme: Ministry of University and Research. Sicilian Micronanotech Research And Innovation Center – SAMOTHRACE (Innovation Ecosystem - cascade call - National Recovery and Resilience Plan (NRRP) - on behalf of the project Coordinator DI PIETRO GROUP srl.
Objective: Development of a prototype of a smart device for respiratory disease self-testing. The proposed device will provide support for disease monitoring through the measurement of hydrogen peroxide concentration in easily accessible biological fluids (saliva and exhaled breath condensate), using a nanostructured biosensor previously developed by the partnership. The device will also include data processing systems, as well as Internet of Things (IoT) communication functions to allow real-time transmission of data to healthcare personnel to facilitate disease monitoring.
Click here for more information

RADIATIONS
Studio e valutazione dell'effetto RADiobiologico di nanopartIcelle polimeriche innovative di origine nATurale radiomarcate con radioIsotopO Lu-177 in linee cellulari di caNcro della proStata

Funding Agency/Programme: Ministry of University and Research. Innovation Ecosystem "THE – Tuscany Health Ecosystem". National Recovery and Resilience Plan (NRRP). Cascade call managed by CNR-INO as Spoke 1.
Objective: synthesis and radiobiological validation of natural-based polymeric nanoparticles and theranostic nanogel (NG) radiolabelled with Lutetium-177 (a beta radioisotope, suitable for both diagnosis and therapy scopes) in prostate cancer cell lines. The expected result is the development of innovative NPP/NG from the synthetic and biocompatibility, cytotoxicity and internalization point of view, as well as from a functional point of view (diagnosis and therapy for prostate cancer).
Click here for more information

GRANTS

2024 ONGOING SCIENTIFIC PROJECTS

PROJECTS IN PARTNERSHIP WITH SCIENTIFIC AND/OR HEALTH CARE INSTITUTIONS

Exploiting the power of human induced pluripotent stem cell extracellular vesicles as a new anti- inflammatory drug for lung ischemia reperfusion injury

Funding Agency/Programme: Ministry of Health. National Recovery and Resilience Plan (NRRP) – M6/C2/I2.1.
Objective: assessing technical and commercial feasibility of an innovative cell-free nanomedicine strategy based on extracellular vesicles (EV), human induced pluripotent stem cells and a young cell source such as cord blood. The project is focused on a patent which highlights the strong anti-inflammatory role of EV isolated from cord blood mesenchymal stromal induced pluripotent stem cells.
Click here for more information

Benign and malignant esophageal stricture, an innovative approach to address an unmet clinical need:

a biohybrid polymer - extracellular matrix, drug-eluting, esophageal prosthesis able to provide sustained mechanical support, actively prevent re-stenosis and induce constructive tissue remodeling

Funding Agency/Programme: Ministry of Health. National Recovery and Resilience Plan (NRRP) – M6/C2/I2.1.
Objective: approximately 35% of patients who have undergone surgery to address esophageal stenosis experience a recurrence of the condition. To reduce this risk, a biohybrid medical device will be developed using advanced tissue engineering technologies, able to provide sustained mechanical support, release active pharmaceutical ingredients, and deliver bioactive components derived from the extracellular matrix to induce constructive tissue remodeling.
Click here for more information

Early Drug Discovery to identify novel inhibitors of Prenylcysteine oxidase 1 (PCYOX1), a novel target in cardiology and oncology

Funding Agency/Programme: Ministry of Health. National Recovery and Resilience Plan (NRRP) – M6/C2/I2.1.
Objective: to validate the druggability of PCYOX1 and identify potential hit compounds directed against it for the future development of cardiovascular and anticancer drugs.
Click here for more information

PRISMA

Prediction of ischemia risk in atrial fibrillation through machine learning

Funding Agency/Programme: Ministry of University and Research. Innovation Ecosystem "THE – Tuscany Health Ecosystem". National Recovery and Resilience Plan (NRRP). Cascade call managed by Università degli Studi di Firenze as Spoke 2, 3, 5.
Objective: PRISMA aims at developing a telemedicine platform based on machine learning to improve the stratification of thromboembolic risk in patients with atrial fibrillation. The system will integrate synthetic models of the left atrial appendage, anatomical-physiological and fluid-dynamic parameters. It will employ neural networks to provide a personalized risk assessment, supporting the selection of the optimal therapeutic approach and promoting precision medicine.
Click here for more information

CASTOR&POLLUX

Centre for data acquisition, storage and processing from multiomic platform for three-dimensional cellular models

Funding Agency/Programme: Ministry of University and Research. D34Health – Digital Driven Diagnostics, prognostics, and therapeutics for sustainable Healthcare – National Plan for Complementary Investments to the NRRP. Cascade call managed by Spoke 4 – "Biological and bioengineered *in vitro* models for care through Digital Twin approaches", Politecnico di Torino.
Objective: to enhance the current Genomics/Transcriptomics laboratory with the necessary equipment for extracting genetic material from a single cell and install a dedicated server for processing and storing acquired data. Standardized experimental protocols will be developed for the creation and sequencing of DNA or RNA libraries for bulk and/or single-cell analysis, as well as computational protocols for appropriate bioinformatics analyses.
Click here for more information

Life Science TTO Network

Funding Agency/Programme: Ministry of Health. National Plan for Complementary Investments to the NRRP – "Innovative Health Ecosystem" Program – Investment E.3.
Objective: establishing and consolidating a nationwide open and sustainable Technology Transfer Office (TTO) Network, which will connect, coordinate and align Network Partners and stakeholders (Research and Care Institutes (IRCCS), Universities, National Health System, Investors, SMEs, Industry, National and International Consortia) as well offer world-class services in a synergistic valuable way at national and international level.
Click here for more information

BIOMITRAL

Engineering the mitral valve: bioinspired control of structure and function for enhanced *in vivo* performance

Funding Agency/Programme: European Commission HORIZON 2020 – ERC Consolidator Grant (ERC-2020-COG).
Objective: developing an innovative prototype of a mitral valve by engineering the chordal apparatus and reconnecting the left ventricle with the valve leaflets.
Click here for more information

BioChord

Biomimetic engineered chordae tendineae for valve repair and regeneration

Funding Agency/Programme: European Commission Call ERC-2023-POC (Proof Of Concept).
Objective: to develop better Mitral Valve repair techniques that are simple, effective, and durable, further advancing and validating BioChord, the first ever polymeric bioengineered regenerative Chordae Tendinae, designed to first repair the MV by replacing the diseased CT.
Click here for more information

Green MID-PLACE

Green MIcrofluiDic PLAtform for advanced tissue on a Chip culturEs

Funding Agency/Programme: Ministry of University and Research - PRIN Call 2022 (Progetti di Ricerca di Rilevante Interesse Nazionale/ Research Projects of Relevant National Interest) on behalf of the project Coordinator Università degli Studi di Palermo.
Objective: to develop an eco-sustainable Organ-on-Chip (OoC) platform for stem cell growth and differentiation.
Click here for more information

Complex graphical models for biological network science

Funding Agency/Programme: Ministry of University and Research - PRIN Call 2022 (Progetti di Ricerca di Rilevante Interesse Nazionale/ Research Projects of Relevant National Interest) on behalf of the project Coordinator Università degli Studi di Firenze.
Objective: collection and pre-processing of omics data and interpretation of results obtained by the novel statistical models developed within the project.
Click here for more information

SMART4SCLERO

Smart Injectable Scaffolds for Sclerostin Based Bone Resorption Treatment

Funding Agency/Programme: Ministry of University and Research - PRIN Call 2022 (Progetti di Ricerca di Rilevante Interesse Nazionale/ Research Projects of Relevant National Interest) on behalf of the project Coordinator Consiglio Nazionale delle Ricerche (Napoli).
Objective: developing an advanced *in vitro* model of joints' disorders dependent from bowel-related pathologies. The model will be based either on native than engineered tissues cultured in static, and dynamic conditions. These latter will be fabricated using the support of the bioprinting, as well as other additive manufacturing technologies.
Click here for more information

Ri.MED OVERVIEW

INTELLECTUAL PROPERTY & TECHNOLOGY TRANSFER

PATENT PORTFOLIO

Ri.MED's research activity is strongly patient oriented, but in order to ensure that scientific results reach clinical needs, it is necessary to effectively manage the intellectual property generated by our researchers as well as the subsequent technology transfer process.

From the laboratories, inventions are translated into patents and then into new solutions for the patients.
The protection of intellectual property is a fundamental value for Ri.MED to develop an innovative model of research sustainability. For this reason, Ri.MED has set up an Intellectual Property and Technology Transfer Office to support, promote and foster the progress of translational research through the enhancement of its application effects: patenting, patent license, industrial sponsorship and creation of technological spin-offs.

Ri.MED and a multinational company operating in the cardiovascular area have recently finalized an important license and collaboration agreement having as object Ri.MED's patent family "Triskele" and that is still in full force. This patent family consists of a heart valve prosthesis, a heart valve and their related delivery system and one of the inventors is Gaetano Burriesci, Ri.MED group leader in Bioengineering and Medical devices.

A further crucial step in the valorization of Ri.MED's intellectual property was the conclusion of a license agreement with Neoolife Inc., a startup company founded to commercialize the joint intellectual property of Ri.MED/UPITT, protected by 4 patents (one developed in collaboration with the University of Cincinnati) and focused on technology for the development of regenerative heart valves. In 2023, Neoolife and a world-leading company in the sector entered into an ongoing agreement aimed at this development.

PATENT PORTFOLIO UP TO 31.12.2024

DRUG DISCOVERY

Nitro-oleic acid controlled release platform to induce regional angiogenesis in abdominal wall repair.
WO2019100021
Fondazione Ri.MED - University of Pittsburgh

Novel reversible nitroxide derivatives of nitroalkenes that mediate nitrosating and alkylating reactions
WO2018067709
University of Pittsburgh

REGENERATIVE MEDICINE AND IMMUNOTHERAPY

NK-mediated immunotherapy and uses therefor
WO2018099988
Fondazione Ri.MED - IRCCS ISMETT

Mandrel-less electrospinning processing method and system, and uses therefor
WO2018175234
Fondazione Ri.MED - University of Pittsburgh

Extracts for the regeneration of ligaments
PCT/US2019/019119
Fondazione Ri.MED - University of Pittsburgh

Method of Producing Regulatory Dendritic Cells
US Provisional n. 63/504,494
Fondazione Ri.MED/IRCCS ISMETT/University of Pittsburgh

Kit per la Ricostituzione di un Dispositivo Biomedico Cell-Free ad Uso in Medicina Rigenerativa, Dispositivo Biomedico Così Ricostituito e Relativo Procedimento di Sintesi
ITA N. 102023000019479
Fondazione Ri.MED/IRCCS ISMETT

TISSUE ENGINEERING AND BIOMEDICAL DEVICES

Method and system for the evaluation of the risk of aortic rupture or dissection in an ascending thoracic aortic aneurysm.
WO2018220573
Fondazione Ri.MED - IRCCS ISMETT

Transatrial access for intracardiac therapy
WO2017127682
University of Pittsburgh

Bi-layer extra cellular matrix scaffolds and uses thereof
WO2017044787
University of Pittsburgh

Hybrid Micro Molding-Fiber Deposition Substrate Processing for Cell Biology Manipulation and Local Anisotropy
US 63/091,462
Fondazione Ri.MED - University of Pittsburgh

Double components mandrel for electrospun stentless, multi-leaflet valves fabrication.
WO2016138416
University of Pittsburgh

Retrievable self-expanding non-thrombogenic lowprofile percutaneous atrioventricular valve prosthesis WO2016138423
University of Pittsburgh

Multi-layered graft for tissue engineering applications
WO2019023447
Fondazione Ri.MED - University of Pittsburgh

Treating soft tissue via controlled drug release WO2015134770
University of Pittsburgh

Microfluidic Tissue Development Systems
WO2017062629
University of Pittsburgh

A modular, microfluidic, mechanically active bioreactor for 3D, multi-tissue, tissue culture.
WO2015027186
University of Pittsburgh*

Osteoarthritis treatment with chemokine-loaded alginate microparticles
U.S. Patent Appl. No. 16/241,112, *continuation application of WO2014022685*
Fondazione Ri.MED - University of Pittsburgh

Organ chip to model mammalian joint.
U.S. Patent Appl. No. 16/193,972)
University of Pittsburgh

Recruitment of mesenchymal stem cells using controlled release systems
WO2014022685
University of Pittsburgh

Multi-well mechanical stimulation systems and incubators
WO2019079722
Fondazione Ri.MED - University of Pittsburgh

A stentless biopolymer heart valve replacement capable of living tissue regeneration.
WO2018156856
University of Pittsburgh

An expandable percutaneous cannula
PCT/US2018/017795
Fondazione Ri.MED - University of Pittsburgh

Biodegradable metallic - polymeric composite prosthesis for heart valve replacement
WO2019210059
Fondazione Ri.MED - University of Pittsburgh – University of Cincinnati

Processing method and apparatus for micro-structured rope-like material
US provisional Patent Application 62/874,114
Fondazione Ri.MED - University of Pittsburgh

Semi-rigid annuloplasty ring and method of manufacturing
WO2019220365
Fondazione Ri.MED

Heart valve prosthesis
WO2010112844
Fondazione Ri.MED

Prosthesis delivery system
WO2012052718
Fondazione Ri.MED

Prosthetic heart valve
WO2016203241
Fondazione Ri.MED

Implant for heart valve repair
WO/2022/229667
Fondazione Ri.MED - Université de technologie de Compiègne - Centre National De La Recherche Scientifique (CNRS) - Assistance Publique/Hôpitaux De Paris

Dispositivo Medico Impiantabile
ITA n. 102023000010848
Fondazione Ri.MED/ University of Pittsburgh

Implantable Composition for Use in Cartilage Defects Repair in Postsurgery Rehabilitation
PCT/EP2023/065364
Fondazione Ri.MED – CHOP (Children's Hospital of Philadelphia)

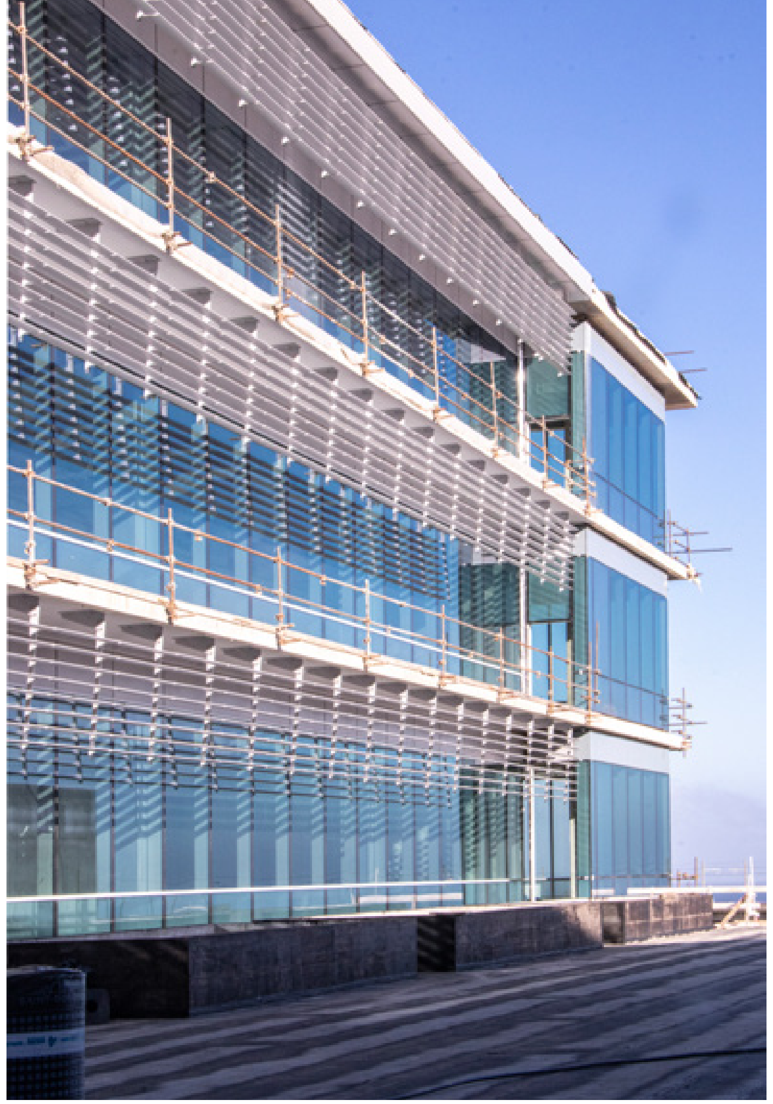
Italian patent application filed in November 2024 related to design and realization of an active bioscaffold for the regeneration of hyaline cartilage in articular joints
applicants: Ri.MED – CHOP – UNIPA.

NOTE:
Also patents where University of Pittsburgh is the only applicant have been co-developed with Ri.MED.

Ri.MED OVERVIEW

Ri.MED RESEARCH CENTER

SOCIO-ECONOMIC IMPACT



The Ri.MED Center, a cutting-edge initiative by the Foundation, is steadily taking shape in Carini, just a few kilometers from Palermo's international airport. This ambitious facility is poised to become a global benchmark for scientific and medical research, playing a leading role in its field.

Construction began in 2020 on a 25,000-square-meter site and is now in full swing. Despite unforeseen challenges such as the COVID-19 pandemic, which necessitated plan modifications and delays due to pandemic-related lockdowns, and the impact of the war in Ukraine on material availability, the resilience, determination, and passion of all involved parties have enabled the Foundation to overcome these hurdles. Today, the campus structure is clearly visible. The project is scheduled for completion by 2026. This revised timeline reflects the ongoing need to constantly update equipment and scientific instruments in line with rapid advancements in research.
Led by the Temporary Association of Enterprises (ATI) with Italiana Costruzioni as the lead firm, and construction management entrusted to a team from Progetto CMR (part of the HOK group that won the international design competition), the facility's design is inspired by the "village street" model. This approach ensures exceptional space flexibility, with 17,070 square meters dedicated to laboratories, common areas, meeting rooms, offices, an auditorium, and a guest house.

With the appointment of Professor Giulio Superti-Furga as Scientific Director, the Center's vision has been updated to reflect the latest theoretical and technical evolutions. Sicily, with its unique genetic and natural heritage and strategic position in the Mediterranean, is considered the ideal location for research exploring the interaction between humans and the environment from nutrition to viral infections, and from life near the sea to solar radiation.

The Ri.MED Center's state-of-the-art laboratories and technological platforms will focus on research into specific organs and their related therapeutic areas, including lungs and respiratory diseases, liver and metabolic diseases, heart and cardiovascular diseases, as well as the brain, gut, skin, and immune system. These activities will be organized into four main areas: "Health," "Research," "Therapeutics," and "Technology."

Once fully operational, the Ri.MED Center is expected to employ approximately 600 highly skilled individuals, generating a significant economic and scientific impact through the technological transfer of research outputs. Discoveries made at the Center will be applicable at IRCCS-ISMETT, the hospital partner, and other Italian hospitals, enhancing the availability of advanced diagnostic and therapeutic tools and patient protocols.

Consistent with the Foundation's institutional objectives, the Ri.MED Center will also host educational and training activities, in collaboration with Italian and international universities. This is expected to have a significant cultural impact on local communities, attracting numerous researchers and their families from around the world, offering job and growth opportunities, and actively contributing to the dissemination of a culture of legality.

Ri.MED RESEARCH CENTER

PLANETARY HEALTH STARTS HERE: A NEW ERA OF MEDICAL RESEARCH BEGINS IN SICILY

by Giulio Superti-Furga

Our new biomedical research center is taking shape in Sicily and will be inaugurated in 2026.

The Ri.MED Research Center in Carini, near Palermo, is being established thanks to the support of five key partners: the Presidency of the Council of Ministers, the Region of Sicily, the National Research Council (CNR), the University of Pittsburgh (Pennsylvania, USA), and the University of Pittsburgh Medical Center (UPMC). This center will also be closely linked to ISMETT, a successful hospital specializing in organ transplantation, and will be operationally integrated with a new, state-of-the-art hospital that will rise on the adjacent grounds—thus creating a comprehensive biomedical campus that spans from research to patient care.

The time has come for a new kind of science— one that holistically explores how genetic predispositions interact with dynamic environmental factors to shape human health. No existing institution is yet rising to this challenge.

It is time to launch innovative research at the intersection of medicine and the environment, with a focus on human health and the ecological dimension. The fundamental principle is simple: health is only possible in a healthy environment. By "environment," we mean nutrition, infections, pollution, and all the forces and conditions that affect human beings directly or indirectly. At the level of the central nervous system, this also includes education, affection, music, poetry—as well as fear, alienation, loneliness, anxiety, and much more. The Ri.MED Center in Carini embraces the concept of "One Health", which we may also call global health or planetary health.

For a biomedical research center aiming to integrate human health with the health of surrounding ecosystems, biodiversity and bioengineering play crucial roles. Biodiversity offers innovative solutions to improve the interaction between humans and their environment, while bioengineering—integrating biology, chemistry, medicine, and physics—helps develop practical strategies to make humanity more resilient to the challenges of the future.

We might describe the evolution of knowledge in biomedical and life sciences as occurring in three phases: the first, descriptive, focused on identifying molecules, genes, proteins, and metabolites; the second focused on understanding their relationships and the biological and physiological mechanisms; the third phase—now upon us—requires applying this knowledge to maintain health through prevention and repair, and inventing solutions to protect humanity and its health-sphere from increasingly complex and

multifactorial challenges, enhancing the robustness and resilience of human systems.

The challenges are manifold and include emerging infections, allergies, lifestyle-related conditions, and climate change impacts such as droughts, heatwaves, desertification, and salinization. Antibiotic resistance, the rise of synthetic diets, and a declining biodiversity in the human biosphere further threaten human and planetary health, increasing vulnerability across ecosystems.

Italy and Europe must support a strong research hub in the South, one that can act as an engine for innovation and a training reference point for the future of biomedical and biotechnological research. Investing additional resources—beyond those already allocated for cutting-edge buildings, state-of-the-art equipment, and operations—represents a strategic investment in the future. Knowledge is the most powerful resource: only those who understand can foresee, prepare, and go beyond immediate and obvious solutions.. Few disciplines will have as great an impact on humanity and the planet's future as medical and biological sciences—especially when empowered by artificial intelligence and guided by a deep humanistic culture.

INTEGRATION WITH HEALTHCARE

The new ISMETT hospital will be built next to the Ri.MED Research Center

→ creating a unique ecosystem that fully integrates advanced research with high-specialty clinical care.

→ set to benefit patients, healthcare systems, and the economic growth.

In this perspective, Sicily assumes a strategic role, thanks to its geographical and political centrality in the Mediterranean—bridging the Global North and South—and its historical ability to create, mediate, and integrate different cultures. Sicily has been a crossroads of civilizations for millennia. I firmly believe that innovative solutions for the future of humanity can best emerge in such a strategic place—one that fosters the meeting of cultures, peoples, and innovative solutions to meet challenges.

Given the scale of funding and the ambition of its mission, the Ri.MED Research Center and the future ISMETT hospital embody a development policy of unprecedented scope in the life sciences sector. This represents an investment worth nearly €1 billion in a highly innovative and strategic field, capable of generating a multiplier effect with broad direct, indirect, induced, and catalytic impact.

We look with interest to leading models of innovation ecosystems, such as VIB in Flanders, Belgium, where an independent study by BiGGAR Economics demonstrated that for every €1 of core public funding, €12 were returned in economic impact. VIB's capacity to translate excellent science into benefits for patients, industry, and society offers an inspiring benchmark—and we believe that Ri.MED can become a similarly transformative force in Southern Europe.

Based on the original vision of the founders and my experience in founding startups and leading research centers, we believe that the transition from discovery to practical, commercial, and social application will be natural and continuous. We envision a center that supports incubation, guided by clear and effective rules, enabling the emergence of scientist-entrepreneurs. The outcomes will not be limited to publications and patents—we also aim to foster innovation ecosystems, startups, and a new generation of translational scientists.

We will attract top global talent while encouraging the return of outstanding Italian researchers, building an international, inclusive, and collaborative work environment. Numerous studies confirm that diversity in research teams is a key driver of innovation, opening new horizons of understanding and solutions.

Not everything will succeed immediately, and mistakes will be part of the journey. But we must dare. The medicine of the future will be increasingly shaped by molecular biology, bioengineering, and advanced technologies and we must be willing to explore new frontiers, not just follow well-trodden paths.

