

DMSC

DEPARTEMENT OF EXPERIMENTAL AND CLINICAL MEDICINE



MAGAZINE

Promoting Research, Sharing Innovation

A space to highlight the scientific excellence of the Department of Experimental and Clinical Medicine and to showcase its research activities nationally and internationally

LncRNAs as Novel Therapeutic Targets for Multiple Myeloma

Since several years, the Medical and Translational Oncology research group, affiliated with the Department of Experimental and Clinical Medicine (DMSC) of the Magna Graecia University of Catanzaro, and led by Professor Tassone and Professor Tagliaferri, focused on the study of new therapeutic targets belonging to the class of non-coding RNAs (non-coding RNA, ncRNA). Micro-RNAs and long-non-coding RNAs (lncRNAs) are the most studied families. Although it is now consolidated that they play a key role in the regulation of physiological mechanisms, including those underlying the onset and progression of tumors, ncRNAs are still considered part of the “dark matter” of the genome because most of them remain unexplored and are therefore the subject of intense research in the biomedical field. Motivated by the promising results obtained from a clinical trial conducted in the phase I centre of the university hospital, in which a targeted therapy against ncRNAs moved from our laboratories to the bedsides of 17 oncological patients (Tassone et. Al, Journal of Hematology & Oncology, 2023), our group was interested in shedding light on new lncRNAs to propose as potential innovative therapeutic targets for the treatment of Multiple Myeloma.

MM is a tumor of the plasma cells of the bone marrow, with an incidence in Italy of about 5,000 new cases per year, and onset mainly in the elderly population: 5-10% of patients are under 40, while 38% are over 70.

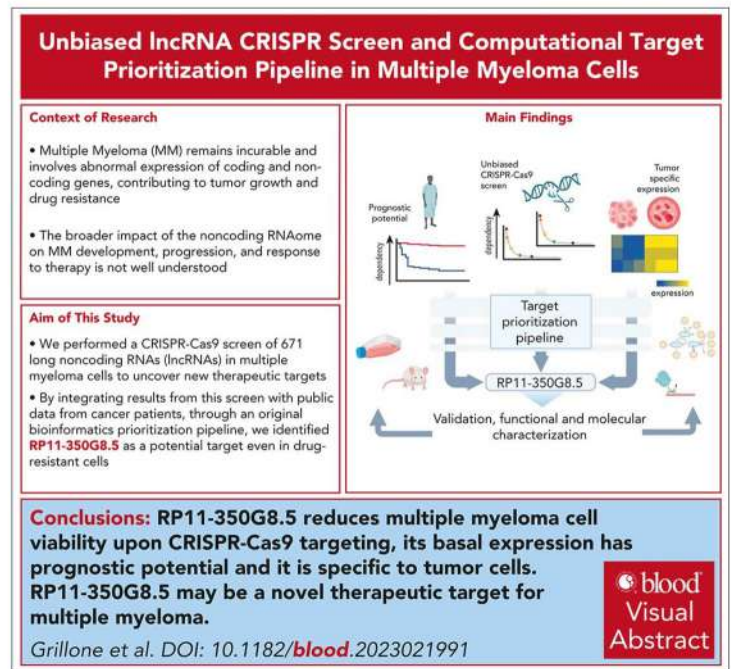
Although the therapeutic scenario has improved thanks to the introduction of new drugs, MM unfortunately remains incurable, patients often have limited therapeutic options and develop resistance even to the most recent therapies. It is therefore necessary to focus on the discovery of new therapeutic targets to propose alternative approaches.

With this aim, in the study of which I am the first author, recently published in the prestigious international scientific journal Blood (Grillone K. et Al., Blood 2024), we highlighted the oncogenic role in MM of RP11-350G8.5, a previously uncharacterized lncRNA. This research work was published on the cover of Blood and was appreciated from the scientific community and the media. In addition to the articles dedicated to our discovery by various newspapers, I was interviewed by TGR Leonardo, and awarded as the best researcher of the DMSC in 2025 both in the context of the “Gran Galà della Ricerca” established by our University and in the context of a national call established by the S.O.S. Solidarietà in Oncologia e Sociale Association based in Bergamo (In the photographs). The discovery was the result of an intense multidisciplinary work carried out in the context of a project funded by the Italian Association for Cancer Research (AIRC).



