

BIOGRAPHICAL SKETCH

NAME: Flavia Biamonte

eRA COMMONS USER NAME N/A (not applicable)

POSITION TITLE: Associate Professor of Applied Biology, Principal Investigator

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Florence, Florence, Italy	B.Sc.	12/2007	Biotechnology
University of Florence, Florence, Italy	M.Sc.	11/2009	Medical, Veterinary and Pharmaceutical Biotechnology
University of Florence, Florence, Italy	PhD	02/2013	Experimental and Clinical Oncology
Magna Graecia University of Catanzaro, Italy	Residency	09/2022	Clinical Pathology and Clinical Biochemistry

A. Personal Statement

I am an Associate Professor of Applied Biology at the “Magna Graecia” University of Catanzaro. My scientific training began during my PhD at the University of Florence, under the supervision of Prof. Alessandro Maria Vannucchi, within an AIRC 5×1000-funded project on Chronic Myeloproliferative Neoplasms. After completing my doctorate, I was awarded a six-year postdoctoral position in Prof. Francesco Saverio Costanzo’s laboratory of Biochemistry and Cell Biology (“Magna Graecia” University of Catanzaro), where I developed solid expertise in redox homeostasis and iron metabolism, progressively focusing on ferroptosis as a therapeutic vulnerability in cancer. Today, my independent research program investigates how the rewiring of iron-handling pathways shapes tumor aggressiveness, stemness, immune evasion, and response to therapy. I lead a fully operational laboratory equipped with advanced *in vitro* platforms, including 3D and co-culture systems, molecular biology (PCR/qPCR), live imaging, flow cytometry, Western blotting, and ELISA assays. My group includes one senior R2 researcher, four PhD students (two senior and two junior), and a research technologist. I share laboratory space and infrastructure with the Biochemistry group of my institution (one PI, two R2 researchers, one PhD student). Together, we have accumulated over ten years of focused experience in iron metabolism and ferroptosis across multiple tumor models. My research is embedded in a national and international collaborative network. I am Principal Investigator of a PRIN 2022 project on ferroptosis in ovarian cancer (“*Ovarian Cancer Cells: from Iron Addiction to Ferroptosis Vulnerability*”, Prot. 2022R85H27), in collaboration with “La Sapienza” University of Rome and the “Federico II” University of Naples (ending February 2026). In parallel, I am co-PI of a PRIN-PNRR project extending ferroptosis paradigms to non-neoplastic diseases, such as psoriasis (“*Multiple Functions of CARD14 in Keratinocyte Differentiation, TLR Response, Ferroptosis and Psoriasis Pathogenesis*”, Prot. P2022RBPHH; ending February 2026), in collaboration with the University of Sannio and CNR of Naples. Internationally, I collaborate with the Champalimaud Foundation (Lisbon), where I spent six months in 2022 as visiting professor, and the University of Coimbra where I contribute to PhD and MSc training programs.

In recent years, my laboratory has expanded its focus to oral squamous cell carcinoma (OSCC). In this context, we have generated compelling preliminary evidence that a subgroup of poor-prognosis OSCCs with perineural invasion (PNI) is selectively enriched in neurogenesis, chemotaxis, and ferroptosis-related biological programs. Functionally, high-risk OSCC *in vitro* models engage in bidirectional crosstalk with neural stem cells, accelerating neuronal differentiation and, reciprocally, enhancing tumor