Ri.MED RESEARCH

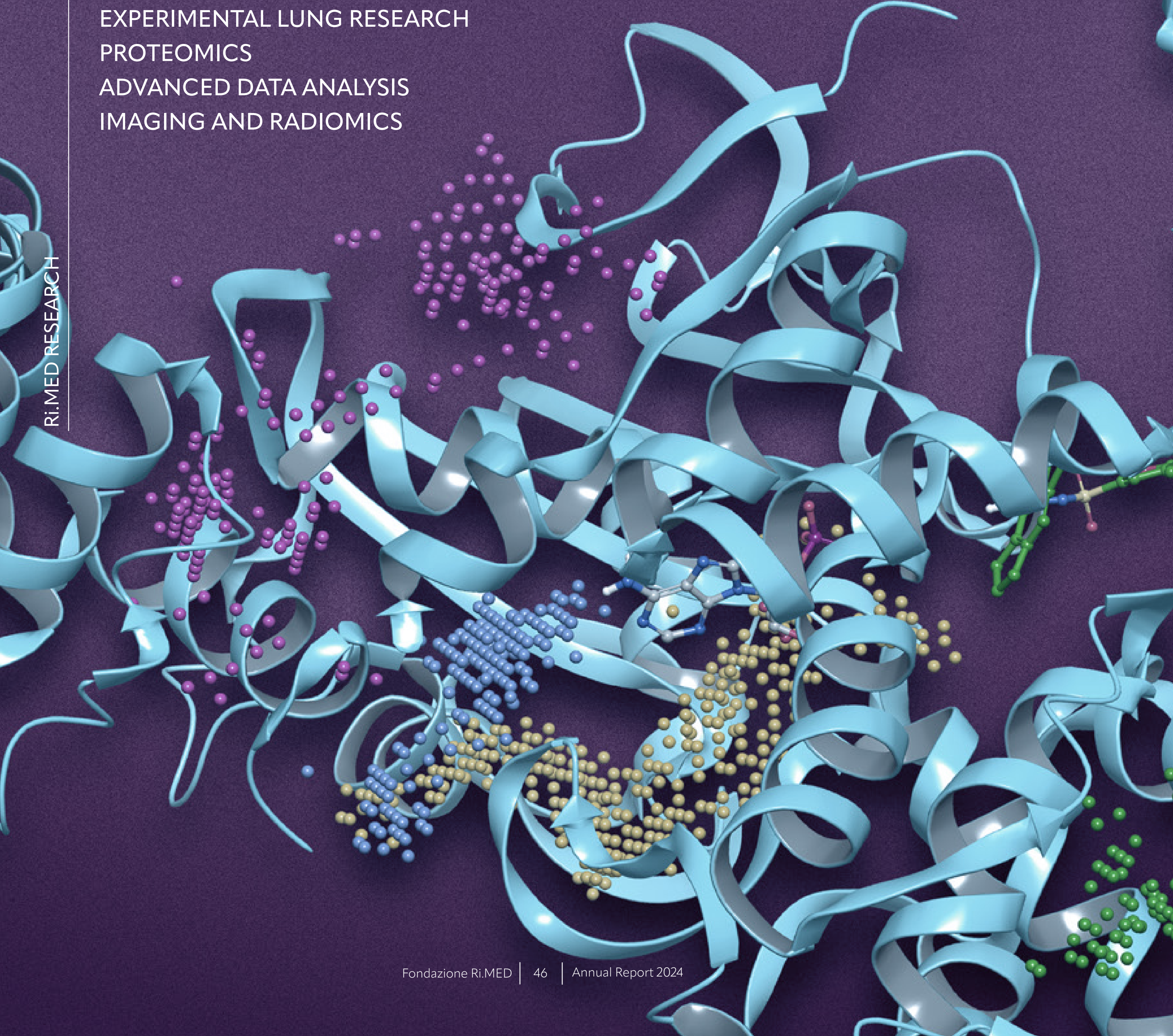
Ri.MED's scientific projects are based on three main areas of interest: regenerative medicine and immunotherapy, aimed at developing advanced therapy medicinal products (ATMP); new drug discovery research; development and tissue engineering and biomedical bioengineering, focused on developing biomaterials, engineered tissues, and medical devices. The activities range from identifying new biologically active molecules to developing cellular products for tissue repair and/or regeneration, and organotypic cultures for regenerative purposes and as models for pharmacology screening, and all the way to simulation of physiological systems and preclinical validation of new generation implantable organs and devices.

Ri.MED's translational research approach is based on therapeutic needs and developed on multiple levels, including the collaboration with our partners: from basic research and pre-clinical research and development, to clinical trials conducted with IRCCS ISMETT.
Ri.MED has a diversified and balanced project portfolio led by a multidisciplinary team with clear product development goals and a "bench-to-bedside" approach. The translational research engine of Ri.MED Foundation envisages the development of skills and technology platforms supporting scientific projects.

DRUG DISCOVERY

STRUCTURAL BIOLOGY AND BIOPHYSICS
MOLECULAR INFORMATICS
MEDICINAL CHEMISTRY
EXPERIMENTAL LUNG RESEARCH
PROTEOMICS
ADVANCED DATA ANALYSIS
IMAGING AND RADIOMICS

Ri.MED RESEARCH



PUBLICATIONS

Texture Analysis in Chronic Liver Diseases
Vernuccio F, Cannella R, Comelli A, Vernuccio L, Lagalla R, Midiri M
Handbook of Texture Analysis: Generalized Texture for AI-Based Industrial Applications
eBook ISBN9780367486099

Shearlet Transform Applied to a Prostate Cancer Radiomics Analysis on MR Images
Corso R, Stefano A, Salvaggio G, Comelli A
Mathematics 2024, 12(9), 1296;
doi: 10.3390/math12091296

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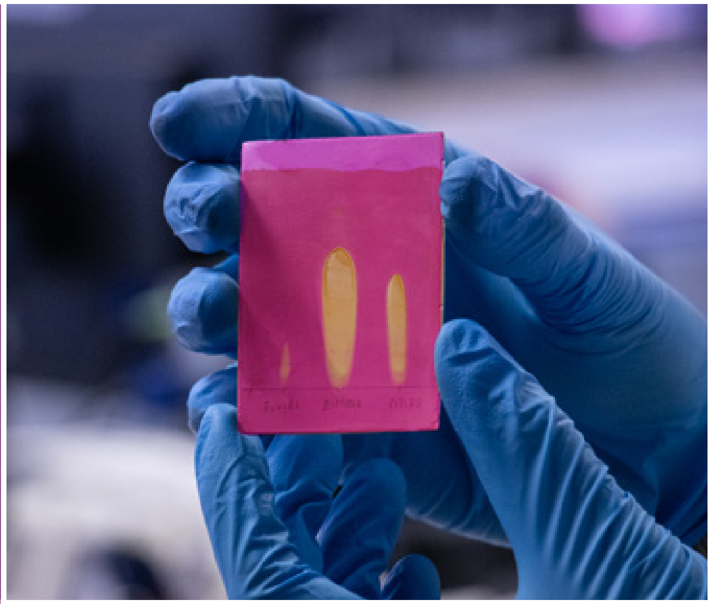

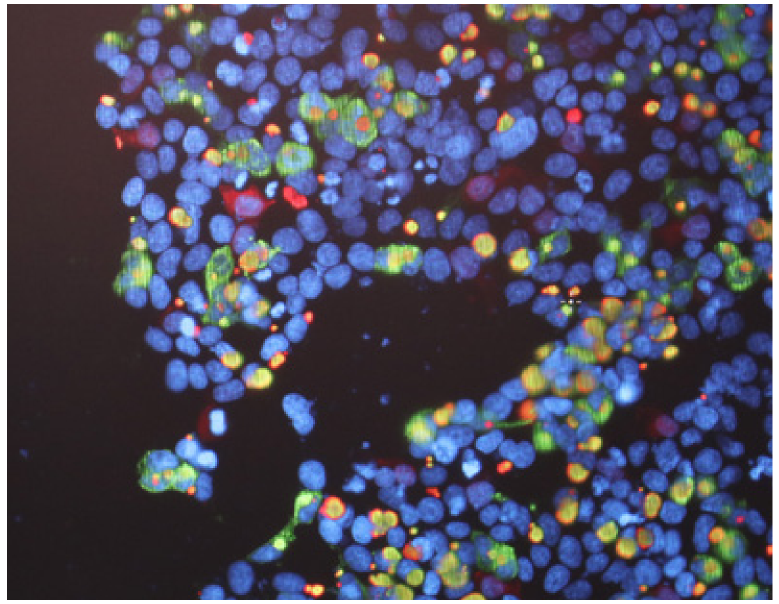

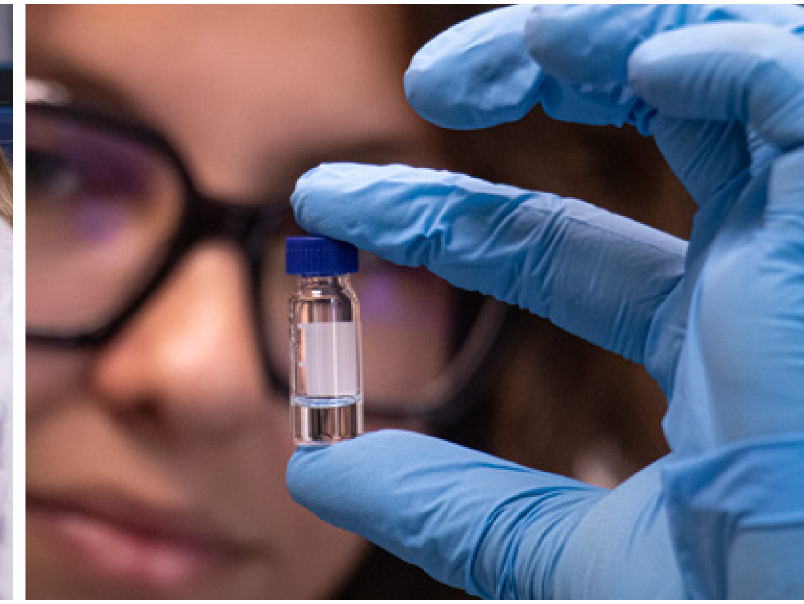

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Correction: PSMA-positive prostatic volume prediction with deep learning based on T2-weighted MRI
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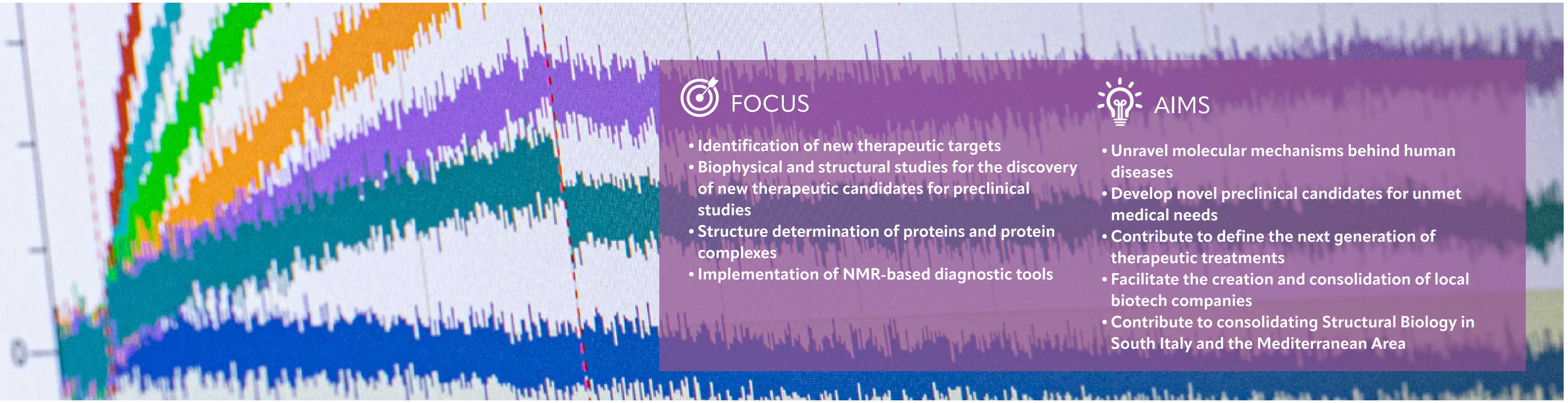

STRUCTURAL BIOLOGY AND BIOPHYSICS

FOCUS

- Identification of new therapeutic targets
- Biophysical and structural studies for the discovery of new therapeutic candidates for preclinical studies
- Structure determination of proteins and protein complexes
- Implementation of NMR-based diagnostic tools

AIMS

- Unravel molecular mechanisms behind human diseases
- Develop novel preclinical candidates for unmet medical needs
- Contribute to define the next generation of therapeutic treatments
- Facilitate the creation and consolidation of local biotech companies
- Contribute to consolidating Structural Biology in South Italy and the Mediterranean Area

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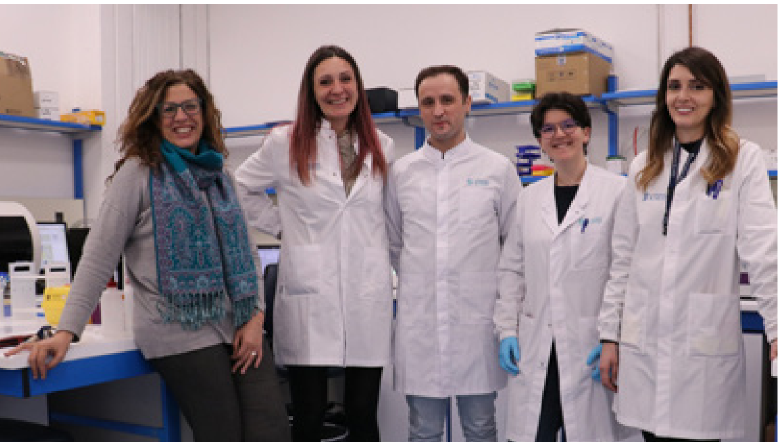
Understanding the folding dynamics, phase transitions, and interactions of proteins both among themselves and with small molecule is essential for uncovering the molecular mechanisms driving key biological phenomena involved in both physiological and pathological processes. Our group focuses on deciphering these processes using an array of experimental structural and biophysical techniques, including high-field nuclear magnet resonance, circular dichroism, isothermal titration calorimetry, interferometry, and fluorescence spectroscopy, complemented by molecular biology and computational approaches. These approaches allow us to investigate the kinetics and thermodynamics of biological phenomena and provide mechanistic details at the atomic level.



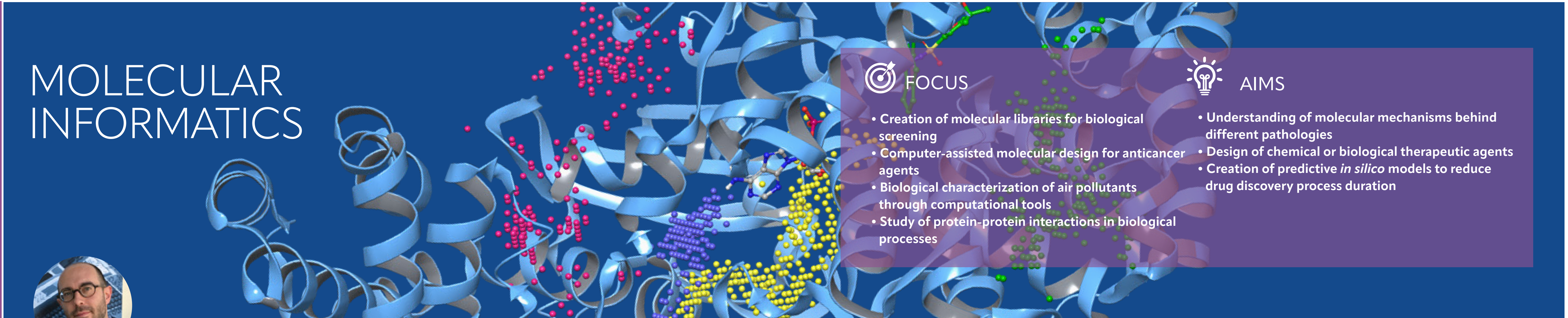
A primary focus of our research is the study of the molecular mechanisms leading to proteins' self-assembly and formation of amyloid-like aggregates, which play a pivotal role in neurodegenerative disorders. Current treatments for these conditions are largely palliative and non-specific, reflecting gaps in the understanding of the disease's molecular basis. Our research aims to unravel the mechanisms of protein misfolding and aggregation behind neurodegenerative diseases and deepen our knowledge of the normal functions and interaction networks of aggregating proteins to design molecules capable of specifically inhibiting pathological aggregation.

Another key project within the group focuses on the structural and biophysical characterization of mussel foot adhesive proteins (Mfps). Similarly to proteins involved in neurodegenerative disorders, Mfps undergo a phase transition and form stable aggregates, but with remarkable adhesive properties. This feature makes Mfps of great interest for developing novel, naturally-derived adhesives for biomedical applications, such as tissue engineering, medical device implantation, and regenerative medicine. However, the molecular basis of Mfps adhesive capability remains poorly understood. Our goal is to elucidate these mechanisms at the atomic level to inform the development of innovative bio-adhesive materials able to work in wet environments.

In addition to these projects, our group is actively involved in small molecule-based drug discovery and the development of protein-based therapeutics, with a particular focus on therapeutic antibodies.

COLLABORATIONS

- Biophysics Institute of the National Research Council (IBF-CNR), Palermo, IT
- University of Palermo, IT
- University of Campania "Luigi Vanvitelli", Naples, IT
- European Brain Research Institute (EBRI) Rita Levi Montalcini, Rome, IT
- King's College London, London, UK
- i3S - Instituto de Investigação e Inovação em Saúde, Universida de do Porto, Porto, PT



MOLECULAR INFORMATICS

FOCUS

- **Creation of molecular libraries for biological screening**
- **Computer-assisted molecular design for anticancer agents**
- **Biological characterization of air pollutants through computational tools**
- **Study of protein-protein interactions in biological processes**

AIMS

- **Understanding of molecular mechanisms behind different pathologies**
- **Design of chemical or biological therapeutic agents**
- **Creation of predictive *in silico* models to reduce drug discovery process duration**

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The Molecular Informatics group at Ri.MED Foundation mainly deals with the creation and use of *in silico* tools for the design, characterisation and optimization of biologically active molecules. The primary aim is to develop reliable *in silico* predictive models that can help understand the molecular mechanisms underlying various diseases to guide the design of chemical or biological therapeutic agents. The approaches used rely on the classical molecular modeling tools for virtual screening as well as modern chemoinformatics tools based on artificial intelligence. Over the years, the team has gained various experiences in the field of medicinal chemistry and computational chemistry. The expertise acquired by the team members is synergistically exploited for the creation of molecular libraries and to create and validate reliable theoretical models for virtual ligand screening (VLS) campaigns. In recent years, the collaboration with academic groups from University of Palermo, Verona, Paris and Vienna has strengthen the development of approaches based on the use of artificial intelligence for the activity prediction of small molecules.

During 2024 the group has been involved in three main projects:

Design of chronic inflammation disease modulators. Cutting-edge in-silico tools including Artificial Intelligence techniques are used to analyze vast datasets, predict molecular interactions, and uncover hidden molecular patterns related to biological activity. The research combines bioinformatics, molecular modeling, and data analysis to identify novel compounds that can regulate the activity of NLRP3. During 2024 a hit family has been discovered and confirmed initiating a hit expansion campaign.

Development of a computational platform for air pollutants characterization and bioactivity prediction. Exploring the intricate link between air pollutants and human diseases, our research aims to provide a comprehensive understanding of environmental factors contributing to human disorders. Through advanced in-silico profiling techniques (also based on Quantum chemistry approaches), we identify and analyze pollutants predicting their potential mechanism of action, offering insights for preventive strategies and public health interventions.

Development of an in-house machine learning tool for the prediction of small molecules activity as G quadruplex (G4) stabilizers. With a specialized emphasis on DNA and RNA G-quadruplex structures, the group strive to develop novel therapeutic interventions. The main focus is leveraging computational models validated through experimental assays to design drugs that can selectively modulate these structures, holding immense potential for treating a variety of diseases, including cancer and viral infections.

The group is also in charge to run the compound management platform with the aim of creating molecular libraries suitable for biological screening and draw up screening plate.

The main outcomes for 2024 have been the completion of the APBIO platform (a tool for air pollutant bioactivity prediction – to be released and published) and the confirmation of a new chemotype active as inhibitor on NLRP3 inflammasome.

Welcome to the Molecular Informatics Group – Where innovation and cutting-edge technology transform molecular research and accelerate discoveries!

COLLABORATIONS

- University of Vienna (Pharmaceutical chemistry department)
- Italian National Council of Research (CNR)
- University of Verona
- University of Paris Citè
- University of Palermo

MEDICINAL CHEMISTRY

FOCUS

- Design and synthesis of new chemotypes
- Identification of new hit compounds
- Family hit expansion and structural optimization
- Structure-activity relationship (SAR) studies
- Hit-to-lead optimization
- Planning, set-up, optimization and scale-up of synthetic routes
- Retrosynthesis
- Analytical characterization of new molecules
- Design and synthesis of novel allosteric inhibitors of NLRP3 inflammasome
- Design and synthesis of potential modulators of PCYOX1 to validate the druggability of the target

AIMS

- Early drug discovery toward disease therapeutic treatment
- Identify new potential target modulators

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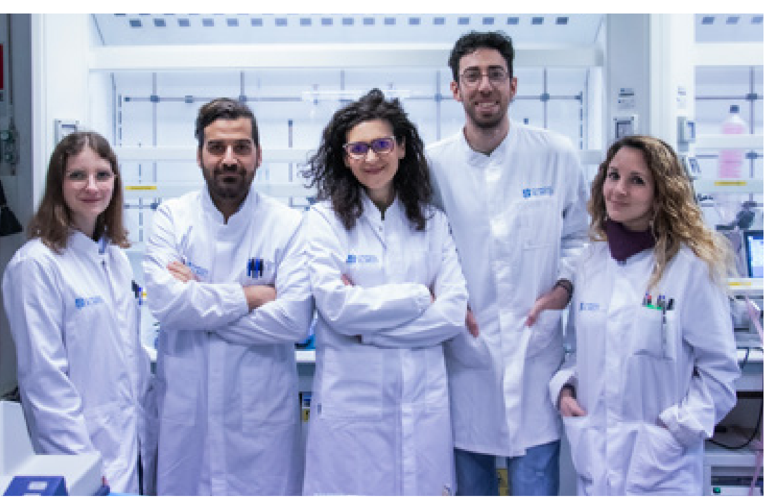


The Medicinal Chemistry group research focuses on discovering new modulators of therapeutic targets of interest. The design, synthesis, and structural characterization of novel small molecules are the main expertise and lead to the creation of compound libraries and building block collections. One of the main projects deals with the design and synthesis of heterocyclic compounds as novel potential inhibitors of NLRP3 (NOD-, LRR- and pyrin domain-containing protein 3) inflammasome. NLRP3 is a validated target for chronic inflammation in age-related diseases (neurodegeneration, autoimmune disorders, etc.).
In 2024, we synthesized a library of indole structure-based sulfonamides, and the compounds were obtained in high yield and purity grade. In the single dose screening (25 µM) several compounds showed a percentage of inhibition higher than 50%. The IC_{50} curves are on the way.

In parallel, the group supports the Drug Discovery area during the screening campaigns and the main tasks include the structure confirmation of preliminary hits and the re-synthesis (when not commercially available or in case of purity issues); the hit(s) family expansion toward the lead compound(s).
Toward the end of the year 2024, we started to investigate and optimize the synthetic routes for the preparation of several structural close analogues of the primary actives retrieved from a virtual screening campaign (by the Molecular Informatic group) and biologically validated and confirmed *in vitro* by the High-throughput Screening group (2023-2024).

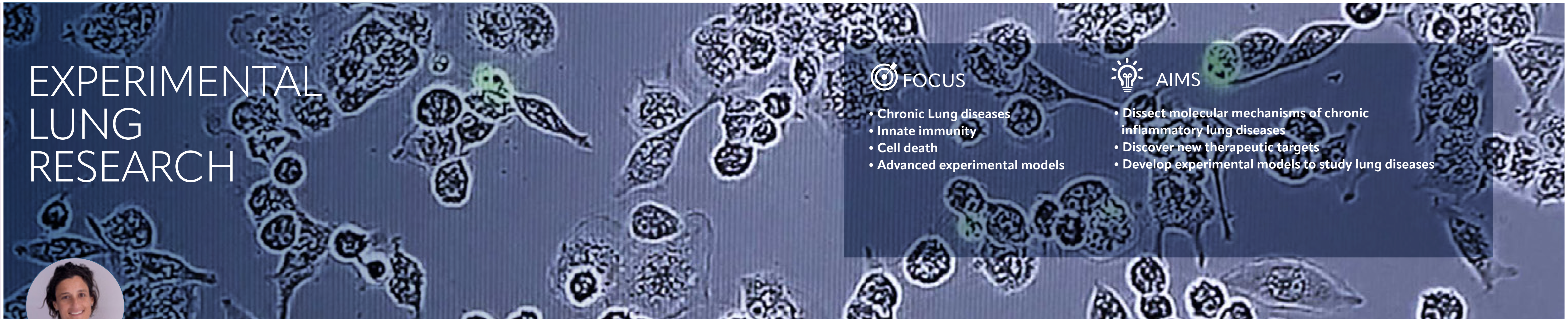
A second project of high interest regards the validation of prenylcysteine oxidase 1 (PCYOX1), as a novel target in cardiology and oncology. In collaboration with the Istituto Europeo di Oncologia; Centro Cardiologico Monzino and Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione, the Medicinal Chemistry and Molecular Informatics groups of Ri.MED Foundation aim to validate the druggability of PCYOX1, and identify potential hits compounds development of cardiovascular and anticancer drugs.
We designed and planned the synthetic route of many structural close analogues of two potential inhibitors recently disclosed. The newly synthesized compounds will be profiled *in vitro* by the collaborators to clarify and explain the mechanism of action, while *in silico* studies will help us to rationalize their binding mode.

We published two peer-reviewed perspectives. In the first one, we overviewed the peptidomimetics developed in the past ten years for treating hepatitis C infection. In the second manuscript, we reviewed the role of the benzoxazole heterocycle in developing antiproliferative, brain-penetrant, and anti-inflammatory agents.

We prepared a third perspective about the applications of bridgehead heterocycles in drug design and medicinal chemistry, and it is under a peer-review process. Moreover, in collaboration with the Molecular Informatics group and the University of Palermo, we contributed to a manuscript (under review) about a fragment virtual screening campaign to identify new hits targeting sirtuin 6 (Sir6).