Award ceremony of the Gran Galà della Ricerca held on 7 May 2025 at the Teatro Politeama in Catanzaro and, on the left, award ceremony for the “Special Mention” for research, obtained on 13 June 2025 at Cascina San Carlo in Bergamo by the members of the board of directors of the SOS Association and the supporters who donated the award.

We applied the sophisticated CRISPR-Cas9 system to conduct a screening aimed at investigating the role of ≈ 700 lncRNAs in MM cell lines sensitive and resistant to the conventional drug Bortezomib. This screening consists in evaluating the effect induced on the tumor cell by the loss of hundreds of genes, with the aim of identifying those whose depletion causes cell death or reduction of the uncontrolled proliferation typical of tumors. Subsequently, in collaboration with the Computational Biology group of the Human Technopole in Milan, led by Dr. Iorio, we have designed a bioinformatics prioritization pipeline capable of combining functional data obtained in the laboratory with clinical data from datasets of patients affected by MM, to evaluate the prognostic value of our candidates. We have thus identified 8 lncRNAs essential for the growth and vitality of tumor cells, which are also highly expressed in tumors and associated with an unfavorable prognosis in patients. Among these, we focused on the most promising candidate, RP11-350G8.5. By depriving a panel of MM cell lines of this lncRNA we highlighted how both sensitive and resistant cells to Bortezomib treatment reduced the ability to form colonies, the proliferation rate and induced death by apoptosis. RNA-sequencing studies have highlighted the molecular mechanisms underlying this effect, linked to alterations in the degradation system of misfolded proteins, the Achilles heel of MM, and also to the induction of immunogenic cell death.



In summary, if we target this lncRNA we are able to induce not only a direct and selective toxicity effect on tumor cells, as demonstrated in vitro and in vivo, but also to stimulate the action of the immune system to fight MM cells. In collaboration with computational chemistry and pharmacological chemistry groups, we have also performed prediction and biophysical validation studies of the 2D and partly of the 3D structure of the lncRNA that had never been characterized before, in order to pave the way for the subsequent development of targeted therapies. We are currently working on designing potential targeting approaches and evaluating the role of RP11-350G8.5 in other tumor types.

Quoting Professor Tassone:

“The discovery of a new lncRNA, never described before, as a possible therapeutic target for Multiple Myeloma, is an important new step in the search for new treatments. It is also a concrete success for AIRC and its supporters, as well as a substantial Italian contribution to the opening of a new frontier of research in the emerging context of RNA therapeutics”.



Cover of Blood depicting one of the images presented in the manuscript Grillone K. et al. 2024 and on the left the Visual Abstract summarizing the work.

Katia Grillone

C-Peptide: a possible therapeutic innovation to counter osteosarcopenia

Sarcopenia and osteoporosis are among the major health challenges associated with ageing. The former increases the risk of falls, the latter the risk of fractures; both contribute to the onset of disability and frailty in the elderly population. Often coexisting and acting synergistically, these conditions contribute to the development of osteosarcopenia syndrome, which compromises functional autonomy and has significant implications for public health and healthcare-related social costs.

Our research group is pursuing a line of investigation on C-peptide, a molecule long considered inert, demonstrating its potential active role in protecting bone and muscle tissue. In particular, one of our studies showed a positive correlation between serum C-peptide levels and lumbar bone mineral density in non-diabetic postmenopausal Italian women, suggesting an insulin-independent action of this molecule on bone metabolism. In collaboration with research groups at the University of Padua and the University of Catanzaro, we demonstrated that the administration of C-peptide in diabetic rats improves trabecular thickness and increases RUNX2 levels in the femur, thereby enhancing bone quality.

We also observed that treatment with C-peptide preserves muscle mass and reduces markers of muscle degradation in animal models of sarcopenia. Data from non-diabetic postmenopausal women confirmed that reduced muscle mass is associated with lower circulating levels of C-peptide.

