NAME: ***MILILLO, CRISTINA***

POSITION TITLE: ***Scientific and Technical Specialist***

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
"G. d'Annunzio" University of Chieti-Pescara, Italy	Master's degree in Pharmaceutical Chemistry and Technology	10/2012	03/2019	Pharmaceutical and Toxicological Chemistry
"G. d'Annunzio" University of Chieti-Pescara, Italy	PhD in Earthquake and Environmental Hazards	11/2020	09/2024	Pharmacology and Toxicology
"G. d'Annunzio" University of Chieti-Pescara, Italy	Post-doctoral Research Fellow	03/2024	present	Pharmacology

A. Personal Statement

I am a Scientific Laboratory Technician (Category D) at the "G. d'Annunzio" University of Chieti-Pescara (Italy) in the Laboratory of Molecular Pharmacology and Pharmacogenetics (MPP-Lab), led by Prof. Patrizia Ballerini. My collaboration with the principal investigator's research team began during my PhD in Earthquake and Environmental Hazards, during which I worked on a project entitled *"Pulmonary toxicity of polystyrene nanoplastics in human bronchial epithelial cells grown at the air-liquid interface."* Throughout my PhD, I conducted research in collaboration with multiple groups at the Center for Advanced Studies and Technology (CAST) at the "G. d'Annunzio" University of Chieti-Pescara. Additionally, I spent four months at the Complutense University of Madrid, in the Department of Biochemistry and Molecular Biology, under the supervision of Prof. Eva Batanero Cremades. During this period, I developed experimental methodologies to investigate the toxic effects of nanoplastics in a 3D cell culture model at the air-liquid interface. Furthermore, in collaboration with Prof. Batanero Cremades, I established an experimental protocol for functionalizing nanoplastics with environmental biomolecules to study the toxicological impact of so-called *biocoronated* nanoplastics. The findings from this research are currently being compiled into a manuscript and were recently presented at the 42nd National Congress of the Italian Society of Pharmacology (SIF).

Moreover, during my PhD, I completed a two-week training period at the Eugenia Menni Center of Excellence (CREM), Fondazione Poliambulanza in Brescia, under the supervision of Prof. Ornella Parolini. There, I was trained in the isolation and culture of mesenchymal stem cells derived from full-term human placentas.

I am also a member of the research team at the Pharmacogenetics Unit at CAST, where we conduct diagnostic analyses to detect genetic polymorphisms in enzymes involved in the metabolism of chemotherapeutic drugs. Most recently, I was admitted to the School of Specialization in Biochemistry and Clinical Pathology at the "G. d'Annunzio" University of Chieti-Pescara.

During my scientific research career (2020–2024), I have published seven articles in international peer-reviewed journals, with approximately 70% as first or co-first author.

B. Positions, Scientific Appointments and Honors

- **2026 – Present** Scientific and Technical Specialist (Permanent Position), Department of Innovative Technologies in Medicine & Dentistry, "G. d'Annunzio" University of Chieti-Pescara, Italy
- **2024 – 2026** Postdoctoral research fellow, Laboratory of Molecular Pharmacology and Pharmacogenetics (MPP-Lab), Center for Advanced Studies and Technology (CAST), "G. d'Annunzio" University of Chieti- Pescara, Italy
- **2024 – Present** Clinical Pathology and Clinical Biochemistry specialist trainee, "G. d'Annunzio" University of Chieti-Pescara, Italy
- **2020 – 2024** PhD Student in Earthquake and Environmental Hazards, "G. d'Annunzio" University of Chieti-Pescara, Italy (Tutor: Prof. Ballerini)
- **2018 – 2019** Internship at Pharmaceutical and Toxicological Chemistry Laboratory ("G. d'Annunzio" University of Chieti-Pescara, Italy) for the thesis project "Synthesis of N-acylsulfonamide derivatives of fenofibrate inhibitors of carbonic anhydrase (Tutor: prof. Ammazzalorso)

C. Contributions to Science

My scientific production is documented by:

- **12 publications in Peer-Reviewed Journals**

Bibliometric indicators:

- Total citations: **179** ***(from Scopus)***
- H-index: **6** ***(from Scopus)***