COLLABORATIONS

- Istituto Europeo di Oncologia (IEO), Milan, Italy
- Centro Cardiologico Monzino, Milan, Italy
- Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione (ISMETT), Palermo, Italy
- University of Palermo, Palermo, Italy



EXPERIMENTAL LUNG RESEARCH

FOCUS

- Chronic Lung diseases
- Innate immunity
- Cell death
- Advanced experimental models

AIMS

- Dissect molecular mechanisms of chronic inflammatory lung diseases
- Discover new therapeutic targets
- Develop experimental models to study lung diseases

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Chiara Finocchio
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- University of Palermo, ITA;
- University of Messina, ITA
- Institute of Translational Pharmacology (IFT) – National Research Council (CNR), ITA;
- Institute for Biomedical Research and Innovation (IRIB) – National Research Council (CNR), ITA;
- Institute for Lung Research, Philipps University Marburg, GER
- Institute of Innate Immunity, University of Bonn, GER.
- La Maddalena spa, Palermo (ITA)
- ARNAS Ospedali Civico Di Cristina Benfratelli, Palermo, ITA

We study innate immunity in lung diseases, both in chronic conditions caused by exposure to external insults such as cigarette smoke as well as in acute settings such as infections. Under homeostatic conditions, alveolar macrophages are the most abundant myeloid cells in the alveolar space and play a key role in orchestrating first line host defenses.

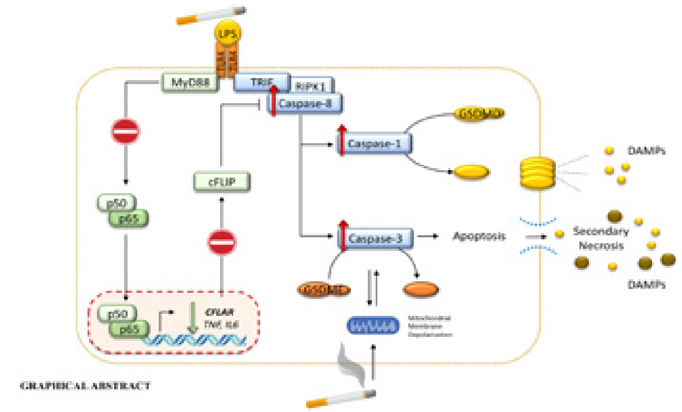
Our research focuses on macrophage-associated immune responses. We are particularly interested in studying how inflammasomes, caspases, and regulated cell death participate to inflammatory reactions in health and disease.

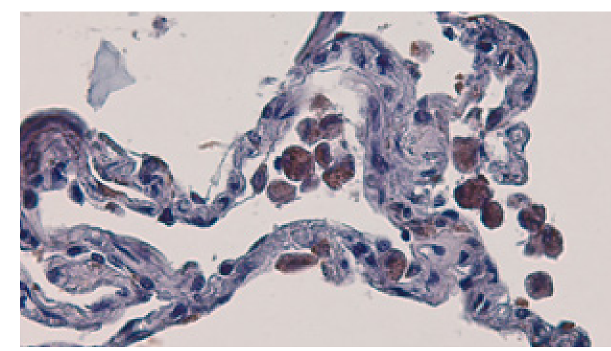
In this respect, growing evidence suggests that fine-tuning cell death may provide a tool for treating chronic inflammation. In particular, we are interested in studying the impact of the pore-forming proteins gasdermins (GSDMs) on the surrounding inflammatory milieu. GSDMs are activated downstream of inflammasomes and/or apoptotic caspases. Upon their activation, GSDMs promote unconventional secretion of IL-1 family cytokines as well as of small damage-associated molecular patters (DAMPs) and eventually lead to pyroptosis, a litic form of regulated cell death.

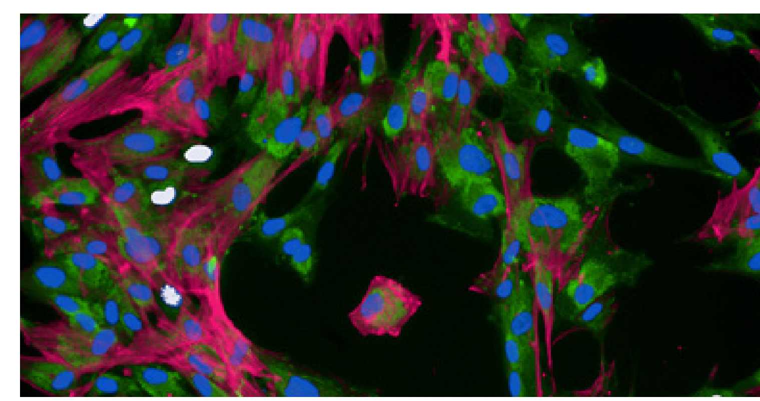
We are currently investigating the impact of GSDMs pore formation on the release of cytosolic proteins in human macrophages and how this affect cellular cross-talk.

A key asset of our lab is the availability and the continuous set-up of new experimental models using human primary cells that we isolate from buffy coats and lung resections. These experimental models are also used as a tool for the development and validation of innovative biosensors for monitoring oxidative stress and inflammation within a consolidated collaboration with the Engineering Department at the University of Palermo.

Our Lab is currently hosted by the National Research Council of Palermo and hosts the Screening Lab of the Ri.MED Foundation Drug Discovery Unit.







PROTEOMICS

FOCUS

- Utilize mass spectrometry-based approaches to investigate the functions of ADAM17 and its cofactors, iRhom1 and iRhom2.
- Demonstrate that iRhom2 contributes to ischemia-reperfusion injury (IRI) *in vivo* and that its ablation mitigates liver damage during graft perfusion.
- Identify predictive and prognostic biomarkers for various clinical conditions, including post-transplant complications, through high-resolution proteomics.

AIMS

- Identify novel functions of ADAM17 and iRhoms, and elucidate the molecular mechanisms underlying iRhom-mediated regulation of ADAM17 activity.
- Discover molecular targets and biomarkers to advance healthcare solutions.
- Develop and optimize proteomic methodologies to support studies of varying scales in health and biotechnology research.

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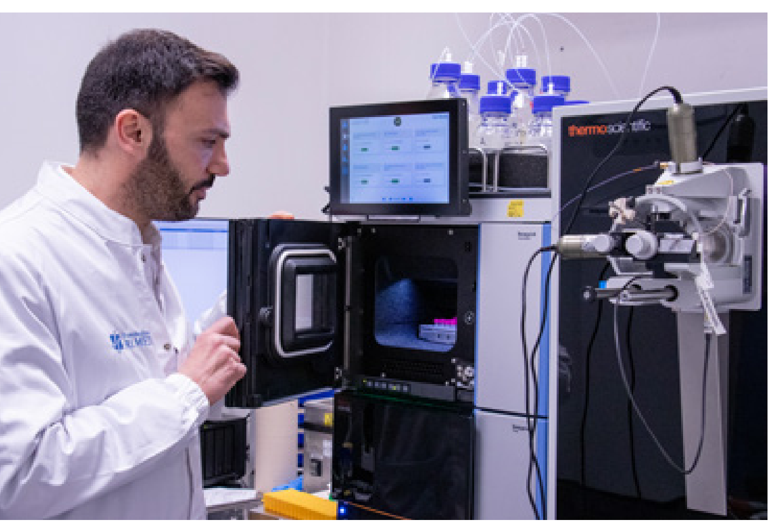
COLLABORATIONS

- ISMETT - Istituto Mediterraneo per i Trapianti Ismett IRCCS, ITA
- University of Palermo, ITA
- IRIB-CNR, Palermo ITA
- Univesity of Pisa, ITA
- University of Udine, ITA
- Istituto Ortopedico Rizzoli, ITA
- German Center for Neurodegenerative Diseases (DZNE) Munich, DE.
- Hospital fo Special Surgery, Weill Cornell University, NY, USA.
- University of East Anglia, Norwich UK
- University of Nottingham, UK
- University of Liverpool, UK

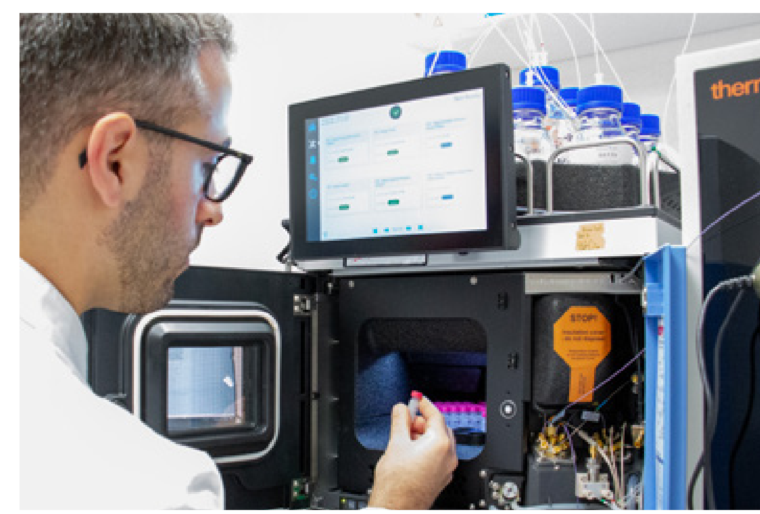


The Proteomics Group is focused on elucidating the roles of a class of membrane-tethered proteases, known as ADAMs (A Disintegrin and Metalloproteinases), in health and disease. Due to their ability to release cell surface proteins, ADAMs are involved in several cellular processes, including cell communication, cell adhesion, and molecular transport. The Proteomics Group uses a synergistic array of proteomic, cell biology, biochemistry, and *in vivo* models to identify substrates of ADAMs, validate them by orthogonal methods, and uncover the functional consequences of their ADAM-dependent release *in vivo*.

Among these proteases, **ADAM17** is of major pharmaceutical interest, as it is responsible for the release of TNF and EGFR ligands, and is therefore involved in the development of autoimmune diseases and cancer. We have developed mass spectrometry-based approaches to characterize the functions of ADAM7 and its two essential cofactors, **iRhom1** and **iRhom2**. iRhom2 specifically regulates the activity of ADAM17 in immune cells. Its genetic ablation in mice prevents TNF release and is protective against rheumatoid arthritis and other autoimmune diseases.

We have recently discovered a new function of iRhom2 in stabilizing MHC class I molecules at the cell surface and regulating antiviral responses. We are currently testing whether this mechanism has functional consequences in the recognition of cancer or virus-infected cells by the immune system. Additionally, we are investigating whether **iRhom2 inactivation** could mitigate ischemia-reperfusion injury - a TNF-driven inflammatory condition that is detrimental in organ transplantation - and improve transplantation outcomes.

The Proteomics Group has also established methods to analyze the plasma proteome and the proteome of liquid biopsies for clinical research. This has enabled the initiation of several research projects in collaboration with the Ri.MED Foundation's partner ISMETT and Palermo University Hospital, aimed at identifying predictive and prognostic biomarkers for various pathological conditions, including ischemia-reperfusion injury in organ transplantation.



ADVANCED DATA ANALYSIS

FOCUS

- The molecular aspects of aging, cancer and degenerative diseases
- Understanding the role of non-coding RNA (microRNA and long non coding RNA)
- Alternative splicing and its modulation

AIMS

- Analysis and interpretation of biological big data
- Omics data analysis through customized algorithms
- Discovery novel biomarkers and pathways
- Design of RNA-based therapeutics through machine-learning based approaches

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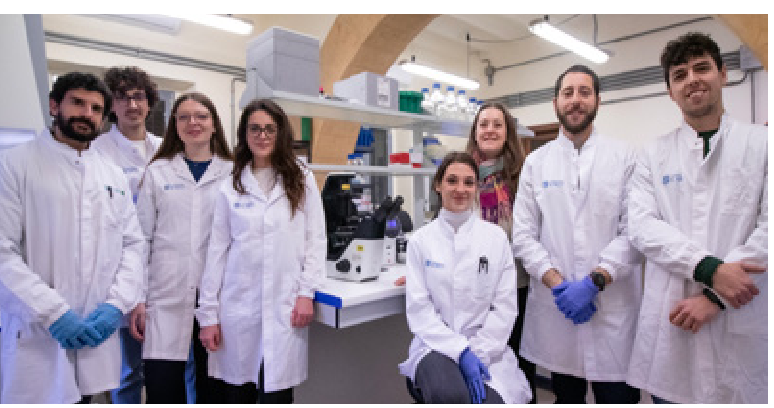
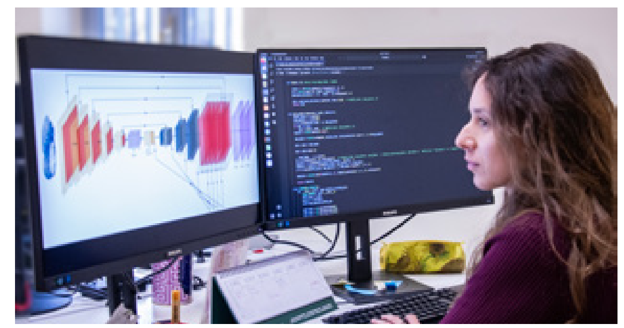


COLLABORATIONS

- University of Palermo, Palermo, Italy
- National Research Council (CNR), ITA
- IRCSS ISMETT, Palermo, Italy
- Università degli Studi di Rome "Foro Italico", Roma, Italy
- University of Pittsburgh, PA, US
- University of Texas Medical Branch at Galveston, TX, US

The Advanced Data Analysis group integrates different layers of expertise spanning from wet lab to big data analysis, with the goal of unraveling biological complex systems by developing customized experimental and computational pipelines. In fact, we constantly put at the service of other research groups our expertise on the analysis of biological big data, both leveraging established algorithms and developing new ones, also based on machine learning and deep learning approaches.

We actively participate in the Drug Discovery area activities by supporting other groups in high throughput screening experimental design and their data analysis. Our main interest is in biological regulatory networks. In particular, we study the regulatory role of non-coding RNA, e.g., microRNA and long noncoding RNA, in the context of aging, cancer and degenerative diseases.



We seek the role of non-coding RNA in gene expression modulation and the occurrence of alternative splicing events, by integrating the analysis of multiple omics data platforms and network analysis methods. Regulatory interactions that have been computationally predicted are validated in wet lab, e.g., with luciferase assays for microRNA-target interactions. We grew expertise with the OXFORD Nanopore and Illumina technologies, which provide a complete picture of the samples at transcriptomics level, useful for our investigations on gene expression and alternative splicing occurrences. Unraveling cellular senescence was our main focus in 2024.
In this concern, we continued to work on SMART and SUNFOX project, funded by PNRR through the National Center for RNA-based Therapeutics, born in 2022. The two projects are focused on finding new approaches for the gene expression regulation of two targets, LMNA and FOXO4 respectively, both involved in senescence pathway. In addition, in collaboration with two department of the University of Palermo, i.e., DiFC and DSEAS, we follow projects focused on classifying senescence cells by single cell's morphological or transcriptomic information, with the aim of detecting time course behavior and contagion effects.

Finally, we set up a new laboratory, with cellular and molecular biology equipment, useful to develop experimental approaches to validate the predictions obtained by novel bioinformatics algorithms developed by the group itself. The experimental activity will be initially focused on microRNA target validation and anti-sense oligonucleotide's application for gene expression and alternative splicing modulation.

IMAGING AND RADIOMICS

FOCUS

- **Artificial Intelligence and Radiomics in Precision Medicine**
- **Radiomics for the quantitative evaluation of Treatment Efficacy and Prediction**
- ***In Vitro* and *In Vivo* Theranostic studies: New Radiopharmaceuticals for Diagnosis and Therapy**
- **Radiobiology Studies for Dosimetry-Time Effectiveness of Radiopharmaceutical Therapy**

AIMS

- **Develop Artificial Intelligence and Radiomics systems to support Biomedical decision-making**
- **Develop tools for target Detection, Segmentation and Classification in biomedical Imaging**
- **Develop Radiomics tools for Preclinical Biodistribution analysis of Radiopharmaceuticals**
- **Study the effects of ionizing radiation on cellular systems (*in vitro*) and *in vivo* in the context of radiopharmaceutical nanotheranostics**

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Paolo Giaccone
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Simone Valenti
PhD Student
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PhD Student
Ghazal Basirina
PhD Student
Gaspare Centineo
Trainee
Silvia Caronna
Trainee
Roberta Ingargiola
Trainee

The Imaging and Radiomics Group is a multidisciplinary team united by multimodal imaging research. A synergy of transversal expertise is the basis of this team; in particular, the group is made up of Computer Scientists, Biotechnologists, specialized Medical Doctors and Engineers from different sectors. The focus of the group is twofold. Part of the research concerns the development of Artificial Intelligence (Machine Learning and Deep Learning algorithms) and Radiomics applied to Multispectral and Biomedical Images (Cellular, Preclinical and Clinical) to support Biomedical decision-making. Additionally, this research group utilizes new innovative and translational approaches to support Nuclear Medicine and Precision Medicine through *in vitro*, *ex vivo*, and *in vivo* studies in the fields of radiopharmaceutical therapy, nanoparticles, and biodiversity.

COLLABORATIONS

- Georgia Institute of Technology (GIT), Atlanta, GA 30332, USA
- National Institutes of Health (NIH), USA
- Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, (PROMISE) University of Palermo, Palermo, ITA
- Pharmaceutical Factory, La Maddalena S.P.A., Palermo, ITA
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- Department of Engineering, University of Palermo, Palermo, ITA
- Experimental Zooprophylactic Institutes of Sicily (IZS Sicily), Palermo, ITA
- The Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT-IRCCS), Palermo, ITA
- Department of Agricultural, Food and Forests Sciences University of Palermo, Palermo, ITA
- Texas A&M University – Corpus Christi, 6300 Ocean Dr, Corpus Christi, TX 78412, United States
- Institute of Bioimaging and Complex Biological Systems (IBSBC) CNR (Palermo and Milan), ITA

In 2024, the Imaging and Radiomics Group was awarded the grant funded by THE - Tuscany Health Ecosystem (Innovation Ecosystem - cascade call - National Recovery and Resilience Plan (NRRP). Ministry of University and Research, entitled "study and evaluation of the RADiobiological effect of innovative polymeric nanoparticles of natural origin radiolabeled with radioIsotopO Lu-177 in prostate cancer cell lines" – RADIATIONS. In addition, the Imaging and Radiomics Group maintained and strengthened the GIT and NIH collaboration in the radiomics analysis of magnetic resonance angiography of mice affected by a particular type of anemia, presenting the preliminary results at the BMES 2024 conference organized by the Biomedical Engineering Society in Baltimore, Maryland in October 2024. As part of their collaboration with the Institute of Bioimaging and Complex Biological Systems (IBSBC-CNR, Milan), the group is conducting preclinical PET and MRI studies to detect early degeneration of neuronal in Parkinson's disease. In addition, the group has conducted the following research areas in the field of preclinical and clinical molecular imaging with positron emission tomography (PET) in the field of biodiversity, gene therapy in inflammation and cancer:

- Theranostic Approaches for Gastric Cancer: An Overview of *In Vitro* and *In Vivo* Investigations
- Biodistribution Assessment of a Novel 68Ga-Labeled Radiopharmaceutical in a Cancer Overexpressing CCK2R Mouse Model: Conventional and Radiomics Methods for Analysis
- Recent Developments in Nanoparticle Formulations for Resveratrol Encapsulation as an Anticancer Agent
- A Review of Advances in Molecular Imaging of Rheumatoid Arthritis: From *In Vitro* to Clinic Applications Using Radiolabeled Targeting Vectors with Technetium-99m

Clinical research activities in Magnetic Resonance Imaging included:

- Shearlet Transform Applied to a Prostate Cancer Radiomics Analysis on MR Images
- PSMA-positive prostatic volume prediction with deep learning based on T2-weighted MR
- New Parametric 2D Curves for Modeling Prostate Shape in Magnetic Resonance Images
- PSMA-positive prostatic volume prediction with deep learning based on T2-weighted MRI
- Grading and Staging of Bladder Tumors Using Radiomics Analysis in Magnetic Resonance Imaging

Additionally, the group was involved in the development of:

- Quantitative Evaluation by Digital Pathology of Immunohistochemical Expression of CK7, CK19, and EpCAM in Advanced Stages of NASH
- High-Risk HPV CISH Detection in Cervical Biopsies with Weak and/or Focal p16 Immunohistochemical Positivity
- Digital Pathology: A Comprehensive Review of Open-Source Histological Segmentation Software

Several research studies were conducted by the group in the field of:

- Stereotactic Radiotherapy for Penile Metastasis: Case Report and Systematic Literature Review
- Radiomics Analysis of Preprocedural CT Imaging for Outcome Prediction after Transjugular Intrahepatic Portosystemic Shunt Creation
- Artificial Intelligence and Statistical Models for the Prediction of Radiotherapy Toxicity in Prostate Cancer: A Systematic Review;
- Texture Analysis in Chronic Liver Diseases

REGENERATIVE MEDICINE AND IMMUNOTHERAPY

EXPERIMENTAL IMMUNOTHERAPY
HEPATOBILIARY REGENERATIVE MEDICINE
REGENERATIVE MEDICINE - CELLULAR THERAPIES
GMP CELL FACTORY
PRECLINICAL *IN VIVO* RESEARCH

Three - dimensional biliary cell colture.
Courtesy of the Hepatobiliary Regenerative Medicine Group

PUBLICATIONS

A Nonenzymatic Procedure to Obtain Human Mesenchymal Stromal Cells from the Dermis
Iannolo G, Calascibetta F, D'Arpa S, Amico G, Tinnirello R, Conaldi PG, Chinnici CM
Methods Mol Biol. 2024; 2835:17-27
doi: 10.1007/978-1-0716-3995-5_2

Modulating the release of bioactive molecules of human mesenchymal stromal cell secretome: Heparinization of hyaluronic acid-based hydrogels
Palumbo FS, Fiorica C, Carreca AP, Iannolo G, Pitarresi G, Amico G, Giammona G, Conaldi PG, Chinnici CM
Int J Pharm. 2024 Mar 25; 653:123904
doi: 10.1016/j.ijpharm.2024.123904

Extracellular Vesicles in Lung Cancer: Implementation in Diagnosis and Therapeutic Perspectives
Carreca AP, Tinnirello R, Miceli V, Galvano A, Gristina V, Incorvaia L, Pampalone M, Taverna S, Iannolo G
Cancers (Basel). 2024 May 22; 16(11):1967
doi: 10.3390/cancers16111967

Human Amniotic MSC Response in LPS-Stimulated Ascites from Patients with Cirrhosis: FOXO1 Gene and Th17 Activation in Enhanced Antibacterial Activation
Pampalone M, Cuscino N, Iannolo G, Amico G, Ricordi C, Vitale G, Carcione C, Castelbuono S, Scilabra SD, Coronnello C, Gruttadauria S, Pietrosi G
Int J Mol Sci. 2024 Feb 28;25(5):2801
doi: 10.3390/ijms25052801

XXVIII Annual Meeting of the Italian Association for Laboratory Animal Sciences
Galligioni V, Campagnol M, Fuochi S, Pagano, V , Raspa M, Sabbioni S, Zarattini P
Biol. Life Sci. Forum 2024, 32(1)
doi: 10.3390/blsf2024032001

Building Basic and Clinical Research Around Lung Transplantation
Vitale Miceli, Alessandro Bertani, Valeria Pagano, Claudio Centi & Pier Giulio Conaldi
Contemporary Lung Transplantation. Organ and Tissue Transplantation. Springer, Cham
doi: 10.1007/978-3-319-20788-9_48-1

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Building Basic and Clinical Research Around Lung Transplantation
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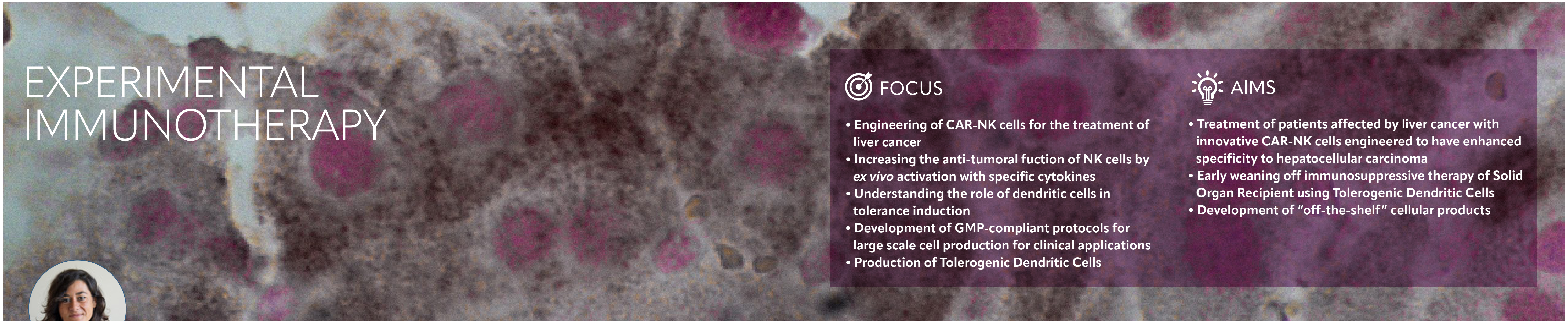
Serologic screening and molecular surveillance of Kaposi sarcoma herpesvirus/human herpesvirus-8 infections for early recognition and effective treatment of Kaposi sarcoma herpesvirus-associated inflammatory cytokine syndrome in solid organ transplant recipients
Mularoni A, Cona A, Bulati M, Busà R, Miele M, Timoneri F, Di Bella M, Castelbuono S, Barbera F, Di Carlo D, Volpe L, Gallo A, Maria de Luca A, Coniglione G, Todaro F, Barozzi P, Riva G, Pietrosi G, Gruttadauria S, Bertani A, Vitulo P, Fontana A, Cipriani M, Rizzo S, Arcadipane A, Luca A, Mikulska M, Conaldi PG, Grossi PA, Luppi M
Am J Transplant. 2024 Nov 16:S1600-6135(24)00697-X
doi: 10.1016/j.ajt.2024.11.013