Building on these results, our group has obtained both national and European patents for an innovative pharmacological formulation combining C-peptide and bisphosphonates, the latter traditionally used in the treatment of osteoporosis. This is the first therapeutic application designed to act simultaneously on bone and muscle, with the aim of preventing the progressive loss of mass and function in the musculoskeletal unit. The rationale behind this invention lies in the ability of bisphosphonates to bind firmly to the bone matrix, acting as a “carrier” for C-peptide and enhancing its local and systemic efficacy on the bone-muscle axis.



Gran Galà della Ricerca Award - Best Patent 2025
 In the photo, from right: Professor Tiziana Montalcini (DMSC), Dr Samantha Maurotti (DMSC), Dr Elisa Mazza (DMSC), and Dr Yvelise Ferro (DSMC).

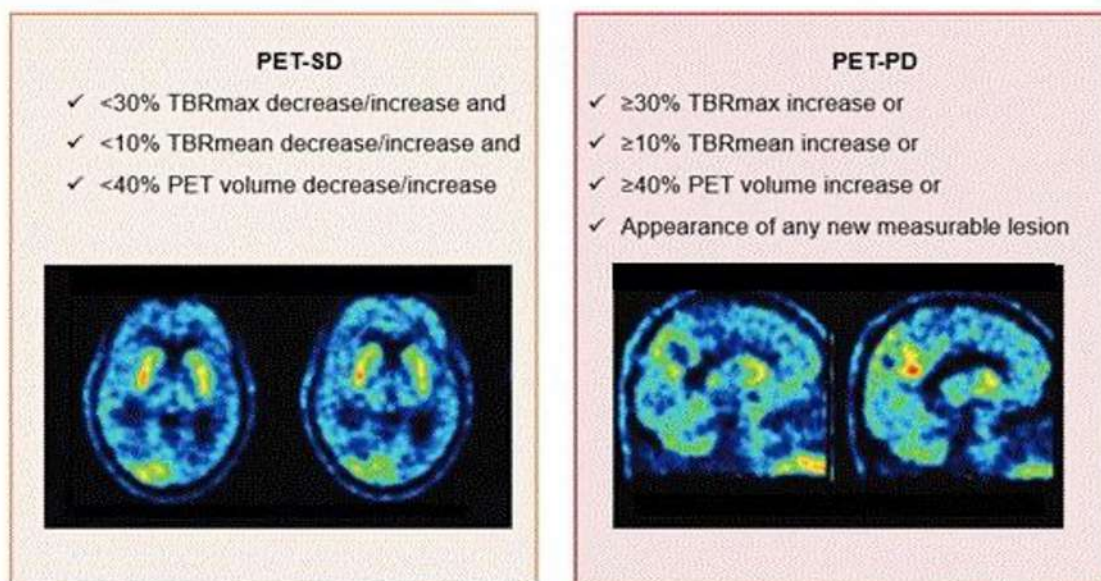
The formulation is currently undergoing preclinical validation, and strategies for future clinical application are now being defined. This line of research was awarded at the Gran Galà della Ricerca in recognition of its conceptual originality, the innovative value of the discovery, and its potential for technology transfer.

In a context of rapid demographic ageing, investing in integrated therapies that simultaneously protect bone and muscle means promoting health, autonomy, and sustainability for the healthcare system. Our next objective is to initiate early-phase clinical studies and define an industrial development plan in synergy with academic and industrial partners, in order to translate this discovery into a concrete therapeutic option.