migration and invasion. Notably, these high-risk OSCC cells are highly susceptible to ferroptosis, an especially relevant vulnerability in a tumor type frequently refractory to apoptosis-based therapies. The project proposed for the Human Technopole call emerges directly from this line of investigation and leverages an interdisciplinary framework, integrating collaboration with our molecular biology group (expert in neuroscience and iPSC-derived neural stem cells) and with the clinical Unit of Oral Pathology and Surgery of our University Hospital. We hypothesize that a discrete OSCC subpopulation couples ferroptosis sensitivity with neurotropic programs, enabling tumor–nerve crosstalk and driving PNI. The main bottleneck we now face is technological: the inability to resolve, at sufficient molecular depth, the cellular states emerging during neuron–tumor interactions. Single-cell RNA sequencing is essential to dissect these programs and reconstruct the bidirectional transcriptional rewiring between tumor and neural compartments. The proposed work “Dissecting ferroptosis-sensitive, neurotropic oral cancer subpopulations through single-cell transcriptomics” will establish a mechanistic framework linking ferroptosis sensitivity, neural responsiveness, and aggressive tumor behavior in OSCC, with direct implications for patient stratification and for the rational design of combination therapies targeting neuron–tumor signaling and ferroptotic vulnerability. Access to the Human Technopole single-cell facility is a scientific necessity. Through the “access with training” modality, I propose the R2 researcher of my group, Dr. Anna Martina Battaglia, as user. Together, we bring complementary expertise in ferroptosis biology, OSCC models, stress-response mechanisms, and translational redox research. I aim for her to acquire full proficiency in single-cell experimental design, sample preparation, and data interpretation, enabling the durable integration of single-cell technologies into our research program.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2025 – National Scientific Qualification as Full Professor in Applied Biology (BIOS/10A), Italian Ministry of University and Research

2024 to present – Lecturer, Doctoral Program in Experimental Biology and Biomedicine (PDBEB), CNC Advanced Courses, University of Coimbra, Portugal

2022 – Visiting Professor, Champalimaud Foundation, Lisbon, Portugal

2021 to present – Associate Professor of Applied Biology (BIOS/10A), Department of Experimental and Clinical Medicine, University “Magna Graecia” of Catanzaro, Italy

2021 to present – Lecturer, Master’s Degree Program in Molecular Biology, University of Coimbra, Portugal

2020 to present – Faculty Member, Doctoral School in Molecular Medicine, University “Magna Graecia” of Catanzaro, Italy

2018–2021 – Senior Researcher (Type B; Law 240/2010, art. 24.3-b), Applied Biology, University “Magna Graecia” of Catanzaro, Italy

2013–2018 – Research Fellow, Department of Experimental and Clinical Medicine, University “Magna Graecia” of Catanzaro, Italy

2012 – Visiting Ph.D. Student, Applied Biosystems, Glasgow, United Kingdom

2009 – Visiting Student, Laboratory of Onco-Hematology, University of Cambridge, United Kingdom

Selected Honors and Distinctions

2024 – Best Oral Communication Award, European Association of Oral Medicine Biennial Conference (London, UK)

2024 – Candidate for “Tarone Under 45” Award, Italian Association of Biology and Genetics (AIBG) National Congress

2021 – Best Poster Award, Italian Association of Cell Cultures (AICC) Annual Conference

C. Contributions to Science

To date, I am the author of 59 peer-reviewed publications indexed in Scopus, with an h-index of 25 and a total of 3,197 citations. My research addresses how iron metabolism and redox stress responses

shape cancer cell plasticity, immune escape, and treatment failure, with a central focus on ferroptosis as a druggable vulnerability in solid tumors. Across ovarian cancer and oral squamous cell carcinoma (OSCC), I combine mechanistic biology with advanced in vitro models (including 3D spheroids and neuron–tumor co-cultures) to identify actionable resistance nodes and translational biomarkers.

1) Iron trafficking and ferroptosis resistance mechanisms in ovarian cancer

A major axis of my work dissects how ovarian cancer cells reprogram iron handling to survive oxidative stress and escape ferroptotic death. We identified iron-dependent determinants of stem-like growth in non-adherent conditions and demonstrated that manipulating iron availability can override resistance to canonical ferroptosis inducers. More recently, we uncovered an intercellular mechanism of resistance based on CD63-mediated exosomal expulsion of iron-rich ferritin, revealing a previously underappreciated route by which tumor cells buffer intracellular iron toxicity and evade ferroptosis. Collectively, these studies provide mechanistic rationale for therapeutic strategies that combine ferroptosis induction with targeting iron storage/export pathways.