Topical application of a hyaluronic acid-based hydrogel integrated with secretome of human mesenchymal stromal cells for diabetic ulcer repair
Palumbo FS, Calligaris M, Calzà L, Fiorica C, Baldassarro VA, Carreca AP, Lorenzini L, Giuliani A, Carcione C, Cuscino N, Pitarresi G, Scilabra SD, Conaldi PG, Chinnici CM
Regen Ther. 2024 Jul 27;26:520-532
doi: 10.1016/j.reth.2024.07.008. eCollection 2024 Jun



EXPERIMENTAL IMMUNOTHERAPY

FOCUS

- **Engineering of CAR-NK cells for the treatment of liver cancer**
- **Increasing the anti-tumoral fuction of NK cells by *ex vivo* activation with specific cytokines**
- **Understanding the role of dendritic cells in tolerance induction**
- **Development of GMP-compliant protocols for large scale cell production for clinical applications**
- **Production of Tolerogenic Dendritic Cells**

AIMS

- **Treatment of patients affected by liver cancer with innovative CAR-NK cells engineered to have enhanced specificity to hepatocellular carcinoma**
- **Early weaning off immunosuppressive therapy of Solid Organ Recipient using Tolerogenic Dendritic Cells**
- **Development of "off-the-shelf" cellular products**

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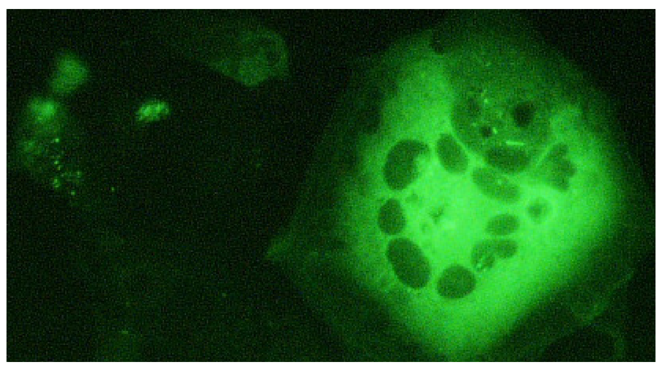

COLLABORATIONS

- The Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT-IRCCS), Palermo, ITA
- Thomas E. Starzl Transplantation Institute, University of Pittsburgh School of Medicine, USA
- University Of Pittsburgh Medical Center (UPMC)
- The University of Pittsburgh, McGowan Institute of Regenerative Medicine (MIRM), USA
- Experimental Zoopròphylactic Institutes of Sicily (IZS Sicily), IT
- National Research Council (CNR), ITA

Our research is focused on the development of cell-mediated therapies aiming at increasing the life expectancy of patients in solid organ transplantation and cancer. During 2023 we focused our research on novel treatment to improve the prognosis of hepatocellular carcinoma (HCC), such cell-mediated immunotherapy. A second project developed in our lab investigates the role of tolerogenic Dendritic cells in the induction of operational immune tolerance in solid organ recipients. HCC is a malignant epithelial tumor arising from hepatocytes. Treatments for HCC include hepatectomy, liver transplant or chemotherapy which are not always effective for advanced forms of HCC and the risk of recurrence is high. Therefore novel treatment strategies are urgently needed. Natural killer (NK) cells play an important role in the innate host immune response against viruses and tumors.
The frequency and function of NK cells in the peripheral blood and liver are associated to the recurrence and survival rates of patients with resectable HCC. Thus, hepatic NK cells are thought to play an important role in mediating the immune function of the liver. We have patented a method to isolate high numbers of viable NK cells from an alternative source such as the liquid perfusate of the liver of deceased donors. We have also optimized a protocol to expand these cells obtaining clinically relevant cell concentrations. We have recently demonstrated that NK cell conditioning with cytokines such as interferon-alpha (IFN-α) significantly increase their anti-viral an anti-tumor response both *in vitro* and in preclinical studies *in vivo*. Having therefore performed all the proof-of-concept studies, our cellular product is ready to move on to the clinic. ISMETT is equipped with a Cell Factory which will support the production of this cellular product for downstream clinical applications.
Genetic modification techniques have been developed to improve the specificity and efficacy of NK cell cytotoxicity to tumor cells. For example, the approach using Chimeric Antigen Receptor (CAR) engineering for NK cells has enhanced the specificity and efficacy of NK cell therapy. In our laboratory we are investigating the use of a novel CAR construct to engineer NK cells with specificity for a tumor antigen described in HCC and known as Glypican-3 (GPC3). The 4th generation lentiviral construct is designed to also secrete soluble cytokines such as interleukin-15 (IL-15), known to sustain NK cells proliferation, function and survival, and IFN-α. The vector we designed also expresses the suicide gene Epidermal Growth Factor Receptor in a truncated form (EGFRt) as safety switch. In close collaboration with the researchers at ISMETT, we have optimized the protocol of transduction of liver derived NK cells, obtaining about 35-40% of CAR-expressing cells. We have demonstrated that these CAR-NK specifically recognize GPC3-expressing tumor target cells and that release IFN-α upon engagement of the CAR receptor. Further, we have shown the correct function of the suicide gene. The experimental protocol for the preclinical studies is currently under evaluation by the Istituto Zooprofilattico Sicilia (IZS), our partner for the *in vivo* experimentation.
Lately, we are exploring the role of the ADAM-17 in the NK-mediated innate response to cancer by knocking out the expression of this metalloproteinase, which is involved in the stabilization of the surface protein CD16 that concurs to NK cell killing of target cells.
Our lab is also interested in developing a cell-based approach to induce operational tolerance in liver/kidney using tolerogenic Dendritic cells. One major caveat of organ transplantation is graft rejection. Accordingly, immunosuppressive therapy is provided for life to transplanted patients, though it is accompanied by severe side effects such as kidney failure. The use of cellular therapies such as the administration of donor derived tolerogenic Dendritic Cells for early weaning of liver transplanted patients is a novel strategy to prevent graft loss. Our strategy in the use of the liver perfusate from deceased donors as source of DCs precursors.

HEPATOBILIARY REGENERATIVE MEDICINE

FOCUS

- Development of artificial bile ducts.
- Advancement of biliary organoid models.

AIMS

- Refining the vascular network within bioartificial CBDs to enhance integration with host tissue and ensure proper nutrient exchange for tissue regeneration.
- Investigating the safety and effectiveness of artificial CBDs *in vivo*.
- Advancing biliary cell culture techniques, including 3D organoids, to create scalable, reproducible, and functional cell sources for disease modeling, drug screening and therapeutic applications.

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COLLABORATIONS
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- McGowan Institute for Regenerative Medicine (MIRM), PA, USA

The Hepatobiliary Regenerative Medicine group, led by Dr. Francipane, focuses on regenerative medicine strategies for treating conditions of the biliary tree. A significant challenge in liver and biliary disease treatment is managing complications that arise after surgery, such as biliary strictures following liver transplants or cholecystectomy. These strictures can lead to biliary tract obstruction, cholestatic liver failure, and even liver (re)transplantation.

Endoscopic retrograde cholangiopancreatography is the standard for diagnosing and treating strictures, with plastic stents used to dilate bile ducts. However, these stents require frequent replacements, increasing risks like infections, pancreatitis, and bleeding. Self-expanding metal stents are an alternative, with fully covered versions (FCSEMS) offering similar effectiveness but requiring fewer replacements. However, FCSEMS carry a migration risk, causing further complications.

The landscape of biliary complication treatment is evolving, with a focus on developing biodegradable polymeric stents that are naturally resorbed by the body, eliminating the need for replacement or removal. A major challenge in this area is balancing the degradation rate of the polymeric scaffold with the regeneration rate of biliary tissue. The scaffold must degrade to prevent chronic inflammation and scar tissue formation, while the mechanical properties must be replaced by newly formed tissue.

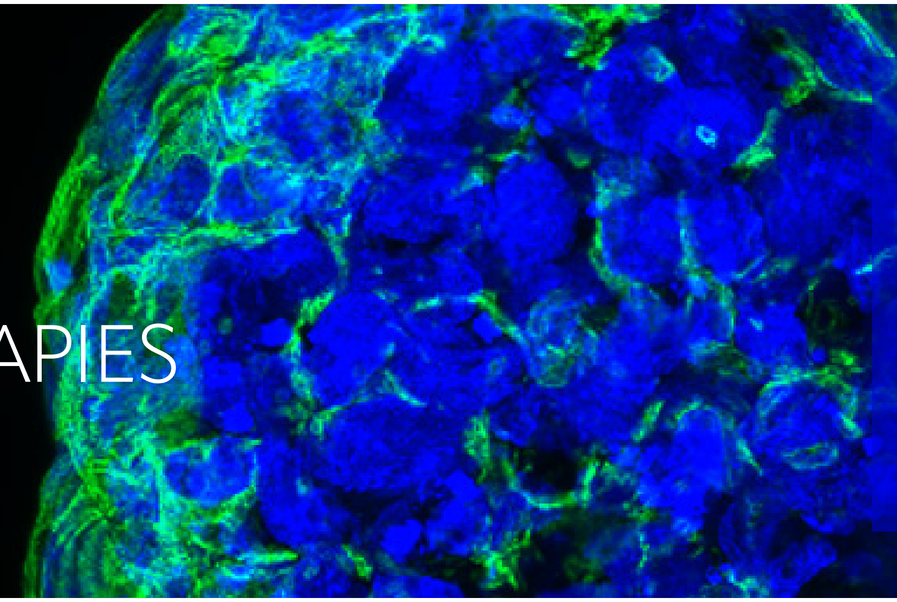
While tissue-engineered constructs using biodegradable biomaterials have been explored, many fail to replicate the complex biological properties of native ducts. In response to this need, Dr. Francipane's group has developed artificial common bile ducts (CBDs) - both acellular and cellularized - using tissue engineering techniques. These CBDs match the native size and combine two biomaterials with different degradation rates within a three-phase tubular structure. One biomaterial supports biliary epithelial cell growth (either from seeded cells in the cellularized version or recruited cells in the acellular version), while the other provides mechanical strength.

Through histological, ultrastructural, and biochemical analyses, the group has shown the creation of a viable and functional biliary-like epithelium in the cellularized version. Tests have confirmed the artificial CBDs' homogeneity, stability, mechanical strength, handleability, and leak-free properties, positioning them as a promising solution for biliary tissue regeneration.

The group is also exploring the inclusion of endothelial or mesenchymal stromal cells, with pre-clinical assessments planned. If these devices prove safe and effective *in vivo*, they could offer new treatment options for CBD-related diseases, reduce hospital admissions, and lower healthcare costs. Efforts to protect the innovation are also underway, with a patent specification close to being filed.

Additionally, efforts are focused on advancing biliary cell culture techniques and establishing organoids for disease modeling, drug testing, and regenerative medicine applications. To enhance reproducibility, orbital shaking technology is used to promote uniform mixing, consistent oxygenation, and improved nutrient exchange. The use of the W8 cytometer for quality control ensures consistency across organoid batches. The group is also working to endow the organoids with a capillary-like network to enhance their physiological relevance.

REGENERATIVE MEDICINE: CELLULAR THERAPIES



FOCUS

- **MSC-derived biotherapeutics:** Developing cell-free therapy based on secretome and EVs
- **Secretome/EV-laden biomaterials:** Creating combined devices with enhanced therapeutic efficacy.
- **Target gene discovery:** Identifying novel genes relevant to diseases.
- **RNA therapeutics:** developing miRNA- and siRNA-based therapeutics.
- **RNA delivery:** developing nanosized delivery systems for RNA-based therapeutics.

AIMS

- **RNA-based therapies for liver disease: developing innovative RNA-based approaches for the treatment of metabolic dysfunction-associated steatohepatitis (MASH) and liver fibrosis.**
- **Cell-free therapies for wound healing: advancing secretome and extracellular vesicle-based treatments for chronic skin wounds.**
- **Optimized drug delivery: enhancing the efficacy of therapeutic agents with biomaterial based-delivery devices**

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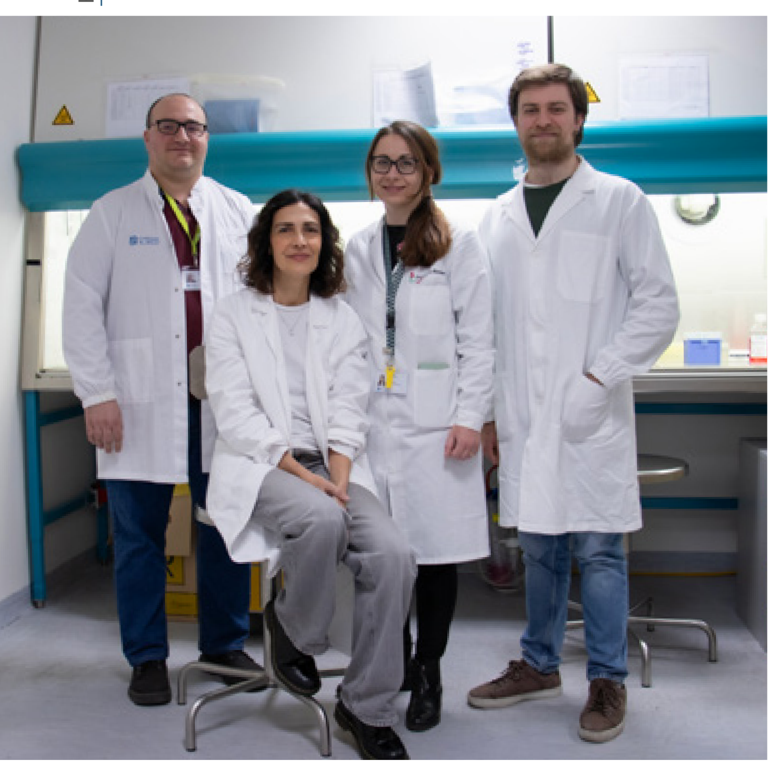

COLLABORATIONS

- Mediterranean Institute for Transplantation and Advanced Specialized Therapies (IRCCS ISMETT), Palermo, ITA
- Lab of Biocompatible Polymers, Dept STEBICEF, University of Palermo, ITA
- Fondazione IRET, Tecnopolo di Bologna, ITA
- Lab of Translational Research, Dept of Medical Sciences, University of Turin, ITA
- National Center for Gene Therapy and Drugs based on RNA Technology, University of Padova, ITA

The Regenerative Medicine – Cell Therapy team focuses on developing strategies that utilize cell-derived products, such as the secretome and extracellular vesicles (EVs) derived from human mesenchymal stromal cells (MSCs), to restore organ function. In this context, the secretome plays a crucial role as a "booster" in regenerative medicine. The bioactive molecules within the secretome, which include proteins, lipids, and RNAs, are often packaged into nanosized extracellular vesicles (EVs), capable of delivering their cargo to target cells. While both the secretome and EVs lack a defined pharmacological classification, they are recognized as biological therapeutics. These products are proposed as alternatives to cell transplantation, as they replicate the therapeutic effects of parental cells without the need for whole cell administration. However, due to their soluble nature, effective delivery is key to optimizing their therapeutic potential. This is accomplished through the development of biomaterial-based

delivery systems that maintain the stability of these soluble agents, protecting them from rapid clearance and *in vivo* degradation. These systems can be designed for specific applications, such as secretome-laden hydrogel patches for topical use (e.g., chronic skin wounds) or injectable EV-laden hydrogel depots for intraperitoneal administration (e.g., liver therapies). In addition to preserving stability, these systems enable sustained release, ensuring prolonged therapeutic activity and delivery to organs. Secretome-laden biomaterials, in particular, are currently being tested for efficacy in animal models of chronic skin wounds. As part of this preclinical evaluation, we have developed polymeric patches incorporating secretome, offering a novel approach to chronic skin wound treatment and enhancing therapeutic outcomes.

A new area of focus is the development of RNA-based therapies for complex, multifactorial diseases, such as metabolic dysfunction-associated steatohepatitis (MASH). MicroRNA (miRNA) therapeutics hold promise for multitargeting approaches, as miRNAs can regulate multiple genes simultaneously. To enhance the effectiveness of RNA therapies, it is crucial to minimize off-target effects and prevent the neutralization of negatively charged RNAs. This can be achieved by utilizing liver-targeting particles, such as newly synthesized nanoparticles or natural EVs, as RNA delivery vehicles. These delivery systems are typically designed for injectable use, enabling systemic administration. As part of this approach, we are currently preparing "engineered" EVs loaded with selected therapeutic miRNAs for preclinical efficacy studies in animal models of MASH, along with preclinical toxicity evaluations. The primary research activities of our team are outlined below:

- Developing RNA-based therapies for liver diseases
- Optimizing the delivery of RNA-based drugs to the liver
- Developing biomedical devices (e.g., secretome-laden biomaterials) for wound healing
- Creating sustainable therapeutic solutions, such as smart, green materials integrated with cell-derived products
- Establishing advanced 3D cellular models for drug testing
- Conducting *in vivo* preclinical studies to assess efficacy and toxicity.

GMP CELL FACTORY

FOCUS

- Cell based therapies for end stage organ failure (e.g. based on MSCs)
- Immunotherapies, e.g. Multivirus specific T lymphocytes

AIMS

- Contribute to translational medicine, providing new ATMPs to patients
- ATMPs release for Phase I studies and single patient use
- Optimization/automation of production processes and Quality Control (QC) tests

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COLLABORATIONS

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- ISMETT- IRCCS policlinico San Matteo, Pavia, ITA
- ISMETT-IRCCS Ospedale Galeazzi- Sant'Ambrogio, ITA
- University of Pittsburgh, USA

The Cell factory group has developed an Advanced Therapy Medicinal Product (ATMP) consisting in polyclonal multivirus specific T cells (MVT-cells) for autologous and allogeneic applications. The protocol is based on the stimulation of T lymphocytes with a mix of peptides of derived from Epstein-Barr virus (EBV), Cytomegalovirus (CMV), BK polyomavirus (BKV) and Adenovirus (ADV). The product, multivirus-specific T cell clones, is capable of containing or treating virus related post transplant complications (i.e. primary infections or virus reactivation). Other ATMPs are also being evaluated for future productions.

The Production Group, in collaboration with infectious disease specialists and researchers from ISMETT IRRCS, is also actively involved in a clinical project aimed at monitoring the clinical conditions and outcomes of solid organ transplant recipients following primary infection or reactivation of the HHV-8 virus, as well as identifying potential neoplastic complications. HHV-8 infection can lead to the development of neoplastic diseases, including Kaposi's sarcoma (KSHV), Castleman disease, and primary effusion lymphoma (PEL), as well as non-neoplastic conditions such as KICS (KSHV-associated inflammatory cytokine syndrome). Currently, no international guidelines or fully effective therapies are available for these diseases. More in detail, the Production Group focuses on the immunological monitoring of patients by analysing the T-cell specific response through the ELISpot assay for INF-gamma production. T cells are collected from patients and stimulated with HHV-8 latent and lytic phase antigens (K8, K12, LANA, GB). The purpose of this analysis is to integrate clinical evidence during patient follow-up. This research activity led to the publication of an article in 2024 in the American Journal of Transplantation, which was described by reviewers as an excellent contribution to the global medical literature. The journal editors commented on the study stating that "the study represents a step forward in our understanding of a rare but potentially fatal event: donor-derived KSHV-related disease, manifesting as KICS". Moreover, in collaboration with the ISMETT Paediatric Unit, the Production Group currently supports diagnostic investigations into the immune response to viral infections in paediatric patients. In this context, INF-gamma production is assessed using the ELISpot assay, following stimulation with Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV) antigens.

The Quality Control group support in research activities included the collaboration with Dr. Mariangela Pampalone on the project: "Evaluation of the Antibacterial and Anti-inflammatory Capacity of Mesenchymal Stromal Cells Isolated from the Human Amniotic Membrane (hA-MSCs) for the Prevention of Spontaneous Bacterial Peritonitis (SBP), a Complication of Liver Cirrhosis." The protocol involved the inoculation of E. coli to induce bacterial peritonitis in the Wistar rat experimental model and the infusion of mesenchymal stromal cells isolated from full-term human placentas as an alternative therapeutic treatment to conventional antibiotic therapy. Multidrug-resistant E. coli was used to induce peritonitis infection, then samples of each group and team point were assessed by the QC group for microbial load, identifying the microorganisms, to evaluate the antibacterial and anti-inflammatory capacity of the mesenchymal stromal cells inoculated at the infected site.

PRECLINICAL *IN VIVO* RESEARCH

FOCUS

- Test surgical, pharmacological, metabolic, gene and immunological therapies on animal models that mimic terminal organ failure
- Safety ed efficacy of scaffold
- *In vivo* Proof-of-concept
- Training for MD and DVM

AIMS

- Welfare of Laboratory animals
- Drafting of the protocol
- Standardization of animal model
- 3R Application (Reduction, Replacement and Refinement)
- Training modules for researchers and personnel who perform procedures (function A), take care of animals (function C), euthanize animals (functionD) and design procedures and projects (function B)

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Nazareno Costa
Animal Care

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- University of Palermo, Palermo, ITA
- Experimental Zooprophylactic Institutes of Sicily (IZS Sicily) Palermo, ITA
- Experimental Zootechnical Institute for Sicily (ISZS) Palermo, ITA

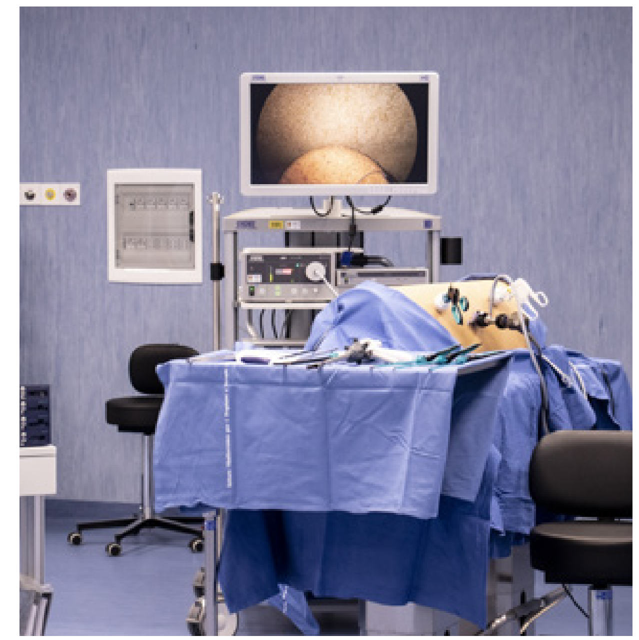
Our research is focused on the development of animal pathological models, the improvement of housing conditions based on specie's needs and their microbiological condition and experimental refinement procedures, in order to improve animal wellbeing, and to standardize protocols to obtain robust data.
To date, as the Ri.MED Foundation does not have its own animal facility, the preclinical *in vivo* group uses animal facilities of our institutional partners (such as IZS Sicilia and ISZ) and acts as an interface between Ri.MED research groups and Competent Authorities to carrying out the *in vivo* projects and to obtain the mandatory authorization .

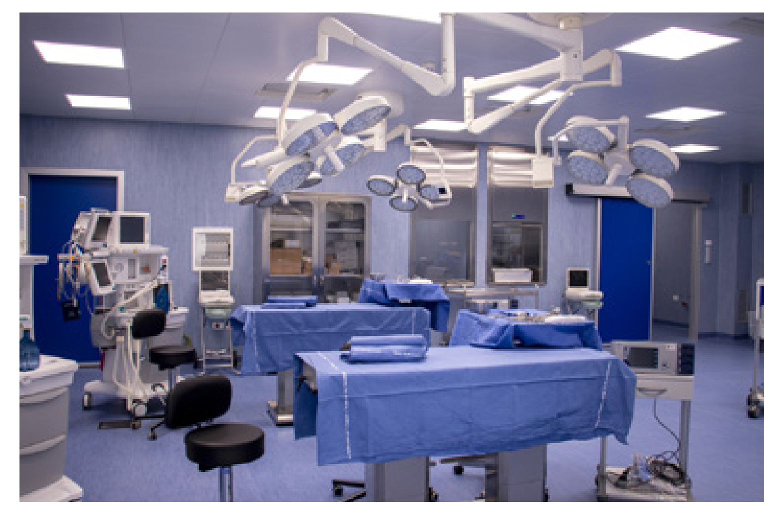
In the course of 2023 we have concentrated our activities giving support to the researchers, supporting them for the drafting of the necessary documents for the Ministerial authorizations and the experimental protocols *in vivo,* by dealing with the application of 3R (refinement replacement and reduction) and obtaining the necessary authorisations for the import, removal and use of organs and tissues for *ex vivo* testing.

In addition, the Preclinical group is following the authorization path of the ISPEMI large animal facility to the Ministry of Health, a structure consisting of an operating room, a pre-surgery and intensive care area and a long-stay area for sheep and pigs.

Moreover, our group has been included in educational projects in local schools, with the aim of offering the means to understand the need for preclinical research *in vivo*, the progress that research has achieved thanks to the conscious use of the animal, assessing them by criticizing them or supporting them, with a critical spirit free from prejudices.

Furthermore, our group takes care of training external and internal personnel for functions a) b) c) d) of the directorial decree on training pursuant to art. 23 Legislative Decree 26/14.