Tiziana Montalcini, Samantha Maurotti, Elisa Mazza

Standardization of acquisition and interpretation criteria of brain tumor imaging with radiolabeled amino acid analogues

PET RANO Brain Metastases 1.0 criteria



In recent years the preferred research topics of prof. Francesco Cicone have been neuroimaging, particularly amino acid positron emission tomography (PET) of brain tumors, and internal dosimetry of theranostic radiopharmaceuticals. Besides conducting spontaneous original research, he has been engaged in collaborative international groups and committees, such as the Response Assessment in Neuro Oncology (RANO) group, the European Organization for Research and Treatment of Cancer (EORTC) Brain tumor group and the European Association of Nuclear Medicine (EANM) Dosimetry Committee. The activity conducted as members of these organizations resulted in the publication of numerous papers in authoritative journals with high impact factor, such as The Lancet Oncology, Nature Medicine, Neuro-Oncology, The Journal of Nuclear Medicine, and others.

For imaging tumors of the central nervous system, the most used PET radiopharmaceutical, [18F]fluorodeoxyglucose ([18F]FDG), has known limitations due to its physiologically high background uptake, and other probes such as amino acid analogues are preferred. These unconventional radiopharmaceuticals, however, still suffer from limited availability and have rarely been included in large clinical trials.

This year, the most relevant achievements of prof. Francesco Cicone have regarded the publication of international guidelines for the acquisition and interpretation criteria of amino acid PET imaging, which may allow for a wider incorporation of molecular imaging into clinical trials evaluating novel treatment strategies for primary and secondary brain tumors.

The publication receiving the greatest international attention has been the article titled "RANO criteria for response assessment of brain metastases based on amino acid PET imaging", published in May 2025 in Nature Medicine (Albert NL et al. 2025 Nat Med 2025;31:1424-1430).

Another relevant article on procedural standardization of molecular imaging of secondary brain tumors published earlier this year was the "Joint EANM/EANO/RANO/SNMMI practice guideline/procedure standard for PET imaging of brain metastases: version 1.0" (Verger A et al. 2025 Eur J Nucl Med Mol Imaging. ;52:1822-1839).

The recommendations included in these papers reflect the experience of several international experts on molecular imaging of brain tumors, and are likely to be adopted by the large majority of specialized centers in this diagnostic field.

Human-centered care: redefining care around the individual

The research team composed of Professor Patrizia Doldo, Professor Silvio Simeone, and research fellows Dr. Caterina Mercuri and Dr. Vincenzo Bosco is actively engaged in the development of innovative educational programs aimed at promoting self-care, through an approach based on nursing counseling. The person and their specific context are genuinely placed at the center of care delivery.

Studies exploring new care approaches for Inflammatory Bowel Diseases (IBDs) are showing promising results in improving the quality of life for affected individuals.

Since the beginning of 2025, the group has produced over ten scientific publications delving into these themes, addressing both pediatric and adult populations, with particular attention to the introduction of diaries in critical care areas. This tool has proven effective in strengthening the relationship between the “patient” and the care team, supporting individuals in a more aware, humane, and participatory care journey. Furthermore, the research group has been involved in important international discussions and scientific investigations on the subject.

The Azienda Ospedaliera Universitaria Renato Dulbecco in Catanzaro has also requested the group to design an educational intervention for healthcare professionals, aimed at further enhancing the institution’s existing orientation toward a comprehensive humanization of care.

These research activities are part of a broader vision that includes the humanization of healthcare and the improvement of clinical and care outcomes, within a context where healthcare is progressively shifting toward community-based settings. This transition supports a model of care that is more accessible to the entire population and better integrated with local services.

The Hidden Side of Cadmium: Iron, Ferroptosis, and Emerging Therapeutic Perspectives for Oral Cancer