Selected publications

- Battaglia AM, Sacco A, Giorgio E, *et al.*; Costa-Silva B; Biamonte F. Expulsion of iron-rich ferritin via CD63-mediated exosome drives ferroptosis resistance in ovarian cancer cells. *Frontiers in Cell and Developmental Biology*. 2025;13:1532097.
- Battaglia AM, Sacco A, Vecchio E, *et al.*; Biamonte F; Costanzo F. Iron affects the sphere-forming ability of ovarian cancer cells in non-adherent culture conditions. *Frontiers in Cell and Developmental Biology*. 2023;11:1272667.
- Battaglia AM, Sacco A, Perrotta ID, *et al.*; Biamonte F; Costanzo F. Iron Administration Overcomes Resistance to Erastin-Mediated Ferroptosis in Ovarian Cancer Cells. *Frontiers in Oncology*. 2022;12:868351.
- Scicchitano S, Vecchio E, Battaglia AM, *et al.*; Biamonte F; Faniello MC. The Double-Edged Sword of Oleuropein in Ovarian Cancer Cells: From Antioxidant Functions to Cytotoxic Effects. *International Journal of Molecular Sciences*. 2023;24(1):842.

2) Ferroptosis, environmental carcinogens, and tumor cell identity in OSCC

I extended ferroptosis research to OSCC to connect iron/redox biology with exposure-related vulnerabilities and clinically aggressive behavior. We demonstrated that acute cadmium exposure triggers NCOA4-mediated ferritinophagy and ferroptosis in OSCC cells derived from never-smokers, while smoker-derived models display relative resistance consistent with metal-detoxification programs. In parallel, I contributed to clarifying how transcriptional drivers of plasticity and local spread intersect with OSCC progression, supporting an integrated view where ferroptosis sensitivity/resistance may track with distinct tumor states relevant to invasion and therapy failure.

Selected publications

- Petriaggi L, Giorgio E, Bulotta S, *et al.*; Battaglia AM; Biamonte F. Acute Exposure to Cadmium Triggers NCOA4-Mediated Ferritinophagy and Ferroptosis in Never-Smokers Oral Cancer Cells. *International Journal of Biological Sciences*. 2025;21(9):4131–4152.
- Sacco A, Battaglia AM, Santamaria G, *et al.*; Biamonte F; Giudice A. SOX2 promotes a cancer stem cell-like phenotype and local spreading in oral squamous cell carcinoma. *PLOS ONE*. 2023;18(12):e0293475.
- Antonelli A, Battaglia AM, Sacco A, *et al.*; Biamonte F; Giudice A. Ferroptosis and oral squamous cell carcinoma: connecting the dots to move forward. *Frontiers in Oral Health*. 2024;5:1461022.
- Biamonte F, Buffone C, Santamaria G, *et al.*; Costanzo FS; Giudice A. Gene expression analysis of autofluorescence margins in leukoplakia and oral carcinoma: A pilot study. *Oral Diseases*. 2021;27(2):193–203.

3) Redox–iron control of therapy resistance and immune escape programs

A third core contribution of my work is defining how iron-driven oxidative stress rewires stress-response networks that support resistance phenotypes, including immune checkpoint upregulation and metabolic

adaptation in 3D. We showed that iron-mediated oxidative stress induces PD-L1 via c-Myc, mechanistically linking iron/redox status to immune evasion. Using multi-omics and advanced 3D models, we also identified metabolic configurations that enable tumor spheroids to grow despite nutrient variability, reinforcing the concept that resistance is sustained by coupled redox–metabolic programs. Complementary synthesis papers helped establish conceptual frameworks for ferroptosis in cancer and in the tumor microenvironment.

Selected publications

- Battaglia AM, Sacco A, Aversa I, *et al.*; Costanzo F; Biamonte F. Iron-mediated oxidative stress induces PD-L1 expression via activation of c-Myc in lung adenocarcinoma. *Frontiers in Cell and Developmental Biology*. 2023;11:1208485.
- De Vitis C, Battaglia AM, Pallocca M, *et al.*; Mancini R; Biamonte F. ALDOC- and ENO2-driven glucose metabolism sustains 3D tumor spheroids growth regardless of nutrient environmental conditions: a multi-omics analysis. *Journal of Experimental & Clinical Cancer Research*. 2023;42(1):69.
- Battaglia AM, Chirillo R, Aversa I, *et al.*; Costanzo F; Biamonte F. Ferroptosis and cancer: Mitochondria meet the “iron maiden” cell death. *Cells*. 2020;9(6):1505.
- Sacco A, Battaglia AM, Botta C, *et al.*; Costanzo F; Biamonte F. Iron metabolism in the tumor microenvironment-implications for anti-cancer immune response. *Cells*. 2021;10(2):303.