BIOENGINEERING AND TISSUE ENGINEERING

BIOENGINEERING AND MEDICAL DEVICES
CARDIOVASCULAR TISSUE ENGINEERING
MUSCULOSKELETAL TISSUE ENGINEERING

Ri.MED RESEARCH

PUBLICATIONS

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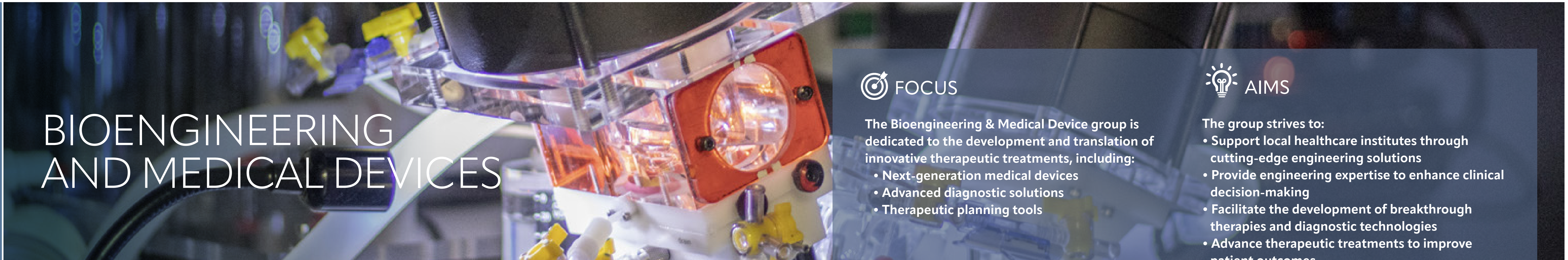
Polymeric sample being mounted in a ultimate tensile testing device.
Ri.MED lab: Cardiovascular Tissue engineering



BIOENGINEERING AND MEDICAL DEVICES

FOCUS

The Bioengineering & Medical Device group is dedicated to the development and translation of innovative therapeutic treatments, including:

- **Next-generation medical devices**
- **Advanced diagnostic solutions**
- **Therapeutic planning tools**

AIMS

The group strives to:

- **Support local healthcare institutes through cutting-edge engineering solutions**
- **Provide engineering expertise to enhance clinical decision-making**
- **Facilitate the development of breakthrough therapies and diagnostic technologies**
- **Advance therapeutic treatments to improve patient outcomes**

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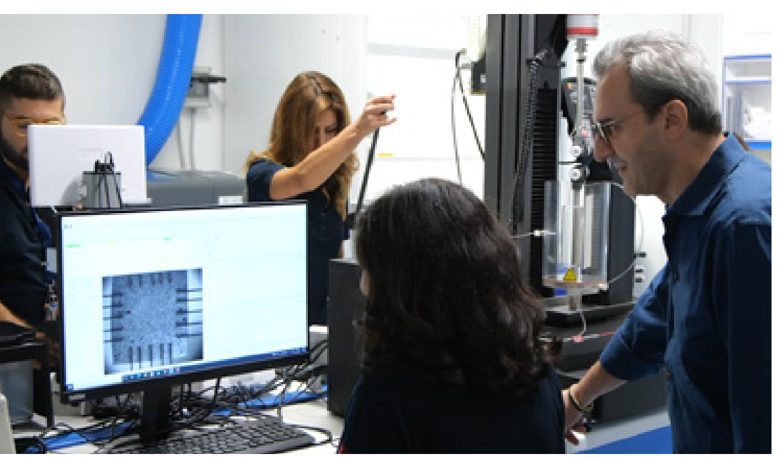
Researcher in Informatics Bioengineering



The Bioengineering & Medical Device group applies engineering principles and physical science to analyse biological systems and develop next-generation biomedical technologies. The group operates mainly in the cardiovascular field, contributing to the conception and optimisation of advanced diagnostic solutions, support tools for therapeutic planning and new generation medical devices based on innovative approaches. It is consolidating as a reference for regional healthcare, for the local academic institutions, and for the small and medium enterprises in the geographic area. Its research team offers solid skills in numerical modelling, fluid-structural analysis, and medical device design and development.

The group is continuously expanding the Foundation's medical technology portfolio, by including novel surgical and minimally invasive cardiovascular repair and replacement solutions. In 2024, the group accelerated clinical translation and strengthened intellectual property, seeing the patent of a novel annuloplasty ring granted in China and Japan, and a new mitral repair device patent published in the EU.

Working with clinical and industrial partners, our team is actively contributing to the translation of these innovations into practice to improve patient outcomes. In October 2024, the first clinical results of the SIKELIA™ transcatheter aortic valve were presented at the TCT Conference in Washington, D.C. The device IP, owned by Ri.MED Foundation, was generated by Gaetano Burriesci, Ri.MED Group Leader in Bioengineering, and licensed to MitrAssist, a multinational cardiovascular company. The solution has become the first polymeric transcatheter valve ever implanted in human, and clinical trial results involving 12 patients from 4 centres confirmed favourable 1-year safety and performance outcomes, with significant improvements in hemodynamics, offering new hope for treating severe symptomatic aortic stenosis.

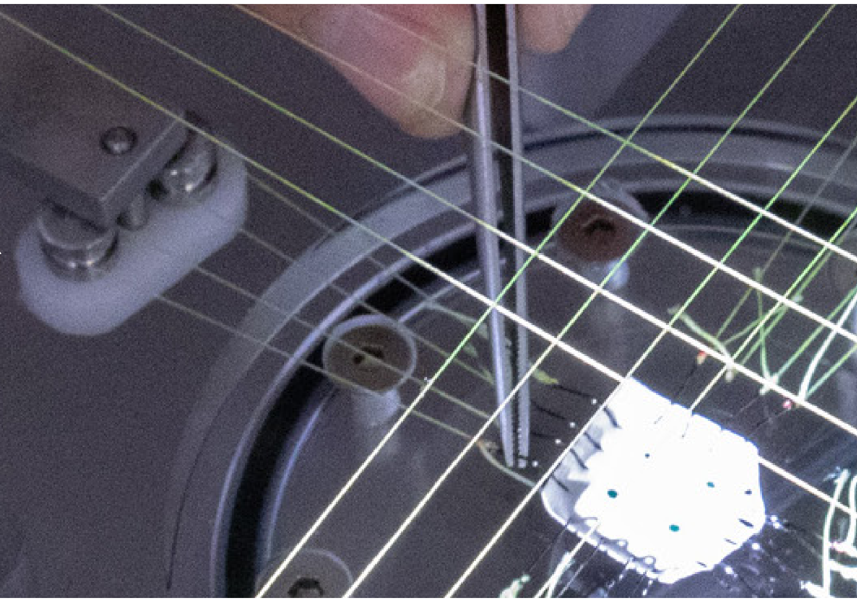
The group also published five new papers in leading journals, covering both fundamental and applied cardiovascular engineering. Key breakthroughs include: i) the characterisation of polymeric membranes and soft tissues, revealing limitations in current experimental methods and proposing a more accurate research protocol; ii) the implementation of a novel meshless particle-based computational approach (in collaboration with the University of Palermo, Italy) to simulate complex cardiovascular fluid-structure interactions; iii) the development of a new intraoperative methods for aortic annulus sizing and balloon valvuloplasty (in collaboration with UCL, UK); iv) the identification of limitations in current left atrial appendage (LAA) morphology classification, highlighting its inadequacy for ischemic event prediction and introducing new hemodynamic parameters for better thromboembolic risk stratification (in collaboration with UCL, UK); v) the analysis of procedural LAA inversion risks based on patient-specific anatomy and showing how pressure variations affect inversion and recovery, with predictable trends (in collaboration with UCL, UK).

These achievements have strengthened the group's international reputation, especially in the LAA research area, leading in 2024 to the PRISMA Project grant. This initiative aims to develop a telemedicine platform integrating machine learning and synthetic LAA models to enhance personalized risk stratification and precision medicine.

COLLABORATIONS

- Adeka, Japan
- Erasmus MC, The Netherlands
- Harvard Medical School, USA
- Imperial College London, UK
- ISMETT- IRCCS, Palermo, ITA
- Magdi Yacoub Foundation, Egypt
- Mitrassist Lifesciences, PRC
- Università degli Studi di Palermo, ITA
- Università degli studi di Padova, ITA
- Université de Technologie de Compiègne, FRA
- University College London, UK
- University of Amsterdam, the Netherlands
- University of Bristol, UK
- University of Minnesota, USA
- University of Pittsburgh, USA

CARDIOVASCULAR TISSUE ENGINEERING



FOCUS

- Tissue-engineered heart valves
- Tissue-engineered vascular grafts
- Tissue-engineered cardiac patches
- Bioreactors for enhanced extracellular matrix elaboration
- Native/engineered tissue image-based structural and histopathological analysis
- Native/engineered tissue numerical models for mechanics and tissue growth

AIMS

- *In silico*, *in vitro*, and *in vivo* models
- Quantitative histology and biomaterial micro-structure image-based analysis
- Structural modelling for cardiovascular tissue engineering
- Mechanical and topological conditioning to duplicate native tissue properties
- Endogenous tissue growth, vascular grafts, and engineered heart valves.

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Joan Dario Laubrie Soto, PhD
Post Doctoral Researcher in Numerical Models

Laura Modica de Mohac, PhD
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Tugba Dursun Usal, PhD
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PhD Student in Precision Medicine

Alfonso Emmanuel Castaneda Serrano
PhD Student in Innovation Sciences and Technologies at the University of Cagliari

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MSc Università degli Studi di Palermo

Beatrice di Caccamo
MSc Politecnico di Torino

Anne Bouwens
MSc Eindhoven University of Technology

Sofia Battaglia
MSc Rome, University Campus Bio-Medico di Roma

Matthias Jacquot
Research Assistant

The D'Amore's Cardiovascular Tissue Engineering group aims to integrate a mechanistic understanding of scaffold–host interaction with the development of novel biomaterials and tissue engineering strategies. The focus of our research is upon unmet clinical needs in cardiovascular diseases. Research interests include six highly interconnected areas: I) quantitative histology and biomaterials micro-structure image-based analysis, II) structural modeling strategies to guide tissue engineering scaffold fabrication, III) mechanical and topological conditioning for tissue elaboration, IV) development of cardiac restrain devices, V) vascular grafts and VI) engineered heart valves.

Our multidisciplinary research team, currently 25 people strong, includes biomedical, mechanical, and structural engineers as well as biotechnologists, biologists, clinicians in addition to a number of interns and Master of Science's degree students.

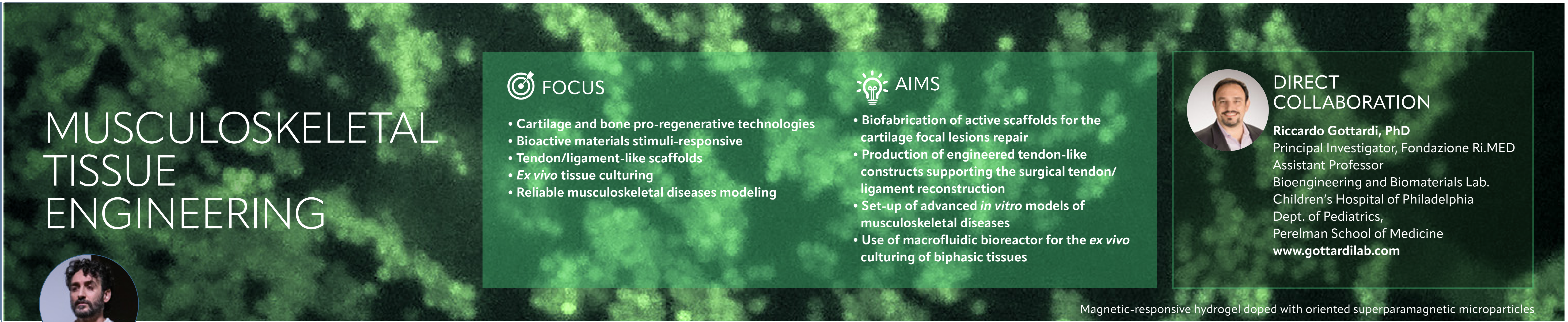
The RiMED laboratory, established in 2020 and graciously hosted by the Departments of: Chimica e Fisica, and STEBICEF, University of Palermo (UNIPA), includes >100 m^2 of fully equipped, independent lab space and 300 m^2 of office and numerical lab space located in buildings 16 and 18 of the UNIPA campus.

Two major technology platforms have been developed since 2020 and cover biomaterials processing and characterization, biological imaging and histology. The group operates also on a second location Additional within the McGowan Institute for Regenerative Medicine, Departments of Surgery and Bioengineering, University of Pittsburgh and includes 70 sq.m of fully equipped wet lab space, and office space.

In 2024, the CVTE group expanded its patent portfolio with 3 issued patents and published 12 scientific papers in leading peer-reviewed journals. Moreover, our group members actively engaged in major international conferences, presenting posters and oral presentations with 16 abstracts accepted in 2024.

COLLABORATIONS

- University of Palermo, Palermo, Italy
- Advanced Technologies Network Center (ATeN Center), Palermo, Italy
- McGowan Institute for Regenerative Medicine (MIRM), Pittsburgh, USA
- University of Pittsburgh Medical Center (UPMC), Pittsburgh, USA
- The Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT-IRCCS), Palermo, Italy
- Universidad Abierta Interamericana (UAI), Buenos Aires, Argentina
- Neoolife, Pittsburgh, USA
- TELEA BioTech, Sandrigo, Italy
- Columbia University Irving Medical Center (CUIMC), New York, USA
- Technical University of Munich, (TUM), Munich, Germany
- University of California Irvine (UCI), Irvine, USA
- Eindhoven University of Technology, Netherland
- Politecnico di Torino, Italy
- Università di Cagliari, Italy
- Policlinico di Milano, Italy



MUSCULOSKELETAL TISSUE ENGINEERING

FOCUS

- Cartilage and bone pro-regenerative technologies
- Bioactive materials stimuli-responsive
- Tendon/ligament-like scaffolds
- *Ex vivo* tissue culturing
- Reliable musculoskeletal diseases modeling

AIMS

- Biofabrication of active scaffolds for the cartilage focal lesions repair
- Production of engineered tendon-like constructs supporting the surgical tendon/ ligament reconstruction
- Set-up of advanced *in vitro* models of musculoskeletal diseases
- Use of macrofluidic bioreactor for the *ex vivo* culturing of biphasic tissues

DIRECT COLLABORATION

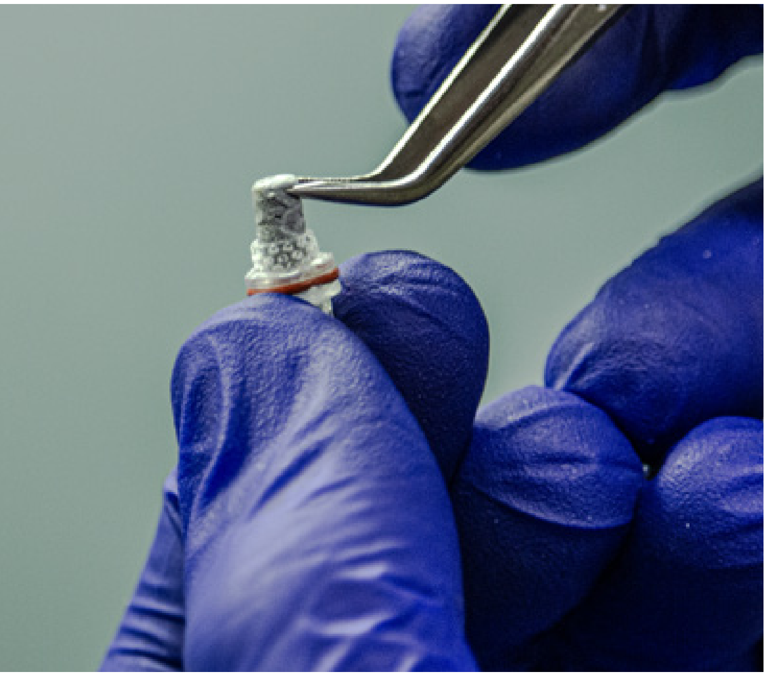
Riccardo Gottardi, PhD
Principal Investigator, Fondazione Ri.MED
Assistant Professor
Bioengineering and Biomaterials Lab.
Children's Hospital of Philadelphia
Dept. of Pediatrics,
Perelman School of Medicine
www.gottardilab.com

Magnetic-responsive hydrogel doped with oriented superparamagnetic microparticles

Roberto Di Gesù, PhD
PRINCIPAL INVESTIGATOR IN
MUSCULOSKELETAL TISSUE ENGINEERING (MSTE)
rdigesu@fondazionerimed.com

Giampiero Vitale
Laboratory Technician

Francesca Romano
PhD student



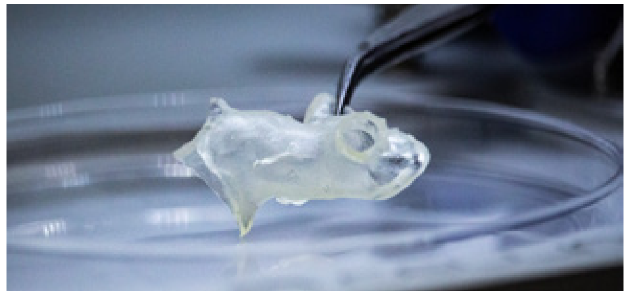
The MusculoSkeletal Tissue Engineering (MSTE) group is dedicated to pursuing as a main objective the advancement of groundbreaking strategies for the treatment of various pathologies that affect ligaments, tendons, cartilage, bone, and muscles.

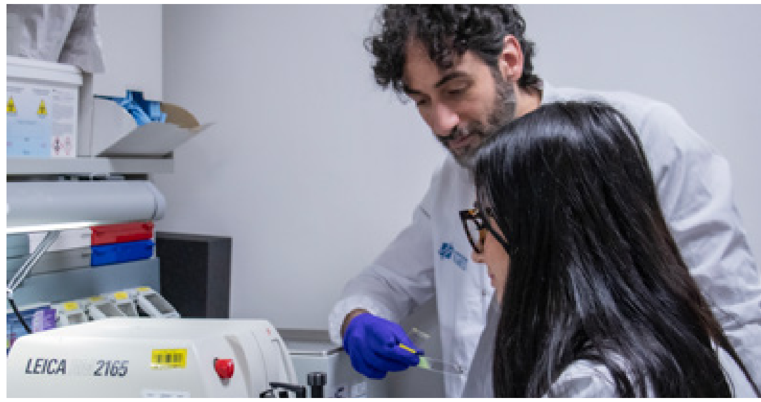
In order to achieve this goal, the MSTE group employs a wide range of innovative approaches relying on tissue engineering technologies. These approaches are based on the most advanced techniques of biofabrication, including but not limited to 3D printing, electric-field induced biofabrication, and bioprinting. Notably, the MSTE research is developed jointly with the Bioengineering and Biomaterials Laboratory at the Children's Hospital of Philadelphia (CHOP, PA - USA) led by prof. Riccardo Gottardi.

The primary focus of the MSTE group is to fabricate bioactive scaffolds able to provide pro-regenerative cues for cells that are either seeded onto or embedded within these kinds of 3D supports. Following this approach, we aim to support reconstructive surgery after tendons/ligaments injuries promoting the regeneration of functional tissue in the mid-term. Analogously, our activity aims to restore the functionality of joints affected by focal chondral defects developing functional scaffolds stimuli-responsive, with a vision toward a clinical translation in the near future. In addition, the MSTE group is leading several projects aimed to the development of highly realistic *ex vivo* models of pathologies affecting the musculoskeletal system. Such an activity is supported by the employment of a proprietary technology based on macro-fluidic bioreactors for the culturing of biphasic tissues in native-like conditions.

The MSTE group is actively involved in numerous collaborations with international partners, which allow the design and management of different interdisciplinary projects. These collaborations serve as a fertile ground for the exchange of knowledge, expertise, and resources, enabling the MSTE group to push forward the boundaries of innovation. In this direction, we are developing engineered models of muscle tissue with a specific focus on fill the gap in the knowledge of the intricate interplay between the pathologies affecting the nervous system and the musculoskeletal apparatus.

This groundbreaking research provides a deeper insight into the mechanisms underlying various neuromuscular disorders and facilitates the exploration of innovative therapeutic approaches.





COLLABORATIONS

- The Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT), ITA
- University of Pittsburgh Medical Center (UPMC), USA
- University of Bologna (Alma Mater Studiorum), ITA
- Buccheri la Ferla clinic, ITA
- University of Palermo, ITA
- The Children Hospital of Philadelphia (CHOP), USA
- MERLN Institute for Technology-Inspired Regenerative MedicineThe Netherlands

TECHNOLOGY PLATFORMS

With its strongly oriented translational approach, Ri.MED strategy provides for the development of skills and technological platforms, significantly enhanced in recent years, also thanks to the funding provided by the Sicilian Region and by the Dipartimento "Casa Italia" of Presidency of the Council of Ministers.

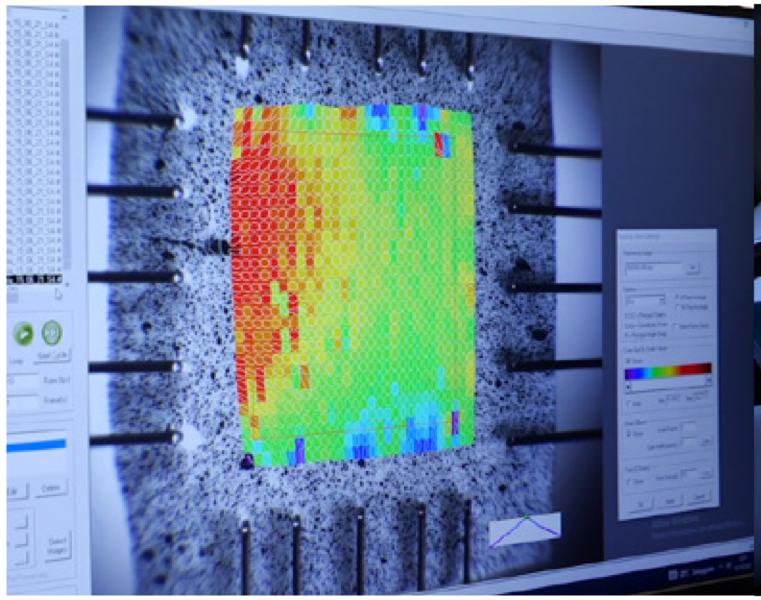
Some example are the automated system implemented for the storage and manipulation of molecule libraries for the **Screening laboratory**; the cardiac simulator and instrumentation supplied to the **Bioengineering Platform** for the characterization of biomaterials and medical devices; an 800 MHz magnetic resonance spectrometer at the **Biophysics and Structural Biology** platform, while the **Biomedical Imaging and Radiomics** platform uses 3T and 7T spectrometers and employs skills for the analysis of multimodal data and images, predictive diagnosis of pathologies and relapses.

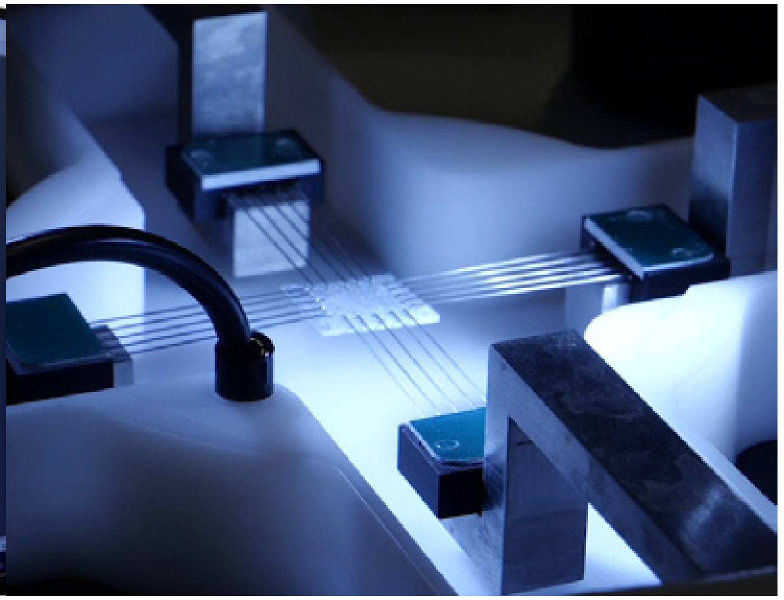
The **Tissue Engineering Platform** allows the mechanical and structural characterization of native and bioengineered tissues and the *in vitro* and *in vivo* study of *de novo* tissue development; it also has software for the elaboration of predictive numerical models for tissue growth and regeneration and instruments for the development of engineered heart valves through the use of a six-degrees-of-freedom robotic arm. The **Bioinformatics** and **Molecular Informatics** groups integrated hardware and software with a virtual screening speed of 5,000 molecules per minute, with proprietary algorithms to study molecular interactions at the cellular level, and with the infrastructure for analyzing chemical-physical properties.

The **Medicinal Chemistry** Platform allows for the structural validation of primary hits and expansion of the chemical family, as well as the structural optimization of biologically promising molecules, up to the identification of small molecules that will enter the preclinical development phase. At IRCCS ISMETT, the **Proteomics** group supports the identification of new pharmacological targets and biomarkers, as well as the study of potential side effects of particular therapeutic molecules, while the **Cell factory** allows for the production of ATMP.

- BIOENGINEERING
- BIOINFORMATICS
- CELL FACTORY
- IMAGING AND RADIOMICS
- MEDICINAL CHEMISTRY
- MOLECULAR INFORMATICS
- PROTEOMICS
- SCREENING
- STRUCTURAL BIOLOGY AND BIOPHYSICS
- TISSUE ENGINEERING

Bioengineering
PLATFORM





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PARTNERSHIPS AND COLLABORATIONS

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- Policlinico Giaccone, Palermo, ITA
- Università degli Studi di Palermo, ITA
- Institute Foundation G. Giglio, ITA
- Università degli studi di Padova, ITA
- Université de Technologie de Compiègne, FR
- Barts Heart Centre at St Bartholomew's Hospital, GB
- Great Ormond Street Hospital for Children, GB
- University College London, GB
- Queen Mary University of London, GB
- University of Bristol, GB
- University of Leeds, GB
- University of Pittsburgh, US
- University of Alabama at Birmingham, US
- MitrAssist, CN
- Adeka, JP

The Bioengineering Platform is equipped with state of the art facilities for the treatment and characterisation of biomaterials, the numerical simulation of complex physiological systems, and the preclinical validation of medical devices of the different classes (from class I to class III).