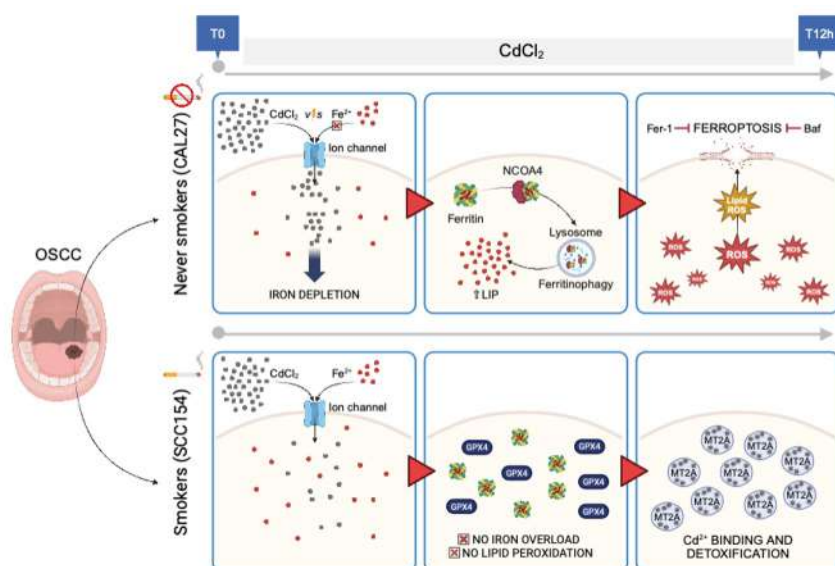
Cadmium is a highly toxic heavy metal released into the environment through industrial activities and tobacco combustion. Once introduced into the body, it progressively accumulates in tissues, damaging vital organs such as the kidneys, liver, and lungs. The International Agency for Research on Cancer (IARC) has classified cadmium as a Group 1 human carcinogen, and it is now recognized as a global public health threat, associated with numerous cancer types, including oral squamous cell carcinoma.

To investigate one of the most insidious effects of this environmental contaminant, the Biochemistry and Cell Biology group from the Department of Experimental and Clinical Medicine (DMSC) has published a study in the *International Journal of Biological Sciences* (IF 10.0) titled: "Acute Exposure to Cadmium Triggers NCOA4-Mediated Ferritinophagy and Ferroptosis in Never-Smokers Oral Cancer Cells." The research was led by Prof. Flavia Biamonte and Dr. Anna Martina Battaglia, with PhD students Lavinia Petriaggi and Emanuele Giorgio (enrolled in the Molecular Medicine Biotechnology Program at DMSC) as co-first authors.

The study demonstrates that acute cadmium exposure exerts a potent cytotoxic effect on oral cancer cells derived from non-smoker patients, triggering ferroptosis - a form of regulated cell death dependent on iron and characterized by extensive lipid peroxidation of cellular membranes.

Cadmium, as a divalent cation, competes with iron for cellular uptake, resulting in a temporary intracellular iron depletion. To compensate for this imbalance, cells activate ferritinophagy, a selective degradation process of ferritin - the primary iron storage protein - mediated by the cargo receptor NCOA4. The consequent release of free iron into the cytoplasm initiates an uncontrolled oxidative cascade which, combined with reduced activity of the antioxidant enzyme GPX4, leads to ferroptosis.

A particularly striking finding from the study is that co-treatment with exogenous iron restores intracellular iron homeostasis and completely abolishes cadmium-induced cytotoxicity. However, this effect is not uniform across all conditions. Oral cancer cells derived from smoker patients, chronically exposed to cadmium through tobacco, display reduced cadmium uptake and upregulated expression of heavy metal detoxifying proteins such as metallothionein 2A (MT2A), which mitigate oxidative stress and prevent ferroptosis activation. In this context, exogenous iron supplementation paradoxically becomes toxic, as it exacerbates oxidative stress and induces cell death.



Graphical abstract del lavoro scientifico

Petriaggi, L., Giorgio, E., Bulotta, S., Antonelli, A., Bonacci, S., Frisina, M., Procopio, A., Prestagiacomo, L. E., Giuliano, A., Gaspari, M., Santamaria, G., Federico, G., Galeano, C., Natali, G., Giudice, A., Costanzo, F., Battaglia, A. M., & Biamonte, F. (2025). Acute Exposure to Cadmium Triggers NCOA4-Mediated Ferritinophagy and Ferroptosis in Never-Smokers Oral Cancer Cells. *International journal of biological sciences*, 21(9), 4131–4152. <https://doi.org/10.7150/ijbs.111228>

Two key implications arise from this study:

- 1. Targeted modulation of ferroptosis could represent a novel selective therapeutic strategy for oral cancer, with personalized approaches based on patients' environmental exposure profiles.**
- 2. The identification of cellular biomarkers of cadmium sensitivity is crucial to protect exposed populations and enable early detection of at-risk individuals.**

This study reflects the outcome of a multidisciplinary collaboration among several research teams at the University "Magna Graecia" of Catanzaro: the Laboratory of Biochemistry and Cell Biology (with extensive expertise in iron metabolism and ferroptosis), groups specializing in proteomics, chemistry, and bioinformatics, and the oral pathology and surgery unit of the "Renato Dulbecco" University Hospital. Additional contributions came from researchers at the Department of Molecular Medicine and Medical Biotechnology of the University of Naples "Federico II."

Flavia Biamonte

From Basic Research to Therapy: A Novel Approach for Lung Cancer

My Experience at the 5th Italian Society of Biochemistry-SIB Workshop "Tumor Biochemistry Group" in Turin

Last June, I had the honor of being selected as a speaker for a short talk at the 5th Workshop of the SIB group "Tumor Biochemistry", held at the Molecular Biotechnology Center in Turin. The event, with its evocative title "Is cancer an inaccessible fortress? Exploiting tumor Achille's heels to foster treatment opportunities", brought together researchers from across Europe to share the latest discoveries in the field of tumor biochemistry.

An International Showcase for Calabrian Research

My presentation, titled "Overcoming BET-inhibitor JQ1 resistance in aggressive non-small cell lung cancer via BRD2-FTH1 axis by inducing ferroptosis", illustrated the results of research we are conducting at the Department of Experimental and Clinical Medicine of the Magna Graecia University of Catanzaro. This work supervised by Prof. Concetta Faniello, addresses one of the most urgent challenges in modern oncology: overcoming drug resistance in non-small cell lung carcinoma.

Scientific Innovation: When Ferritin Meets Epigenetics

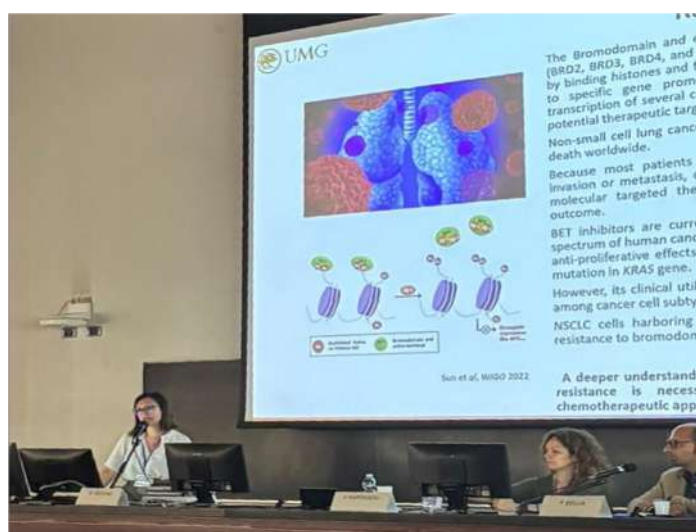
Our research has identified a completely novel mechanism involving nuclear ferritin (FTH1) and BRD2 protein in the regulation of programmed cell death called ferroptosis. This process, characterized by iron accumulation and oxidative stress, represents a new therapeutic frontier. Our results demonstrate that FTH1 silencing can enhance the efficacy of the JQ1 drug in resistant tumor cells, opening unprecedented prospects for treating aggressive forms of lung cancer.

A Stimulating Exchange with European Excellence

The workshop offered an extraordinary panorama of the most advanced research in Europe. Among the most significant sessions, those dedicated to tumor metabolism and the relationships between tumor cells and the microenvironment provided valuable insights for future collaborations.

The presence of researchers from prestigious institutions such as IFOM Milan, University of Cambridge, and the Centre for Genomic Regulation in Barcelona created an environment of scientific exchange at the highest level.

Presenting our research in this international context represented a unique opportunity to receive feedback from the European scientific community and to establish new research contacts. The questions and suggestions received during the speed talk session have already guided some of our upcoming experiments, confirming the importance of open scientific dialogue.