4) Ferritin as a master regulator of redox balance, plasticity, and chemoresistance

A defining and continuous thread of my scientific trajectory is the functional dissection of ferritin heavy chain (FTH1) as a central hub integrating iron storage, redox control, cell fate, and therapy response in cancer. Long before ferroptosis emerged as a recognized form of regulated cell death, my work demonstrated that ferritin is not a passive iron buffer, but an active determinant of tumor cell identity and vulnerability. Using genetic silencing and functional reprogramming approaches across hematological and epithelial cancer models, we showed that FTH1 controls:

- Cell differentiation and lineage commitment, as demonstrated in K562 cells, where FTH1 silencing blocks erythroid differentiation via miR-150/GATA1 rewiring.
- Genome stability and proteostasis, revealing that ferritin depletion induces protein misfolding and stress responses detectable by Raman spectroscopy.
- Epithelial–mesenchymal transition (EMT) and migratory programs, through activation of the CXCL12/CXCR4 axis in ferritin-deficient cells.
- Cancer stem cell expansion, establishing ferritin as a negative regulator of ovarian cancer stemness and EMT.
- Chemotherapy response, showing that FTH1 modulates cisplatin sensitivity in ovarian cancer via ROS control and governs NF- κ B–dependent chemoresistance programs.
- Apoptosis execution by regulating the miR-125/p53 axis.

Selected publications

- Lobello N, Biamonte F, *et al.* Ferritin heavy chain is a negative regulator of ovarian cancer stem cell expansion and epithelial to mesenchymal transition. *Oncotarget*. 2016;7:62019-62033.
- Salatino A, Aversa I, Battaglia AM, *et al.*; Biamonte F. H-Ferritin affects cisplatin-induced cytotoxicity in ovarian cancer cells through modulation of ROS. *Oxidative Medicine and Cellular Longevity*. 2019;3461251.
- Aversa I, Chirillo R, Chiarella E, *et al.*; Biamonte F. Chemoresistance in H-ferritin silenced cells: The role of NF- κ B. *International Journal of Molecular Sciences*. 2018;19(10):2969.
- Zolea F, Battaglia AM, Chiarella E, *et al.*; Biamonte F. Ferritin heavy subunit silencing blocks erythroid commitment of K562 cells via miR-150/GATA-1 repression. *International Journal of Molecular Sciences*. 2017;18(10):2167.
- Aversa I, Zolea F, Ieranò C, *et al.* Epithelial-to-mesenchymal transition in FTH1-silenced cells: The role of CXCR4/CXCL12 axis. *Journal of Experimental & Clinical Cancer Research*. 2017;36(1):104.

- Zolea F, Biamonte F, Candeloro P, *et al.* H-ferritin silencing induces protein misfolding in K562 cells: A Raman analysis. *Free Radical Biology and Medicine*. 2015;89:614-623.
- Biamonte F, Zolea F, Bisognin A, *et al.* H-ferritin-regulated microRNAs modulate gene expression in K562 cells. *PLOS ONE*. 2015;10(3):e0122105.
- Di Sanzo M, Aversa I, Santamaria G, *et al.* FTH1P3, a novel H-ferritin pseudogene transcriptionally active and regulated during differentiation. *PLOS ONE*. 2016;11(3):e0151359.
- Zolea F, Biamonte F, Battaglia AM, *et al.* Caffeine positively modulates ferritin heavy chain expression in H460 cells. *PLOS ONE*. 2016;11(9):e0163078.
- Biamonte F, Battaglia AM, Zolea F, Oliveira DM, Aversa I, Santamaria G, Giovannone ED, Rocco G, Viglietto G, Costanzo F. Ferritin heavy subunit enhances apoptosis of non-small cell lung cancer cells through modulation of miR-125b/p53 axis. *Cell Death Dis*. 2018 Dec 5;9(12):1174. doi: 10.1038/s41419-018-1216-3.