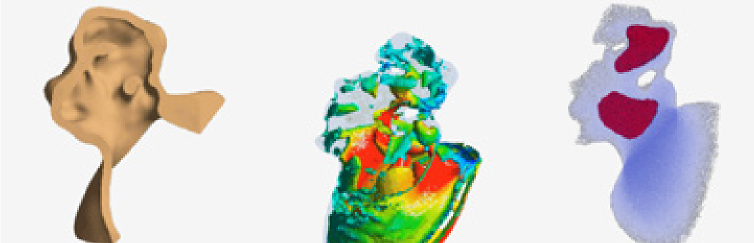
Our research team offers solid expertise in numerical modelling, fluid-structure analysis, design optimisation of medical devices, and pre-clinical evaluations complying with regulatory requirements and good practice. The platform is consolidating as a reference for healthcare providers, academic groups and small and medium-sized enterprises in the region, contributing to stimulate the implementation of clinical innovations emerging from the local excellence and providing the necessary professional training to generate new technical and business competencies in the field.

EXPERTISE

- Mechanical and thermo-mechanical and rheological characterisation of biomaterials and biofluids
- Numerical simulation of physiological systems and their interaction with medical devices (by means of structural, fluid dynamic and fluid-structure interaction analyses)
- Development of numerical codes for the study of cardiovascular problems (e.g. simulation of thrombosis)
- Development of support tools for therapeutic planning
- Development of advanced diagnostic solutions
- Design of medical devices
- Hydrodynamic and structural *in vitro* characterisation of physiological systems and cardiovascular implants

TECHNOLOGY PLATFORM

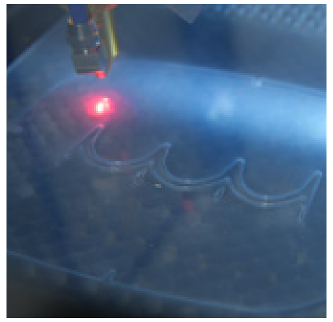
- Codes for the numerical simulation of complex physiological systems (developed in house and commercial)
- Equipment for the treatment and characterisation of biomaterials and biofluids
- Tools for the basic manufacturing of components and prototypes
- Instruments for the preclinical validation of cardiovascular medical devices

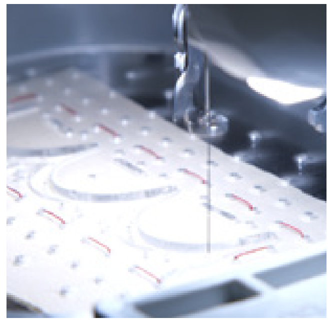


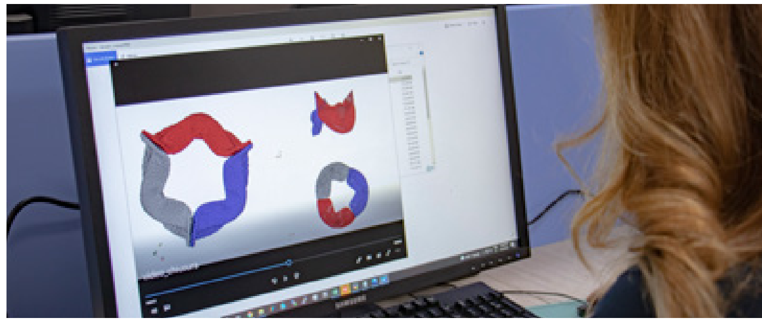
Structural analysis of contracting left atrial appendage.

FSI vorticity analysis of a left atrial appendage.

Clot formation in atrial fibrillation predicted with our code.

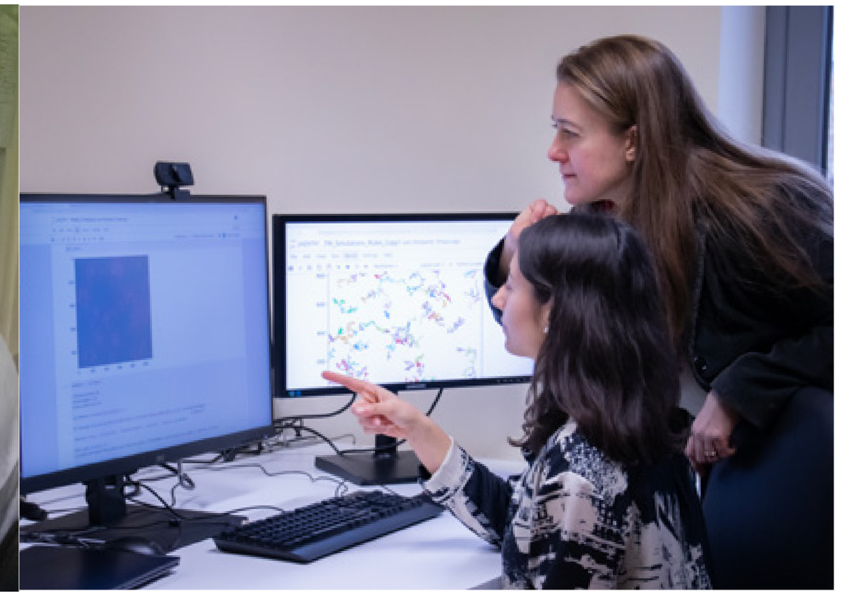


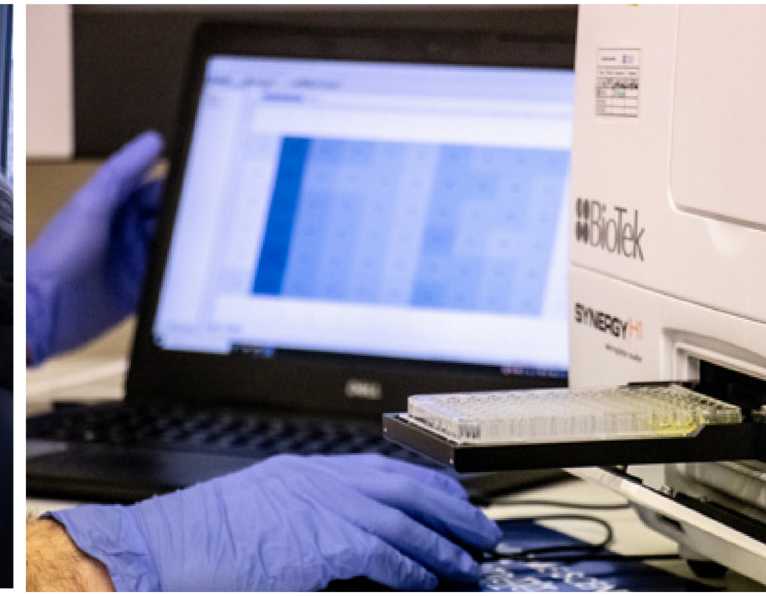




Biroinformatics

PLATFORM





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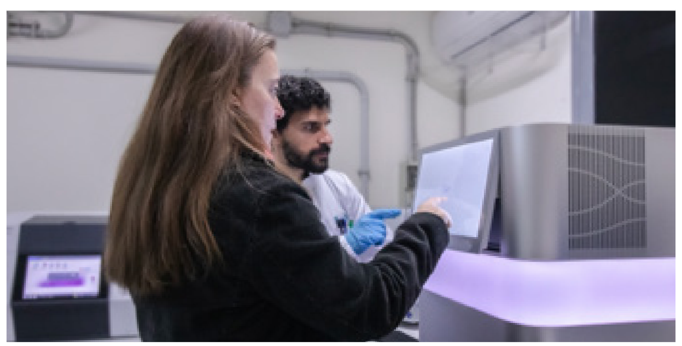
PARTNERSHIPS AND COLLABORATIONS

- University of Palermo, Palermo, ITA
- National Research Council (CNR), ITA
- IRCSS ISMETT, Palermo, Italy
- Università degli Studi di Roma "Foro Italico", Roma, ITA
- University of Pittsburgh, PA, US
- University of Texas Medical Branch at Galveston, TX, US



Bioinformatics platform is devoted to support Ri.MED researchers and collaborators to retrieve the most amount of information from their data, with a particular interest on Biological Big Data. For instance, it supports the Drug Discovery Unit in high throughput screening experimental design and data analysis. It performs standard high-throughput data analysis, applied on a wide range of data source technologies, e.g., microarray or next generation sequencing data, integrated with clinical data if available.

Very often, the biological questions of interest and the associated experimental designs cannot be analyzed by the commercial software available to the scientific community. In this case, we exploit our expertise on computer programming and big data management for analyzing high-throughput data in a customized way. The main scientific interest of the group is the study of biological interaction networks, analyzed by integrating many sources of data.
For instance, one of our projects is dedicated to describe the regulatory interaction network of the endogenous microRNA in a specific tissue of interest, by analyzing its microRNA and gene expression profiles.

EXPERTISE

- Molecular biology, Genetics, Systems biology
- Bulk and single cell RNAseq data analysis, Genomics, Epigenomics, Transcriptomics, Metagenomics
- Statistics, Bioinformatics, Machine Learning, Complex Systems, Network analysis
- Long-read Next Generation Sequencing (Oxford Nanopore Technologies)
- Programming with R, Python, Matlab, Galaxy

TECHNOLOGY PLATFORM

Software

Our scripts for data analysis are realized with open-source language, i.e., Python, R and Bioconductor libraries. Visualization of interaction network is performed with the software Pajek or Cytoscape. In order to better satisfy the collaborators needs we are able to enrich our analysis results by comparing them with the results obtained with the software Ingenuity Pathway Analysis.

Hardware

- Server - CPU: 2x Xeon Gold 6152 2.10 GHz 22 Cores RAM: 128GB
- Server - CPU: 2x AMD Epyc 7402 24 Cores 2.8GHz RAM: 256GB
- HDD: 3x 480GB SSD GPU: 2x Nvidia A100 40GB

RNA-based therapies and NGS Lab equipment:

- Cellular and molecular biology equipment
- Biotek Synergy H1, multimode plate reader
- Agilent AriaDx, Real-Time PCR System
- Qiagen Qiacuity, digital PCR System
- Illumina NextSeq2000
- Oxford Nanopore Promethion 24, P2 Solo and MinION

ACTIVE RESEARCH PROJECTS

SUnFox - *Senescence Undoing by FOXO4 knock down. This project is funded by National Center for Gene Therapy and Drugs based on RNA Technology" (CN3 – Spoke 4)*
Abstract: This is a project that studies a novel senolytic approach for the treatment of aging-associated diseases and senescence-associated diseases. The aim is inducing the apoptotic death of the senescent cells by knocking down FOXO4 via systemic and local delivery of specific ASO/siRNA.
SMART: *(Splicing Modulation by Advanced RNA Technologies)*
Abstract: The project aims to study *in silico* and *in vitro* RNA-based approaches to manipulate pathological splicing events. Classical *in vitro* assays will be supported by imaging and omic studies. Splicing modulation can be obtained by means of i) canonical ASO (that inhibit selected splicing site by occupancy), ii) bifunctional ASO (targeted bifunctional oligonucleotide enhancer of splicing - TOES) and iii) engineered Cas13.

Cell Factory

CONTACTS

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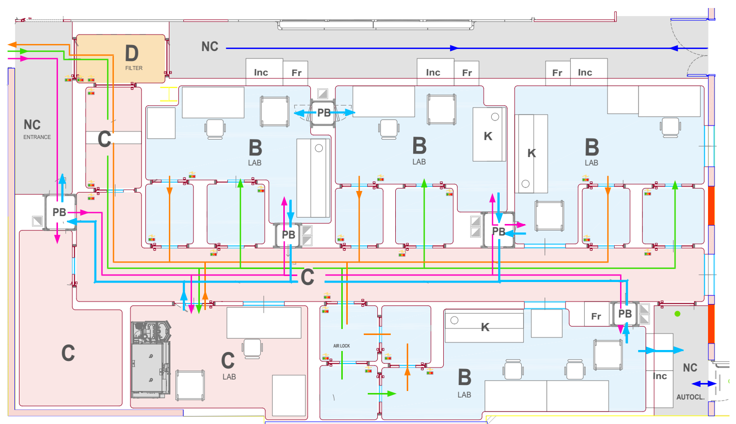
Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT)
Via Ernesto Tricomi 5 - 90127, Palermo, ITA

PARTNERSHIPS AND COLLABORATIONS

- Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT) IRCCS, Palermo, ITA
- ISMETT- IRCCS policlinico San Matteo, Pavia, ITA
- ISMETT-IRCCS Ospedale Galeazzi- Sant'Ambrogio, ITA
- University of Pittsburgh, US



GMP Facility Layout, with personnel and material flows

The new cell factory guarantees flexibility in the type of production and functionality of the different areas. The design of production and quality control layouts for advanced therapies (gene therapy, cell therapy, tissue engineering and combined ATMPs) was approved by AIFA during a Scientific Advice meeting. There are 4 class B laboratories, one of which allows for a higher containment and has an autoclave for waste treatment.

The other 3 class B laboratories can be used in a totally independent way, for the simultaneous preparation of three different products. Alternatively, they can be connected two by two. In the last case, part of the operations can be performed in one lab and other manipulations can be performed in the second lab, passing the intermediate product through a pass box.

An additional class C room is used for cell preparation in specific closed systems. Maintenance can be performed without access to the production rooms, as the engines of the equipment protrude into technical areas.

The Quality Control laboratories are equipped to conduct all the tests on raw materials, intermediates and final products required for product release. These labs can receive and adequately store reagents, materials and products according to GMP. Production areas and QC labs are equipped with a remote monitoring system.

EXPERTISE

- Set up of a GMP compliant Quality Assurance System
- Definition of GMP production protocols
- Development of Quality Control Methods
- Validation of environment, equipment, products
- GMP Training

ACTIVITIES

The facility is being qualified. The cell factory staff will carry out the validation of fundamental general processes (gowning validation, sanitization and clean hold time, passage of materials, etc.). Once the necessary development/ technology transfer data of the first advanced therapy products (adoptive immune therapies) are available, specific validation activities for the production process and related quality control methods will be carried out.
A complete dossier on the first advanced therapy product and its intended clinical use will be submitted as an integral part of the manufacturing authorization application of the new facility. Novel culture methods allowing minimal operators' intervention and automatic QC tests are being tested.
Continuous activities include the maintenance of the GMP compliant Quality Assurance system and the periodic training of internal and external staff.

Biomedical Imaging and Radiomics
PLATFORM

CONTACTS:
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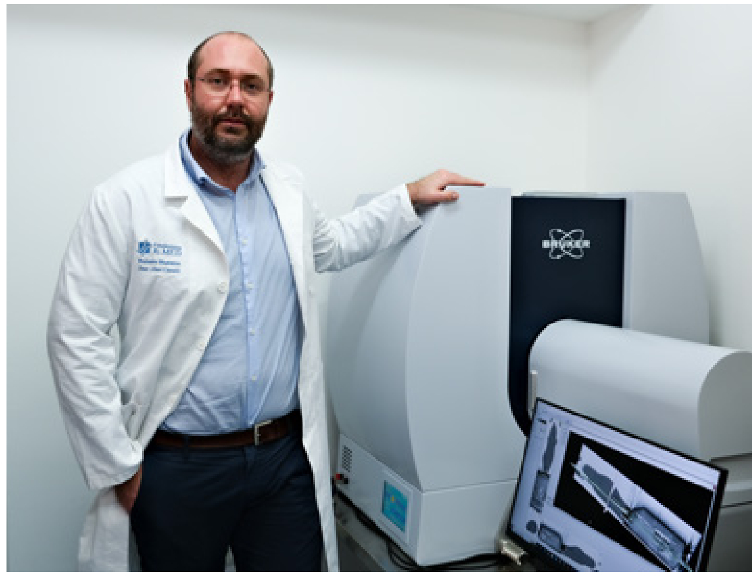
Corso Calatafimi 414, 90129 -Palermo

PARTNERSHIPS AND COLLABORATIONS

- Georgia Institute of Technology (GIT), Atlanta, GA 30332, USA
- National Institutes of Health (NIH), USA
- Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, (PROMISE) University of Palermo, ITA
- Pharmaceutical Factory, La Maddalena S.P.A., Palermo, ITA
- Department of Biomedicine, Neuroscience and Advanced Diagnostics, (BIND)University of Palermo, Palermo, ITA
- University Hospital Agostino Gemelli IRCCS, Rome, ITA
- University of Catania, Catania, ITA
- Ospedale Generale Regionale "F.Miulli", Bari, ITA
- Nuclear Medicine, University of Messina, Messina, ITA
- Biomedical Campus University of Rome, Rome, ITA
- Medical Physics Unit, Cannizzaro Hospital, Catania, ITA
- Nuclear Medicine Department, Cannizzaro Hospital, Catania, ITA
- Department of Engineering, University of Palermo, Palermo, ITA
- Experimental Zooprophylactic Institutes of Sicily (IZS Sicily), Palermo, ITA
- The Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT-IRCCS), Palermo, ITA
- Department of Agricultural, Food and Forests Sciences University of Palermo, Palermo, ITA
- Institute of Bioimaging and Complex Biological Systems (IBSBC) CNR (Palermo and Milan)
- Texas A&M University - Corpus Christi, United States



Biomedical Imaging and Radiomics Platform is primarily focused on oncology and neuroscience research. The Platform supports *in vitro*, *ex vivo*, and *in vivo* experiments, aiming for translation into the clinical application. Image analysis, artificial intelligence and radiomics tools are the driving forces of the platform, which are the basis for the entire workflow. The staff, which is currently increasing, is now comprised of scientific figures who possess transversal skills suitable for supporting the entire translational workflow, including experiments using cellular models and phantoms, scaffolds, tissues and organs within the RadioTheranostics and Biodiversity field. The scientific personnel on this platform are also trained in working with small animal models (mice and rats).

In 2024, the platform was implemented with the radiobiology laboratory (at Corso Calatafimi 414). The radiobiology laboratory, authorized to develop experiments using the following radionuclides such as Tc-99m, F-18, Cu-64, Ga-68, Lu-177, Ag-111, Zr-89 for research purposes, is supporting the RADIATION project won in June 2024 entitled "study and evaluation of the RADiobiological effect of innovative polymeric nanoparticles of natural origin radiolabeled with radioisotope Lu-177 in prostate cancer cell lines". The laboratory is equipped with a Gamma Counter
as well as Dynamic Light Scattering (DLS) instruments suitable for the design and characterizing the radioactive samples and the structure and stability of the nanosystems respectively.

ACTIVE RESEARCH PROJECTS

- Synthesis and functionalization of nanoparticles with plasmonic effects for applications in cancer precision therapy in collaboration with the GIT.
- Radiomic analysis of magnetic resonance angiography of mice suffering from a particular type of anemia in collaboration with the GIT.
- Biodistribution studies of novel radiopharmaceuticals on preclinical PET models in light of the discovery of new PET ligands and neurological receptors, transporters and enzymes in collaboration with the GIT.
- Preclinical PET and MRI studies to detect neuronal degeneration early in Parkinson's disease in collaboration with Institute of Bioimaging and Complex Biological Systems (IBSBC) CNR (MI).
- Radiobiology of Targeted Radionuclide Therapy: *in vitro* radiobiology studies on innovative radiopharmaceuticals through pharmacokinetic, trafficking and cell viability assays (RADIATIONS project) in collaboration with La Maddalena S.P.A.
- *In vivo* biodistribution studies for the evaluation of the efficacy of the treatment of site-directed radiopharmaceuticals on a preclinical mouse model in diagnosis and theranostics (ISOLPHARM project) in collaboration with Institute of Bioimaging and Complex Biological Systems (IBSBC) CNR (PA).
- Innovative approaches to cancer treatment using metal nanoparticle-based therapies in collaboration with Texas A&M University.

EXPERTISE

- Image processing (MR, PET, CT, IVIS, HRCT, microscopy and histology), deep learning for 3D segmentation, radiomic to extract features and machine learning to prediction and classify of pathologies (for example, cancer, COVID19) and relapses as well as medical decision support
- Conducting magnetic resonance imaging scans (T1, T2, DP, DWI, ADC, and DCE)
- Conducting positron emission tomography/computed tomography scans (PET/CT)
- Conducting spectroscopy scans on phantoms, *in vivo* samples, and *ex vivo* samples
- Biodistribution analysis of radiopharmaceuticals: preclinical molecular imaging
- Radiobiology assay, Radiopharmaceuticals application in Theranostics *in vitro* experiments
- Nanotechnology: Applications of nanoparticles in biomedicine
- Python, Matlab, CUDA

TECHNOLOGY PLATFORM

At Imaging and Radiomics Lab - Via Marini 14:

- **Hardware:** two workstations featuring 16-core Xeon CPUs, 128 GB RAM, 1x1TB HD SSD, 4x2TB HDs, and two Nvidia RTX8000 GPUs; one laptop with an Intel Xeon W-11955M CPU, 64 GB RAM, 1x2TB HD SSD, 3x2TB HDs, and two Nvidia A6000 GPUs.
- **Software:** PMOD, TopSpin, Paravision 6.1, Jmrui, Tarquin, Horos, 3DSlicer

At Radiobiology Lab – Corso Calatafimi 414:

- **Cell cultures and imaging**: Incubator 37°C 5%CO2, Biohazard laminar flow biological hood equipped with UV for cells, Thermostated bath, electrophoresis cells for sds page, transblot machine, inverted digital microscope, cell counter, 2 centrifuges with adapters, fluorescence 4-color/transmitted light and color applications, electrophoretic cells for SDS-PAGE, ChemiDoc MP Imaging System with accessories, Dynamic Light Scattering DLS. Other small laboratory equipment (e.g. scales, pH meter, aspirator, sonicator, pipets,..)
- **Radioprotection and radioactivity detection:** Chemical hood with edge for shielded vision and cabin for acids, bases and flammables, Comecer safe for radiopharmaceuticals, Plexiglass screen for Comecer beta emitters, Geiger counter, WIZARD 2470 gamma counter with 10 PerkinElmer detectors
- **Thermal cabins for material storage and cryopreservation:** FRIDGE +4 °C, FREEZER -20°C, FREEZER -80°C, liquid nitrogen rack

At Istituto Zooprofilattico Sperimentale:

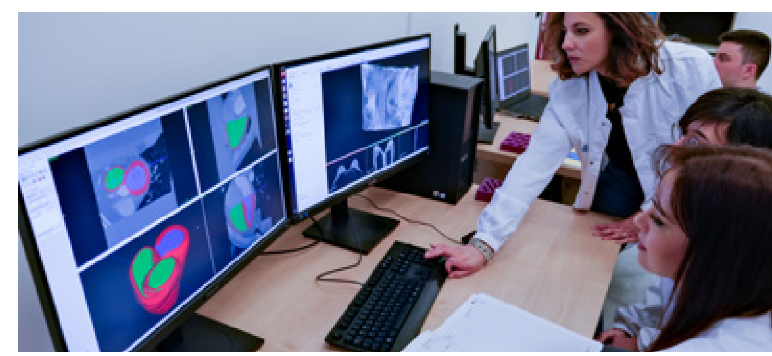
- Bruker Pharmascan 70/16 (7 Tesla).
- IVIS Spectrum Advanced pre-clinical optical imaging.
- microCT Skyscan 1276 CMOS Bruker

At IRCSS ISMETT

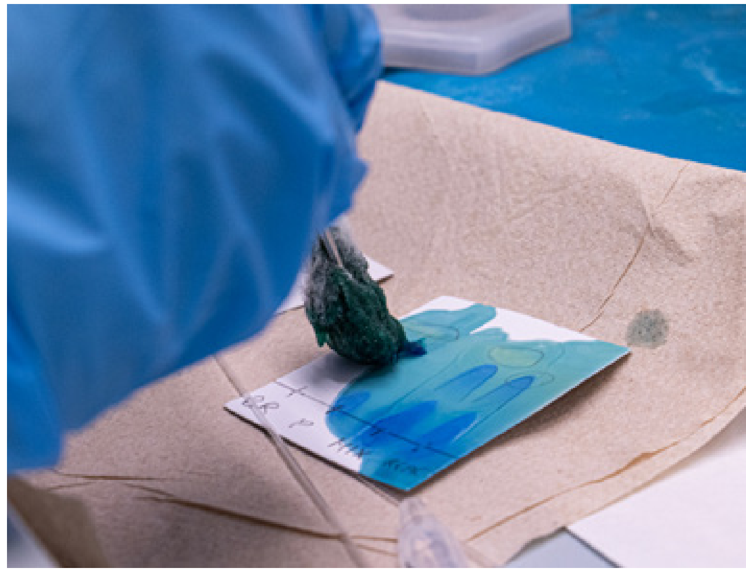
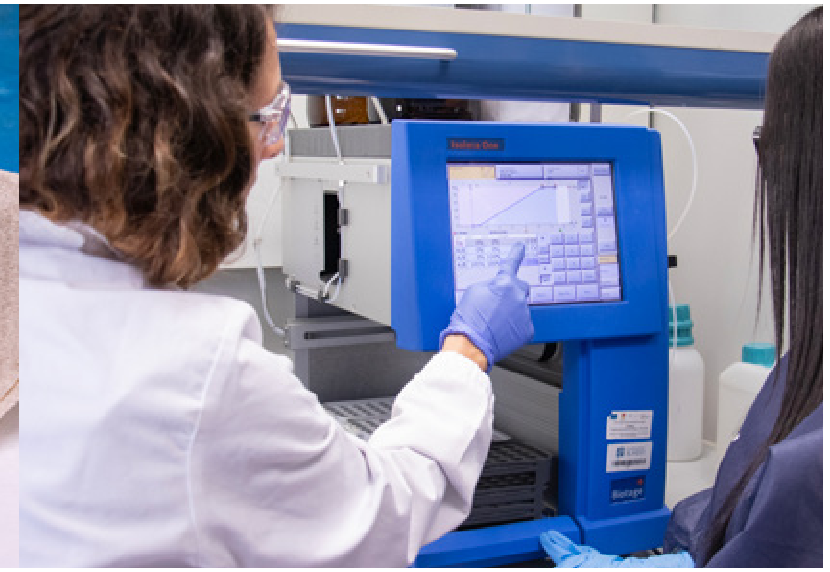
- GE DISCOVERY MR 750 W 3 Tesla High-Field Magnetic Resonance