The results presented in Turin represent only the beginning of a path that could lead to new therapeutic strategies for patients with lung carcinoma resistant to conventional therapies. Our laboratory will continue to explore the role of ferroptosis as a therapeutic target, with the goal of translating these discoveries from basic research to clinical practice. Particularly satisfied that the results obtained have recently been published in a prestigious International Scientific Journal of Biochemistry, the "Federation of European Biochemical Societies" Febs Journal.

This experience once again confirms how research conducted at the Magna Graecia University of Catanzaro can compete at the highest international levels, contributing to scientific progress and, hopefully, to improving treatment prospects for cancer patients.

Breast cancer: new perspectives between epigenetics and patient-specific models

Scientific research in the biomedical field is a constantly evolving area, where the commitment of researchers is essential to deepen our understanding of disease and develop new therapies. In this context, our university actively contributes by hosting innovative, high-quality research projects.

The research activity of the Proteomics and Tumor Biochemistry group, coordinated by Professor Domenica Scumaci, is focused on the study of breast cancer through an innovative biochemical and proteomic approach. The aim is to uncover the molecular mechanisms underlying tumor pathogenesis and progression in order to identify new therapeutic targets.

Histone lipidation: new horizons in cancer epigenetics

One of the areas on which our research group is focusing is the proteomic analysis of non-traditional post-translational histone modifications, with particular attention to lipidation, in breast cancer cell models. While modifications such as histone acetylation, methylation, and phosphorylation have been widely studied and recognized as key regulators of chromatin structure and gene expression, histone lipidation is emerging as a new and promising field of investigation. Our research aims to identify and characterize specific histone lipidations, analyzing their impact on chromatin stability, DNA accessibility, and the modulation of gene expression in neoplastic contexts. The hypothesis is that these modifications may act as molecular switches, influencing the transcription of genes involved in cancer development. Understanding these molecular mechanisms could pave the way for the development of new therapeutic strategies.

The significance of our work was recently underscored by its selection for an oral presentation at the conference "Nutrition, Environment, and Biomembranes: Interaction and Emerging Perspectives." The event, organized by the Italian Society of Biochemistry and Molecular Biology, was held at the University of Bologna from 27 to 29 May 2025. There, I had the honor of presenting the research entitled "Histone Lipidation in Breast Cancer: The Epigenetic Role of BRCA1."

This participation was not only a personal achievement, but also a valuable opportunity to share our findings and engage openly with a panel of renowned experts in the field of biochemistry. It was an important moment for building new connections and stimulating future collaborations.

La lipidazione istonica: nuovi orizzonti nell'epigenetica del cancro

The role of the extracellular matrix in breast cancer: from in vitro studies to patient-derived models

Another area of research concerns the derivation and characterization of organoids from patients with breast cancer. These three-dimensional models, derived directly from surgical resections, reproduce in vitro the tissue structure and the genetic and phenotypic complexity of the original tumor. The use of organoids allows for a more faithful analysis of tumor behavior, overcoming some of the limitations of traditional two-dimensional cell models. The proteomic and biochemical characterization of these organoids will, in the future, allow us to identify possible patient-specific biomarkers and therapeutic targets.

Another interesting aspect of this project is focused on characterizing the interaction between the extracellular matrix and breast cancer cells. The extracellular matrix is not simply a structural support, but a dynamic microenvironment that actively interacts with tumor cells, influencing proliferation, migration, invasion, and chemoresistance. Our study aims to identify the protein composition and post-translational modifications of the extracellular matrix of breast cancer obtained from patients. Understanding these details is essential for unraveling the molecular mechanisms that regulate ECM formation and function in the tumor context.

Preliminary results of this research were recently presented in a poster entitled "Proteomic Profiling of Decellularized Extracellular Matrix in Human Breast Cancer" at the 5th Workshop of the SIB Group "Tumor Biochemistry," Is Cancer an Inaccessible Fortress? Exploiting Tumor Achilles' Heels to Foster Treatment, held at the Molecular Biotechnology Center in Turin from 9 to 10 June 2025 (photo).



Active participation in scientific conferences, such as those mentioned above, is a fundamental aspect of research activity. These meetings offer a unique opportunity for direct exchange with internationally renowned researchers who, through their experience and vision, can provide critical feedback, suggest new directions of investigation, and stimulate synergistic collaborations. Discussion of data, analysis of methodologies, and exchange of ideas not only validate and enrich one's work, but also open new horizons toward multidisciplinary approaches and cutting-edge technologies. It is in these contexts that scientific networks are strengthened and new hypotheses are generated.

The research activity described reflects our group's ongoing commitment to actively contributing to the understanding of the molecular mechanisms underlying breast cancer through innovative approaches, also supported by international scientific exchange.

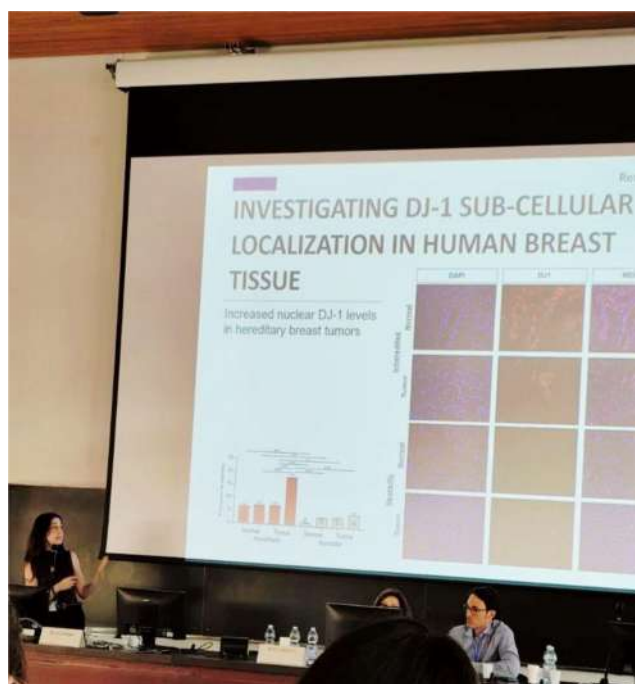
Marilena Pontoriero

Research, Exchange, and New Connections: My Experience at the SIB Congress in Turin

In June, I had the pleasure of participating in the 5th Workshop of the "Tumor Biochemistry" group of the Italian Society of Biochemistry (SIB), held at the Molecular Biotechnology Center in Turin. This event gave me the opportunity to deliver an oral presentation in a high-level and stimulating scientific context, showcasing the doctoral research project I have been working on in the Proteomics and Tumor Biochemistry Laboratory at our University, coordinated by prof. Domenica Scumaci.

My research focuses on the role of phospho-DJ-1, a protein involved in protecting chromatin from metabolic stress by preventing histone glycation. Specifically, our team identified a potential inhibitor of this protein isoform and obtained promising in vitro results, particularly in the HCC1937 cell line—a model of triple-negative breast cancer carrying a BRCA1 mutation. These findings suggest an intriguing link between epigenetic instability and tumor vulnerability.

Beyond the scientific value, what makes events like this truly special is their human and relational dimension. The congress is a valuable opportunity to meet other researchers working in the same field, share ideas, approaches, and challenges, and foster an open, stimulating atmosphere for exchange. Additionally, it was a real pleasure to reconnect with several colleagues from the SIB Tumor Biochemistry group. After five editions of this workshop (one of which was hosted at our University in 2023), strong bonds of friendship and scientific affinity have naturally formed.



Taking part as a speaker in an international-level event was also a meaningful occasion to give visibility to my University and to the work carried out every day in our labs. Bringing scientific contributions to an international context means not only sharing results but also proudly representing the academic community we belong to, helping to build its value and recognition within the broader research landscape.

I return from Turin with new awareness, fresh ideas for my project, and the deep conviction that the value of science grows when it is shared.

Marina La Chimia



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