At Institute of Molecular Bioimaging and Physiology, National Research Council (IBFM-CNR):

- PET/CT Clinical and Preclinical



Medicinal Chemistry **PLATFORM**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PARTNERSHIPS AND COLLABORATIONS
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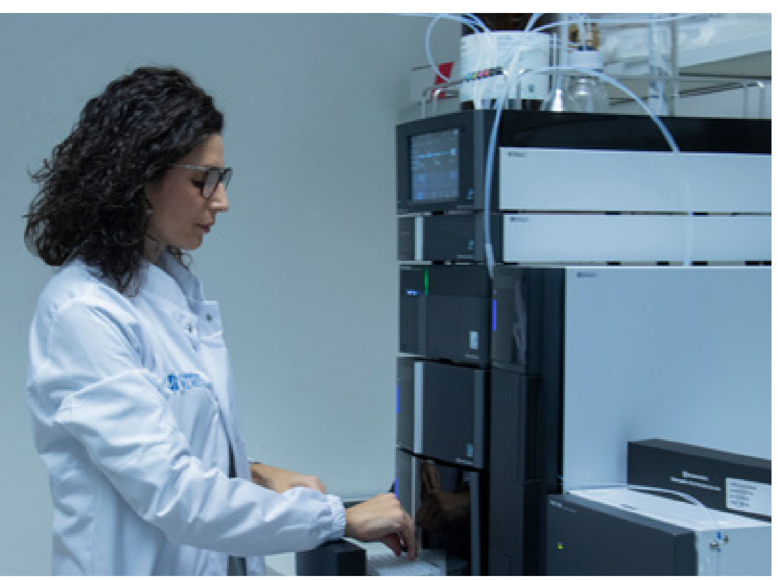
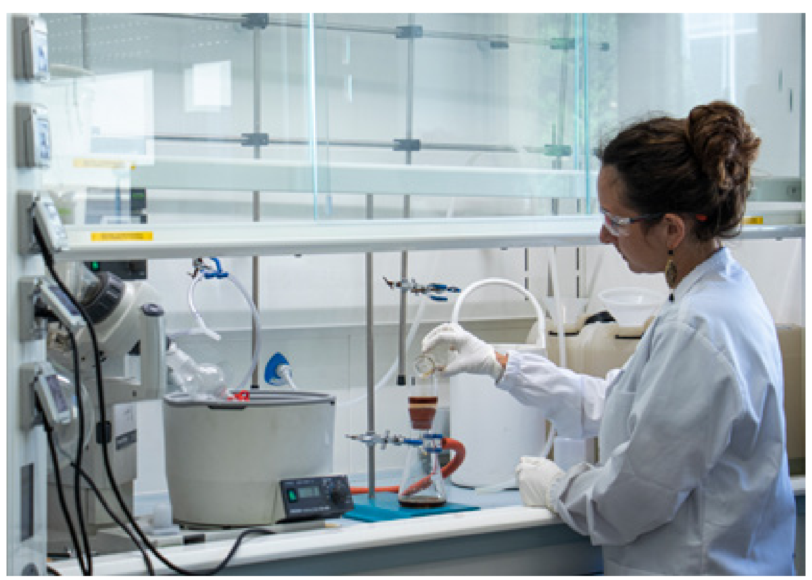
- Centro Cardiologico Monzino, Milan, ITA
- Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione (ISMETT), Palermo, ITA
- University of Palermo, Palermo, ITA

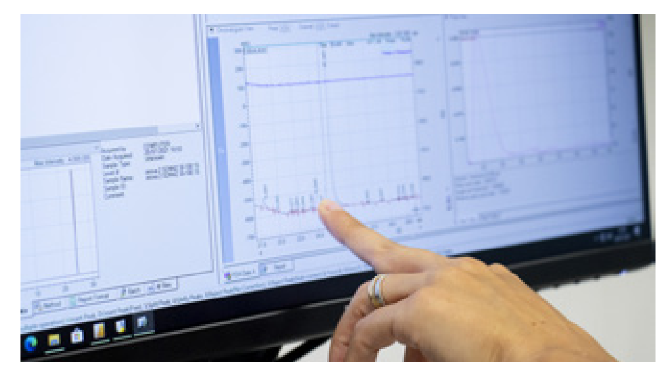
The Medicinal Chemistry platform deals with the design and synthesis of novel small molecules leading to the creation of compound libraries and building blocks collections. The platform supports drug discovery campaigns, with hit structure confirmation, hit re-synthesis, hit series expansion and optimization, hit-to-lead activities. The main expertise covers the design, the planning, and the organic synthesis; the purification and isolation, and the structural elucidation and analytical characterization of the newly synthesized compounds. Moreover, structure-activity-relationship (SAR) studies allow to explore the chemical space of the most promising hits to better define the *in vitro* biological profile. The platform is fully equipped for reactions set-up, work-up and purification of complex mixtures; and for the isolation, structure characterization, and standard purity grade assessment of the title compounds.

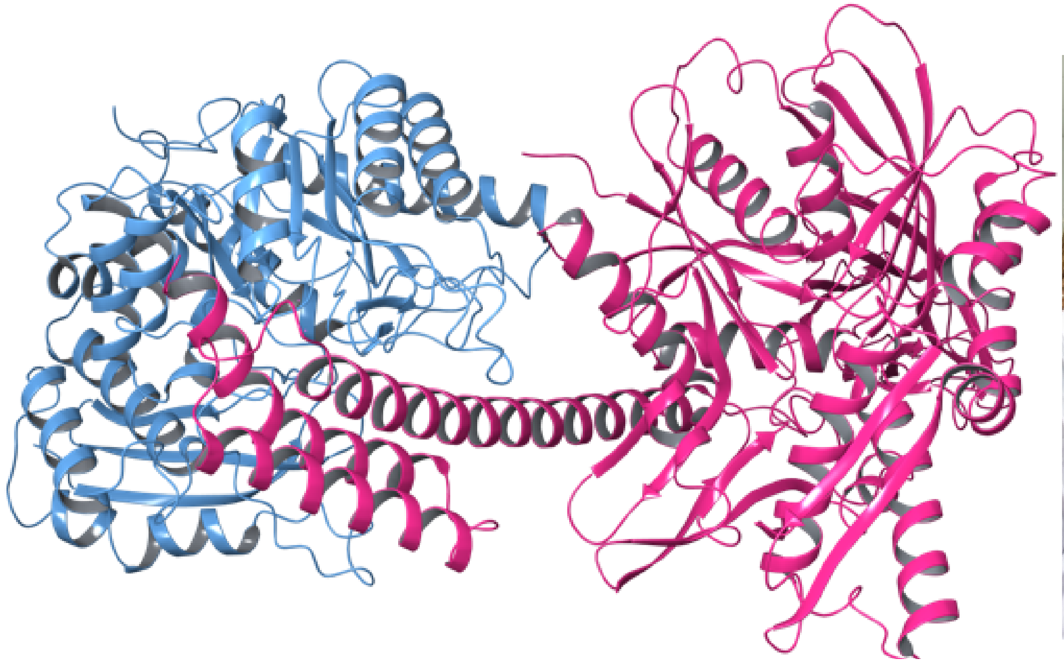



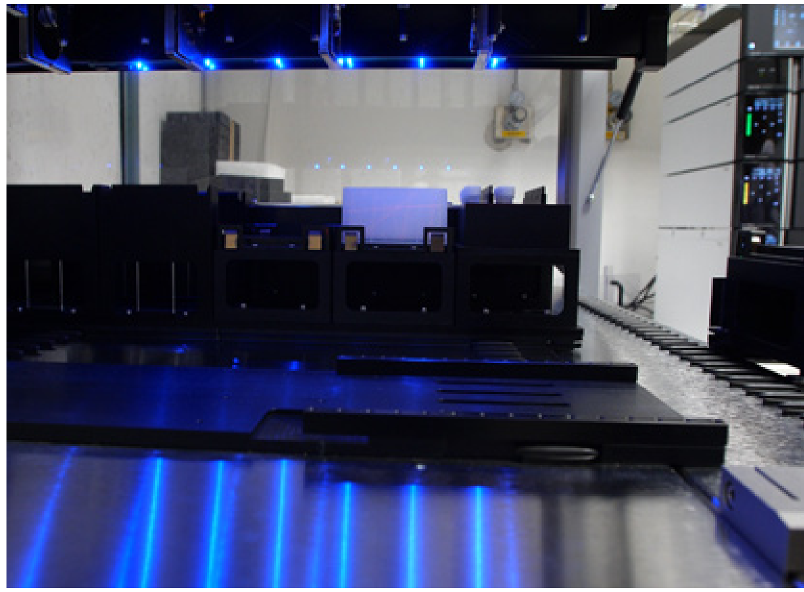
EXPERTISE
- Drug design.
- Planning, development, and optimization of synthetic routes
- (Microwave-assisted) organic chemistry
- Purification of complex mixtures on normal and reverse phase
- Isolation of title compounds
- Structure elucidation and analytical characterization
- Purity grade assessment


ACTIVE RESEARCH PROJECTS
- Design and synthesis of potential inhibitors of NOD-like receptor family, pyrin domain containing 3 (NLRP3) inflammasome as potential anti-inflammatory agents
- Early Drug Discovery to identify novel inhibitors of prenylcysteine oxidase 1 (PCYOX1), a novel target in cardiology and oncology
- Design and synthesis of new sirtuin-6 (Sir6) inhibitors, a validated target for lymphoma treatment

TECHNOLOGY PLATFORM
- Milli Q-3, Merck: Water purifier system for the production of pure and ultra-pure water needed for analytical applications
- Isolera One, Biotage: Flash chromatography apparatus for the isolation (on normal and reverse phase) of compounds of interest from complex reaction mixtures
- Nexera, Shimadzu: High-performance liquid chromatography (HPLC) platform for semi-preparative applications and purity grade assessment
- LC-MS 2020, Shimadzu: Liquid chromatography-mass spectrometry platform for reactions monitoring and analysis of complex mixtures
- Discover 2.0, CEM: Microwave reactor for homogenous and heterogenous catalytic transformations
- Lyovapor L-200, Büchi: Lyophilizer for in vacuo drying from water, preserving the stability and integrity of the samples
- H-Cube Mini-Plus, StepBio: Flow reactor for catalytic hydrogenations, able to safely generate high-pressure hydrogen via water electrolysis
- Glass-Oven B-585, Büchi: Dryer for removal of residual organic solvents combining the use of mild temperatures and vacuum







Molecular Informatics
PLATFORM

CONTACTS

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PARTNERSHIPS AND COLLABORATIONS

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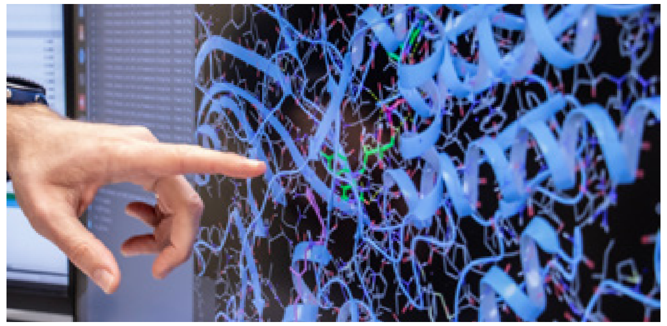
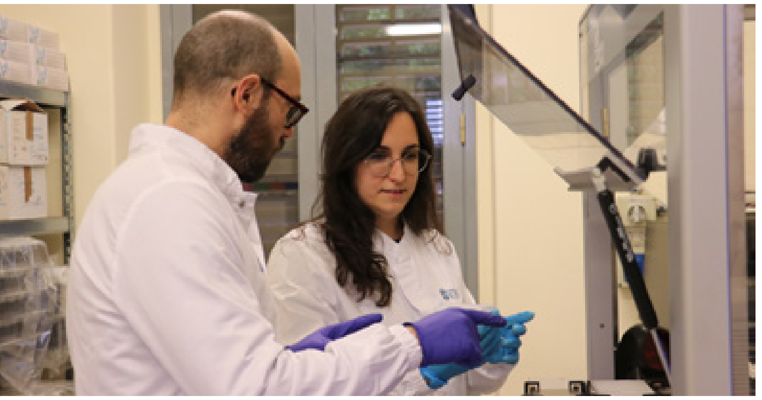
- Italian National Council of Research (CNR), ITA
- University of Verona, ITA
- University of Paris Citè, FR
- University of Palermo, ITA





The Molecular Informatics platform focuses on the identification, characterization, and optimization of biologically active molecules using advanced *in silico* techniques. Its methods range from classical molecular modeling and virtual screening to the integration of modern chemoinformatics with proprietary tools.

The team's collective expertise is leveraged to create molecular libraries, develop and validate reliable theoretical models, and perform subsequent virtual ligand screening (VLS). The platform also plays a key role in exploring and expanding chemical space to generate optimal molecular libraries for biological screening. Recent collaborations with academic groups from the University of Palermo, Verona, Paris, and Vienna have led to the development of AI-based approaches for predicting the activity of small molecules. Additionally, the compound management system within the platform automates the preparation of screening plates from in-house molecular libraries, based on virtual screening results.

ACTIVE RESEARCH PROJECTS

- Development of selective inhibitors of NOD-like receptor family, pyrin domain containing 3 (**NLRP3**)
- Deep learning-based drug repurposing of **Kinases** inhibitors
- Design of protein-protein interaction modulators (**ENO1-HSP70**)
- Bioactivity prediction of Air Pollutants through chemoinformatics approaches
- Computer-aided molecular design of DNA and RNA G-quadruplexes stabilizers

EXPERTISE

- Structure based virtual screening (Docking and Pharmacophore)
- Ligand Based virtual screening (pharmacophore, molecular descriptors based models, QSAR and 3D QSAR)
- Molecular Dynamics
- Dynamic pharmacophore (hybrid technique based on the use of pharmacophores from the molecular dynamics trajectory)
- Chemical Database creation and management
- Chemical data mining
- Machine Intelligence in Drug Design
- Compound Management (plates design and preparation

TECHNOLOGY PLATFORM

Software

- Schrödinger suite for small molecule drug discovery
- Schrödinger suite for biologics drug discovery
- LigandScout expert suite
- Autodock and Autodock Vina
- AlvaDesc/AlvaModel
- DESMOND (OPLS2005 and OPLS3e, OPLS4)
- AMBER
- NAMD
- VMD
- GROMACS
- KNIME

Hardware

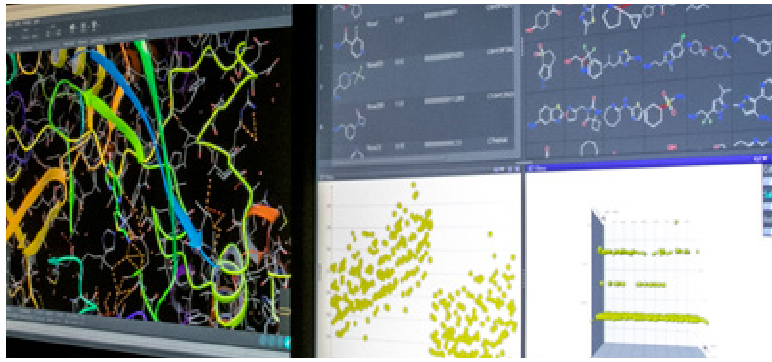
- 5 Workstations
- Server: 80 cores e 2 x NVIDIA Tesla K80
- Server: 96 cores e 2 x NVIDIA A100
- Hamilton compound storage (up to 80K compounds)
- Hamilton liquid handler for plates preparation

Calculation capability:

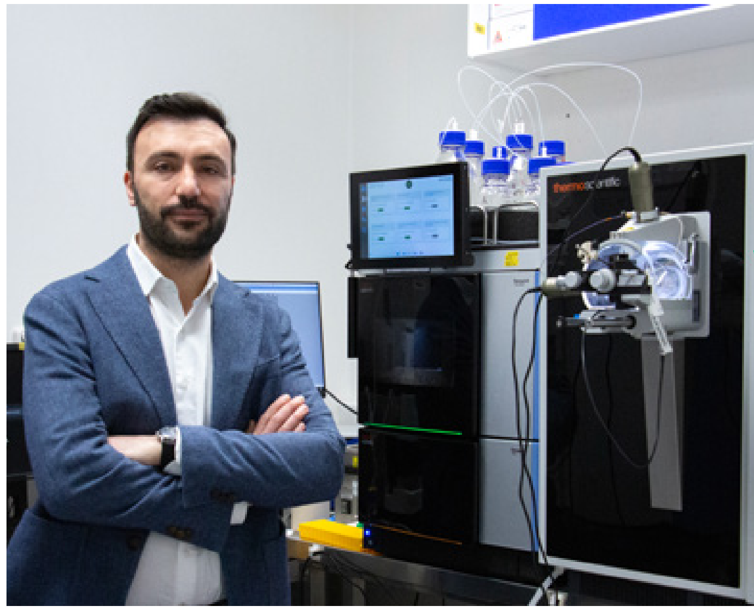
- Library optimisation → ~ 6,000 molecules/min
- Virtual Screening HTVS → ~ 5,000 molecules/min
- Virtual Screening SP → ~ 1,500 molecules/min
- Molecular Dynamics → ~ 200 ns/day/Card (on 40,000 atoms system)

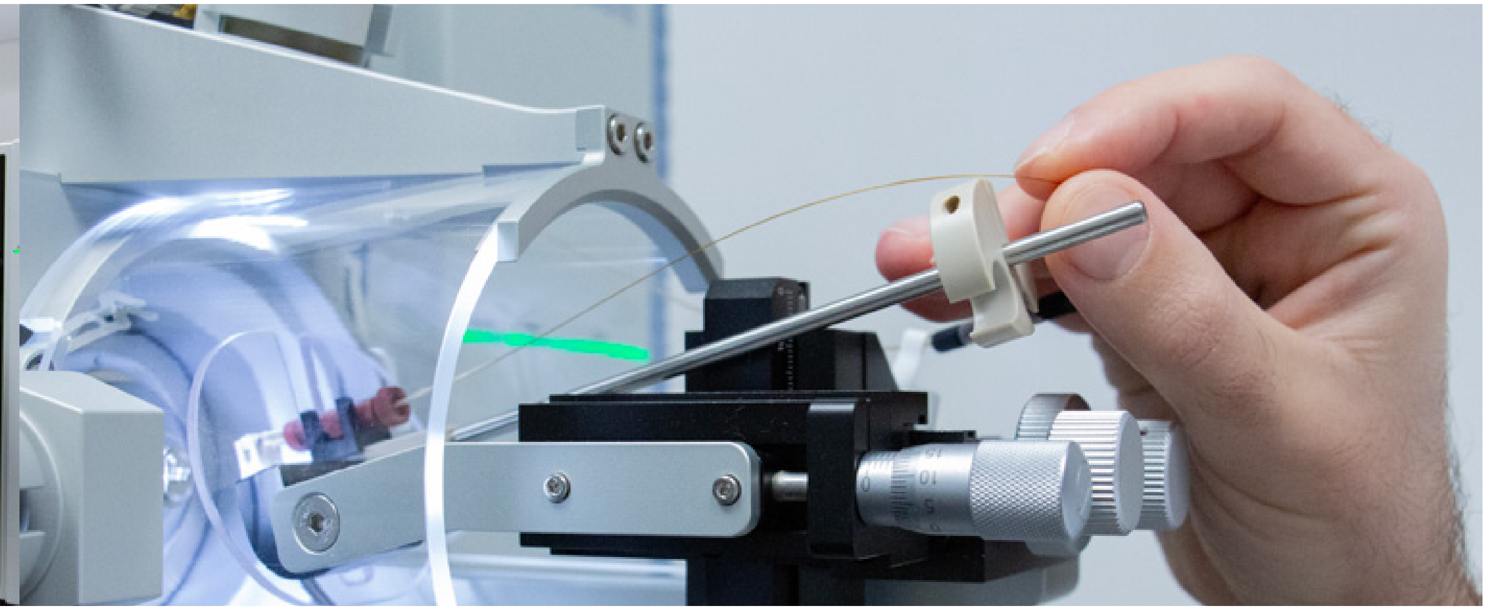
Integrated in Silico Platform

The group is actually working at the creation of an integrated platform for molecular network analysis in collaboration with the Bioinformatics group.



Proteomics
PLATFORM





CONTACTS

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PARTNERSHIPS AND COLLABORATIONS

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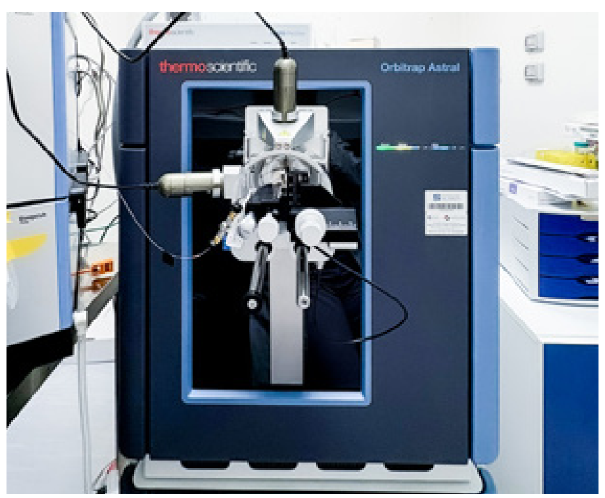
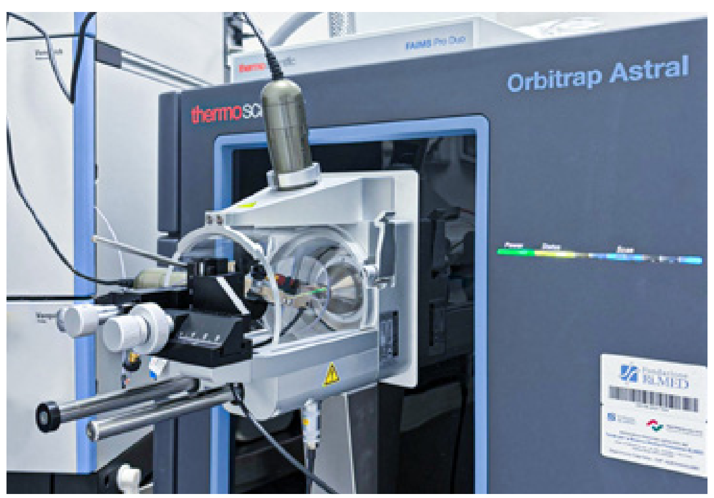
- University of Palermo, ITA
- IRIB-CNR, Palermo ITA
- Univesity of Pisa, ITA
- University of Udine, ITA
- Istituto Ortopedico Rizzoli, ITA
- German Center for Neurodegenerative Diseases (DZNE) Munich, DE.
- Hospital fo Special Surgery, Weill Cornell University, NY, USA
- University of East Anglia, Norwich UK
- University of Nottingham, UK
- University of Liverpool, UK

The proteome represents the complete set of proteins expressed by a cell, tissue, or organism. The systematic, high-throughput study of proteomes, known as proteomics, enables the identification and quantification of proteins and their relative abundance in biological samples. Proteomics also allows for the analysis of differentially regulated proteins across various conditions. Proteomic applications in preclinical and clinical research are extensive, encompassing the identification of novel drug targets, the discovery of disease-associated biomarkers, and the prediction of drug-induced side effects. To support these efforts, Ri.MED has established a state-of-the-art proteomics platform for protein identification and characterization. This platform supports internal research, fosters collaborative studies, and provides services to academic research labs and industry partners.





Ri.MED has established a state-of-the-art proteomics platform equipped with advanced instrumentation, including an Astral, an Exploris 480, and a Q Exactive mass spectrometer, coupled with Vanquish Neo UHPLC and UltiMate 3000 RS LCnano systems. These cutting-edge technologies enable high-resolution, high-sensitivity quantitative proteomic analyses.

Specifically, the platform allows for the chromatographic separation of peptides generated through proteolytic digestion of complex protein mixtures, followed by electrospray ionization and tandem mass spectrometry (MS/MS). The resulting fragmentation patterns—mass spectra defined by unique mass-to-charge (m/z) ratios—serve as molecular fingerprints for peptide identification. Computational analysis of these spectra enables the inference and quantification of individual proteins present in the original sample.

Beyond identification, Ri.MED's instrumentation and dedicated software infrastructure support robust quantitative proteomics, making it possible to compare protein abundance across different biological conditions or experimental groups.
Complementing the proteomics facility, Ri.MED also houses fully equipped laboratories for biochemistry and cell culture. These labs support upstream sample preparation and downstream validation of proteomic findings using orthogonal, immuno-based techniques

Ri.MED's proteomics platform provides cutting-edge tools and expertise, enabling researchers to conduct high-quality proteomic studies that drive advancements in health and biotechnology research.

TECHNOLOGY PLATFORM

- Vanquish Neo uHPLC system connected to an Orbitrap Exploris 480 mass spectrometer
- Vanquish Neo uHPLC system on-line coupled to an Astral mass spectrometer
- Ultimate 3000 HPLC system connected to a Q-Exactive mass spectrometer
- Field Asymmetric Ion Mobility Spectrometry (FAIMS) Pro Interface for HPLC
- BeatBox®: Tissue homogenizer and cell lysis instrument for semi-automated sample homogenization of cells and tissue
- Comprehensive software for data analysis (e.g., Proteome Discoverer software)
- Fully equipped laboratory for biochemical validation of proteomics results

EXPERTISE

- Project planning
- Sample preparation using FASP, SP3, and iST methods
- Protein identification from in-gel or in-solution samples
- High-resolution LC-MS/MS for protein identification and quantification in complex mixtures
- Data acquisition using DDA and DIA methods
- Data analysis and visualization, including Perseus, R, and Gene Ontology analysis

TECHNOLOGY PLATFORMS

Screening
PLATFORM

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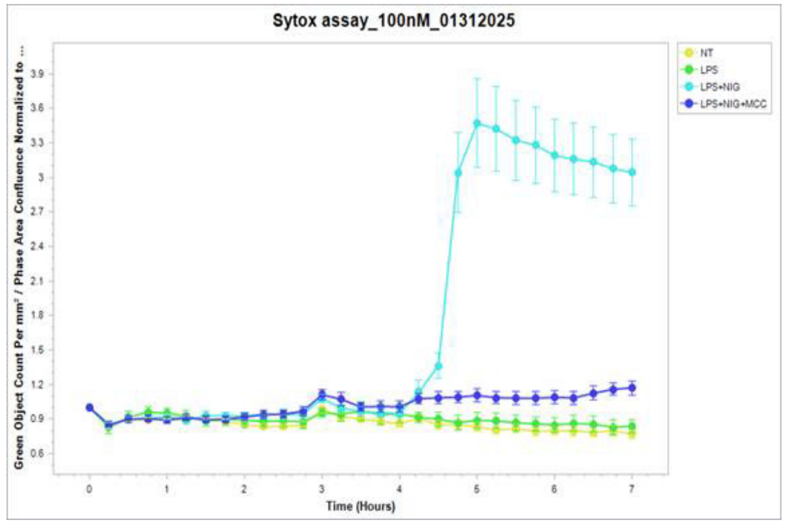
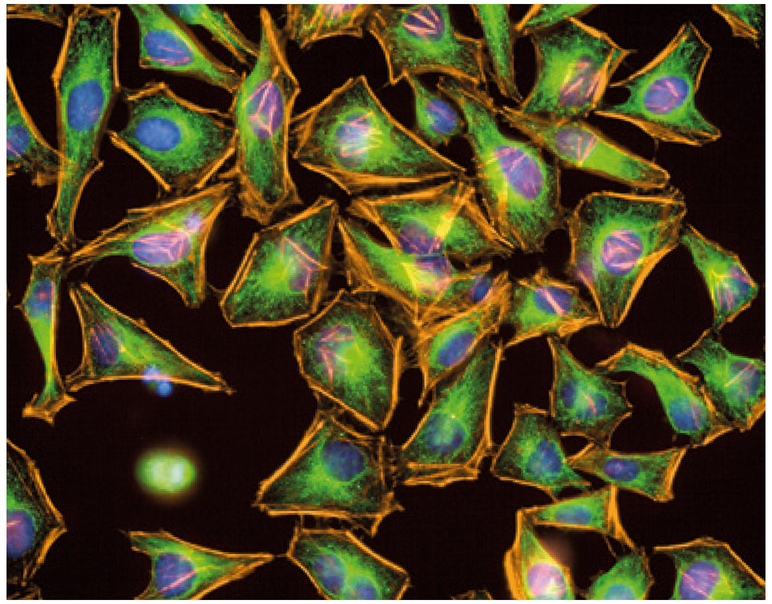
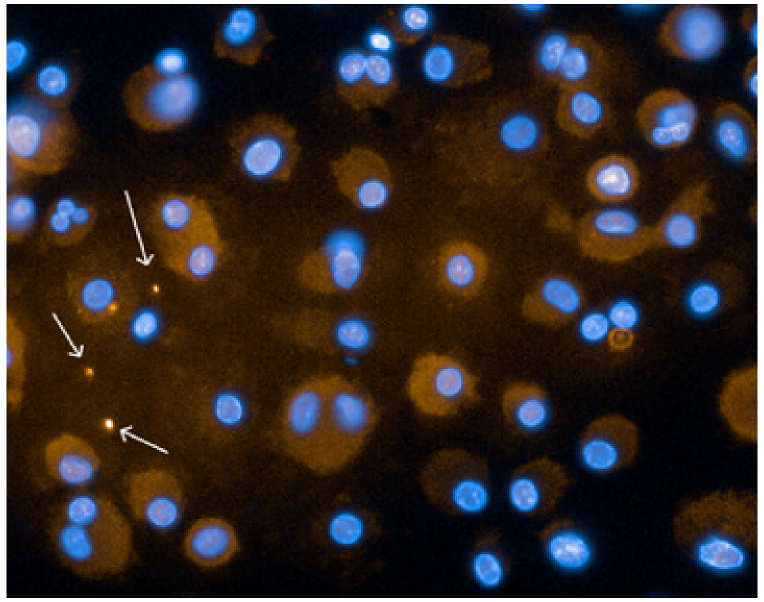
PARTNERSHIPS AND COLLABORATIONS
• Institut de la Vision, Parigi, FR
• University of Campania "Luigi Vanvitelli", ITA
• University of Bologna, ITA
• National Research Council (CNR), ITA

Ri.MED RESEARCH

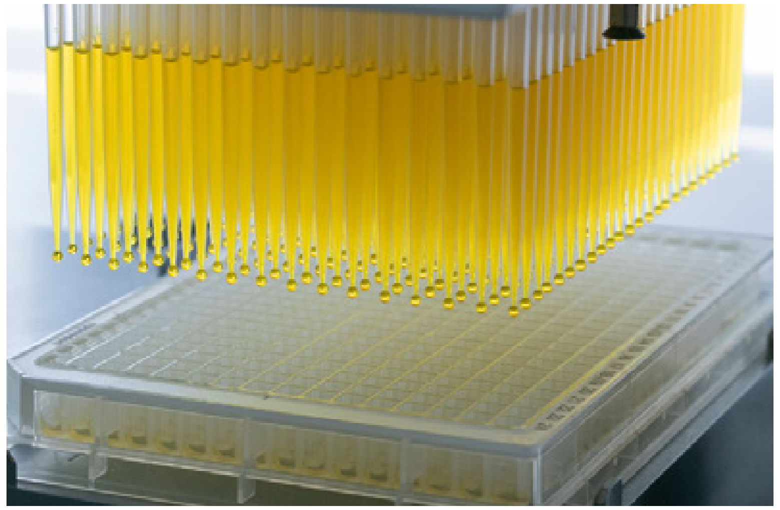


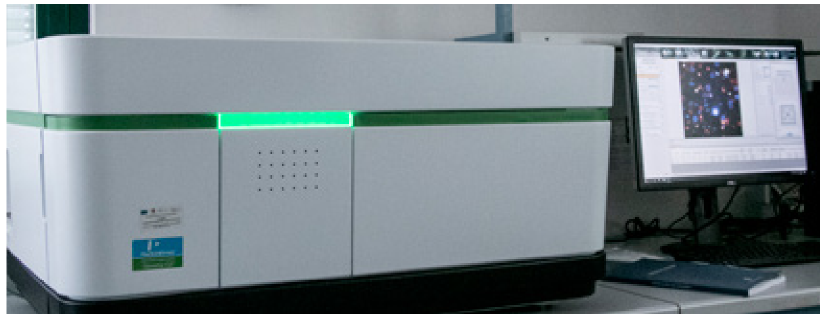


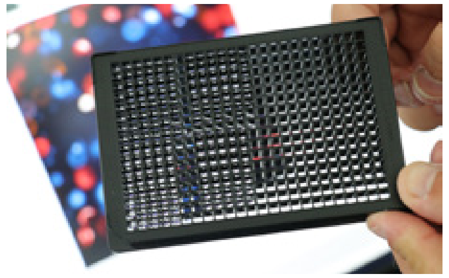


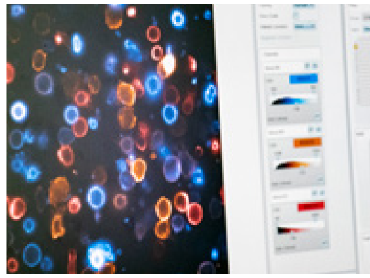
The screening platform provides labs and expertise for the development, miniaturization and validation of biochemical and cellular assays for the screening of libraries of small molecules. Our instrumentation allows the setup of flexible and partially automated protocols using a variety of readouts including absorbance, luminescence, fluorescence, TR-FRET, and imaging. Our lab is equipped with a high-content screening (HCS) system combined with software for image analysis and data evaluation. The platform supports Drug Discovery projects by performing both primary screening as well as dose-response curves, orthogonal and secondary assays.

ACTIVE RESEARCH PROJECTS
Discovery of selective inhibitors of the NOD-like receptor protein 3 (NLRP3) inflammasome for the treatment of chronic inflammatory diseases.



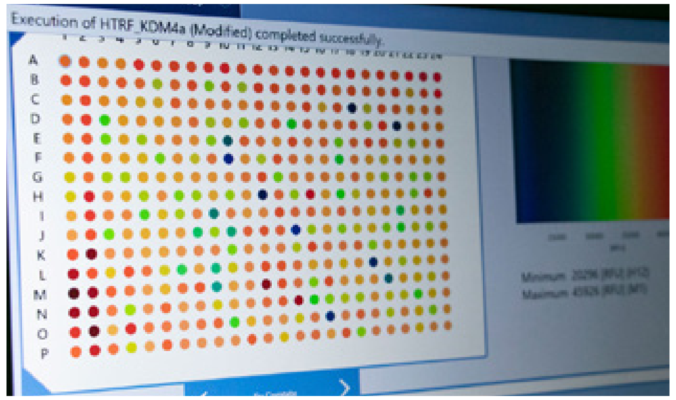


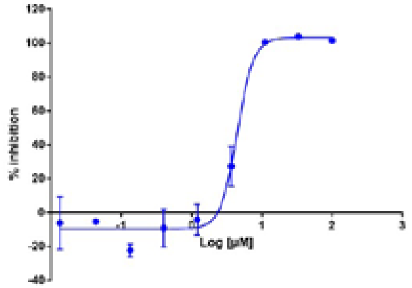


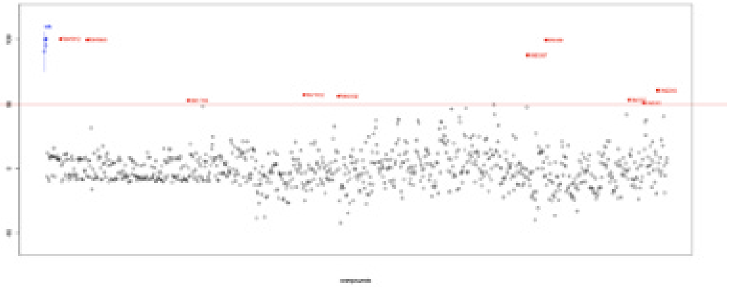


EXPERTISE
- Set-up and validation of primary assay (cell-free and cell-based)
- Different readouts possible including absorbance, luminescence and TR-FRET
- Assay miniaturization (384-well plates)
- High-content imaging (HCI)
- Screening/high-content screening (HCS)
- Data analysis and primary active selection
- Orthogonal and secondary assays
- Toxicity tests

TECHNOLOGY PLATFORM
- Wet lab for cell and molecular biology
- In-Hood-Bravo (Agilent) - liquid handling system
- Spark (Tecan) - multimode microplate reader
- Incucyte® S3 (Sartorius) Live-Cell Analysis System
- EL406 (Biotek) – automatic microplate washer/ dispenser
- Aquamax 4000 (Molecular Devices)– automatic microplate washer for gentle cell washing
- Operetta-CLS (Perkin Elmer)–high-content imaging (HCI) system

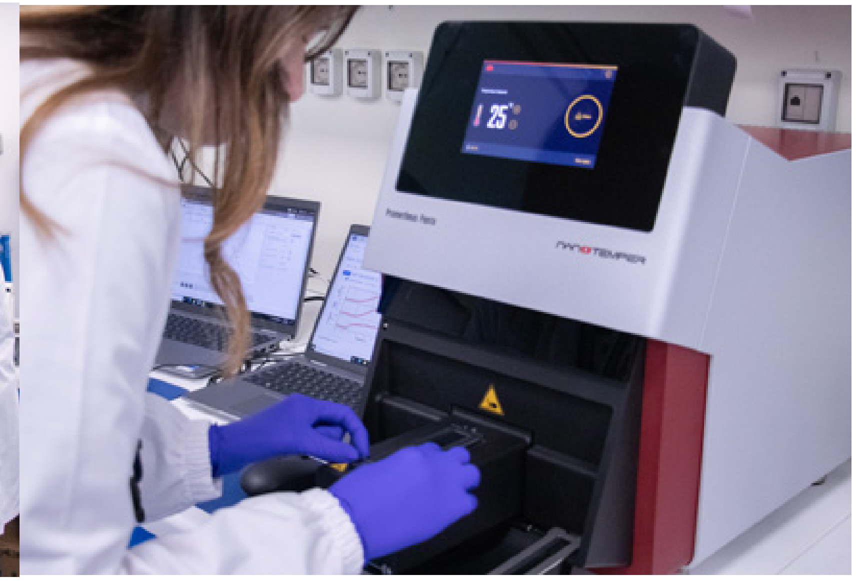






Structural Biology and Biophysics

PLATFORM



CONTACTS

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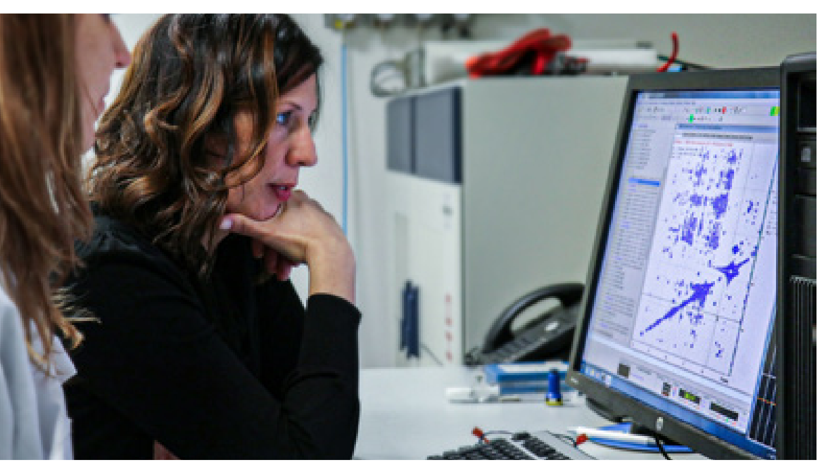
PARTNERSHIPS AND COLLABORATIONS

- Biophysics Institute of the National Research Council (IBF-CNR), Palermo, ITA
- University of Palermo, ITA
- University of Campania "Luigi Vanvitelli", Naples, ITA
- European Brain Research Institute (EBRI) Rita Levi Montalcini, Rome, ITA
- King's College London, London, UK
- i3S - Instituto de Investigação e Inovação em Saúde, Universida de do Porto, Porto, PT

The Structural Biology and Biophysics Platform supports the identification and characterization of biological targets, as well as studies of protein-protein and protein-ligand interactions. Leveraging state-of-the-art equipment, the platform employs a multi-technique approach, including high-field nuclear magnet resonance, circular dichroism, isothermal titration calorimetry, interferometry, and fluorescence spectroscopy, complemented by molecular biology and computational approaches.

The Platform contributes to projects across various therapeutic areas, including neurodegenerative diseases, cancer, and infectious diseases. It provides support at multiple stages of research, from molecular biology manipulation to the production of high-pure recombinant proteins for structural and biophysical studies, and from structural characterization of proteins to studies of the kinetics and thermodynamics of protein-protein and protein-ligand interactions.



The platform's broad expertise and diverse project portfolio highlight its key role in advancing both basic and translational science.

EXPERTISE

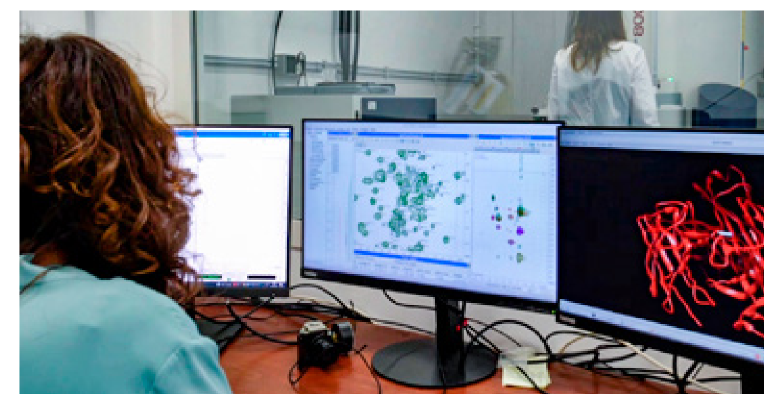
- Proteins Production: from cloning to purified and characterized proteins, including the production of uniformly or selectively labeled proteins
- Determination of size, structure, and stability of biomolecules
- Structural, kinetics, and thermodynamics studies of protein-protein and protein-ligand interactions
- Fragments-based screening by NMR and BLI
- Development and application of customized analytical assays

TECHNOLOGY PLATFORM

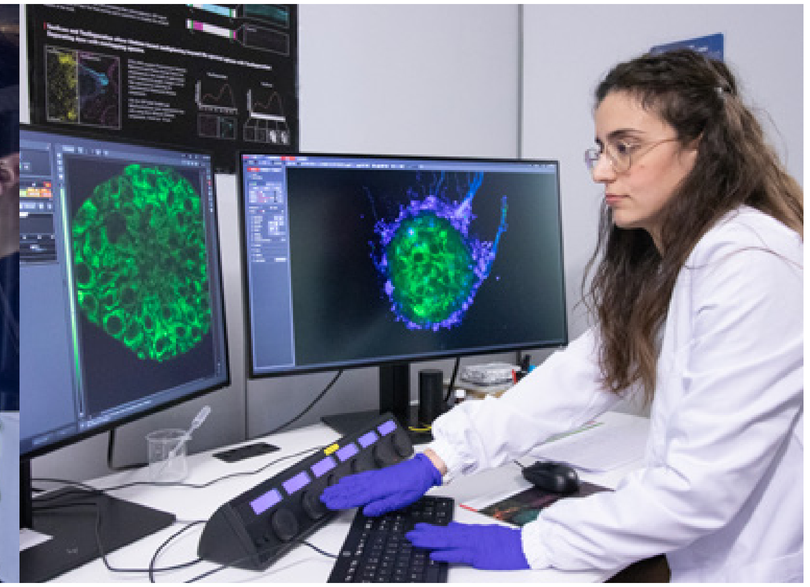
- Molecular biology laboratories for recombinant protein production according to the most modern techniques for cloning, expression, and purification
- AVANCE NEO 800 MHz NMR spectrometer equipped with cryo-probe – Bruker
- MicroCal PEAQ_ITC – Malvern Panalytical
- Bio-Layer Interferometer Octet Red96 – Sartorious
- CD Spectropolarimeter J-1500 – JASCO
- Multi-mode high-performance Microplate Reader CLARIOstar Plus – BMG Labtech
- Monolith X – Nanotemper Technologies
- Prometheus Panta – Nanotemper Technologies

ACTIVE RESEARCH PROJECTS

- Discovery of selective inhibitors of the NOD-like receptor protein 3 (NLRP3) inflammasome for the treatment of chronic inflammatory diseases.
- New drugs and biomarkers for response and pharmacological resistance in colon cancer
- Identification and characterization of interactions among SARS CoV-2 RTC and host proteins.
- Molecular mechanisms of protein misfolding diseases.
- Development of nontoxic bio-adhesives for wet environments



Tissue Engineering
PLATFORM



CONTACTS:
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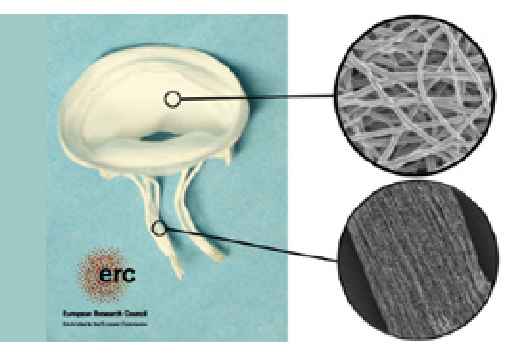
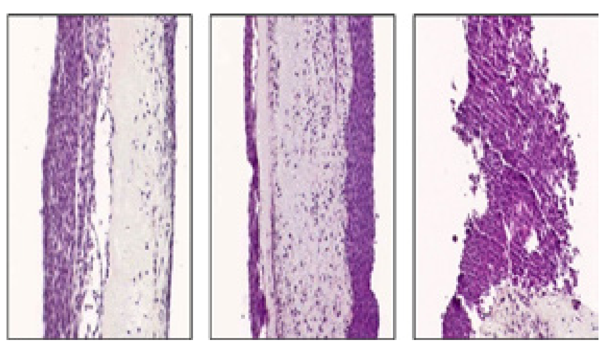
Viale delle Scienze - 90100 Palermo, ITA
Ed.18/A Tissue processing platform
Ed. 16 Tissue characterization platform

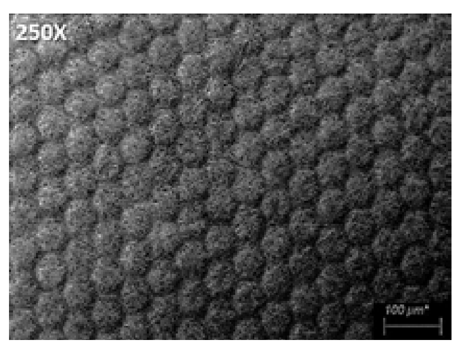
PARTNERSHIPS AND COLLABORATIONS
- University of Palermo, Palermo, ITA
- Advanced Technologies Network Center (ATeN Center), Palermo, ITA
- McGowan Institute for Regenerative Medicine (MIRM), Pittsburgh, USA
- University of Pittsburgh Medical Center (UPMC), Pittsburgh, USA
- The Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT-IRCCS), Palermo, ITA
- Universidad Abierta Interamericana (UAI), Buenos Aires, AR
- Neoolife, Pittsburgh, USA
- TELEA BioTech, Sandrigo, ITA
- Columbia University Irving Medical Center (CUIMC), New York, USA
- Technical University of Munich, (TUM), Munich, DE
- University of California Irvine (UCI), Irvine, USA
- Eindhoven University of Technology, NL
- Politecnico di Torino, ITA
- Università di Cagliari, ITA
- Policlinico di Milano, ITA
- École polytechnique, Paris, FR

The Tissue Engineering program aims to establish a world class and financial sustainable tissue engineering platform at Ri.MED with a focus on clinical translation. The interest of this research platform is upon clinical applications where few effective solutions exist, with an emphasis upon unmet clinical needs in cardiovascular diseases.

The bioprocessing and tissue engineering core platform offers disruptive tools for prototyping and assesing advanced scaffold and biomaterials for tissue engineering applications.
The platform aims to address a broad spectrum of needs within the IRCCS-ISMETT, UPMC Italy and Ri.MED cluster as well as supporting existing and prospective collaborative efforts with invesitgators at the Mcgowan Institute, and Pittsburgh departments of bioengineering and surgery.







EXPERTISE
- Advanced bio-fabrication
- Polymer Synthesis
- Decellularization of organs and tissues
- Mechanical, physical, and chemical characterization of native and engineered tissues
- Qualitative and quantitative histological evaluation of native and engineered tissues
- Formulation and characterization of controlled drug release medical devices
- *In silico* and *in vitro* mechanobiology models
- Structural deterministic models for tissue growth and scaffold degradation
- Pre-clinical evaluation in small and large animal models
- Numerical simulation of physiological systems and their integration with medical devices
- FDA class II and III medical devices prototyping
- Electrospinning
- Double component electrospinning
- Advance valve fabbrication

TECHNOLOGY PLATFORM
- Extraction of ExtraCellular matrix from organ and tissue to produce bio-hybrid medical devices such as cardiac patches, esophageal and vascular grafts
- Numerical codes for the development of simulation models of physiological and predictive systems
- Numerical models to predict *de novo* tissue growth, native tissue remodeling, and polymeric degradation
- Numerical simulation of physiological systems and their integration with medical devices
- Software for quantitative histology analysis
- Software for qualitative and quantitative analysis of microstructure from scanning electron microscopy and multi-photon images
- Innovative methods of morphological analysis of micro and nanostructured materials
- 3D printing on methal, polymer, plastic, gel and cellsoptimization of engineered heart valves
- Electrodeposition, Double component deposition, Mandrelless deposition
- Design and development of bioreactors for stress, flow releated stimulate and topologycal cues
- Prototyping unit with Plastic and Metallic 3D Printers
- Mechanical characterization of the tissue engineered prosthesis including cardiac patches, vascular grafts, and heart valves.
- Melt electronwriting
- Stereolithography

ACTIVE RESEARCH PROJECTS
- Organ level, Meso level, Micro level biomimicry
- Design and development of a minimally invasive cardiac patch implantation system.
- Desing and characterization of esophageal graft
- Development and evaluation of conductive cardiac patches.
- Manipulation of the scaffold microarchitecture in collaboration with the company Telea Biotech.
- Study of the tissue growth, native tissue remodelling and polymeric degradation.
- Development of a bioengineered chordal apparatus for heart valve repair.
- Development of a 3-layer vascular graft to prevent hypelasia of the intima and promote re-endothelialization
- Endothelialization of large surface for blood contacting medical device

WORK IN PROGRESS

Ri.MED Research Center

Fondazione
Ri.MED

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