LIST OF PUBLICATIONS

1. Milillo C, Falcone L, Di Carlo P, Aruffo E, Del Boccio P, Cufaro MC, Patruno A, Pesce M, Ballerini P. Ozone effect on the inflammatory and proteomic profile of human macrophages and airway epithelial cells. Respir Physiol Neurobiol. 2023, 307, 103979. (RESEARCH ARTICLE, FIRST AUTHOR)
2. Lanas A, Tacconelli S, Contursi A, Piazuelo E, Bruno A, Ronci M, Marcone S, Dovizio M, Sopeña F, Falcone L, Milillo C, Mucci M, Ballerini P, Patrignani P. Biomarkers of Response to Low-Dose Aspirin in Familial Adenomatous Polyposis Patients. Cancers (Basel). 2023, 15, 2457. (RESEARCH ARTICLE)
3. Bruno A, Milillo C, Anaclerio F, Buccolini C, Dell'Elice A, Angilletta I, Gatta M, Ballerini P, Antonucci I. Perinatal Tissue-Derived Stem Cells: An Emerging Therapeutic Strategy for Challenging Neurodegenerative Diseases. Int J Mol Sci. 2024, 25, 976. (REVIEW, CO-FIRST AUTHOR)
4. Patrignani P, Tacconelli S, Contursi A, Piazuelo E, Bruno A, Nobili S, Mazzei M, Milillo C, Hofling U, Hijos Mallada G, Sostres C, Lanas A. Optimizing aspirin dose for colorectal cancer patients through deep phenotyping using novel biomarkers of drug action. Front Pharmacol. 2024, 15, 1362217. (RESEARCH ARTICLE)
5. Milillo C, Aruffo E, Di Carlo P, Patruno A, Gatta M, Bruno A, Marinelli L, Dimmito MP, di Giacomo V, Paolini C, Pesce M, Ballerini P. Polystyrene nanoplastics mediate oxidative stress, senescence, and apoptosis in a human alveolar epithelial cell line. Front Public Health. 2024, 12, 1385387. (RESEARCH ARTICLE, FIRST AUTHOR)
6. Upadhyaya P, Milillo C, Bruno A, Anaclerio F, Buccolini C, Dell'Elice A, Angilletta I, Gatta M, Ballerini P, Antonucci I. Nicotine induced genetic and epigenetic modifications in primary human amniotic fluid stem cells. Curr Pharm Des. 2024, 30, 1995-2006. (RESEARCH ARTICLE, CO-FIRST AUTHOR)
7. Bruno A, Dovizio M, Milillo C, Aruffo E, Pesce M, Gatta M, Chiacchiaretta P, Di Carlo P, Ballerini P. Orally ingested micro- and nano-plastics: a hidden driver of intestinal inflammation and cancer. Cancers 2024, 16, 3079. (REVIEW)

8. Gatta M, Dovizio M, Milillo C, Ruggieri AG, Sallese M, Antonucci I, Trofimov A, Khavinson V, Trofimova S, Bruno A, Ballerini P. The Antioxidant Tetrapeptide Epitalon Enhances Delayed Wound Healing in an in Vitro Model of Diabetic Retinopathy. Stem Cell Rev Rep. 2025. (RESEARCH ARTICLE)
9. Recinella L, Acquaviva A, Bruno A, Ciaramellano D, Centulio AP, Dovizio M, Milillo C, Mozzon M, Generali D, Genovesi G, Orlando G, Chiavaroli A, Ferrante C, Ballerini P, Brunetti L, Leone S. Intestinal Protective Effects of a Pomegranate Peel Extract in In Vitro and Ex Vivo Studies. Int J Mol Sci. 2026 Feb 6;27(3):1603. (RESEARCH ARTICLE)
10. Dovizio M, Fink D, Gatta M, Bruno A, Milillo C, D'Ascanio F, Ameen F, Di Carlo P, Chiacchiaretta P, Lanuti P, Amedei A, Ballerini P. Micro-Nanoplastic Exposure and Lung Cancer Biomarkers: The Role of Extracellular Vesicle-Mediated Intercellular Communication. Int J Mol Sci. 2026 May 28;27(11):4887. (REVIEW)
11. Milillo C, Bruno A, D'Ascanio F, Gatta M, Battistelli M, Burattini S, Di Carlo P, Parrón-Ballesteros J, Niccolai E, Dovizio M, Lanuti P, Batanero E, Amedei A, Ballerini P. Polystyrene nanoplastics impair epithelial barrier establishment and modulate extracellular vesicle release in human bronchial cells cultured at the air-liquid interface. Toxicology. 2026 Jun 25;526:154533.doi: 10.1016/j.tox.2026.154533. Epub ahead of print. (RESEARCH ARTICLE)

PARTECIPATION IN INTERNATIONAL AND NATIONAL CONFERENCES

- Milillo C. Assessment of direct biomarkers of aspirin action to develop precision chemoprevention of colorectal cancer. Pescara Meeting 2022, Resolution of inflammation: mechanisms, mediators& biomarkers. May 8-10, 2022, Pescara. **(Oral Presentation)**
- Milillo C. Nicotine-induced genetic and epigenetic modifications in primary human amniotic fluid stem cells. 41° National Conference of the Pharmacology Italian Society. November 16-19, 2022, Rome. **(Poster Presentation)**
- Milillo C. Polystyrene nanoplastics mediate ROS production and apoptosis in A549 cell line. 16th Public Health Conference. November 9-11, 2023, Dublin. **(Oral Poster Presentation)**
- Milillo C. Pulmonary toxicity of polystyrene nanoplastics in human bronchial epithelial cell grown at the air-liquid interface. 42° National Conference of the Pharmacology Italian Society. November 13-16, 2024, Sorrento. **(Poster Presentation)**

TRAINING PERIODS

- **2022 –** One month at Institute E. Menni of Brescia (Italy) to acquire technical skills in the isolation of human amniotic mesenchymal stem cells
- **2023 –** Four months at Complutense University, Madrid (Spain), Department of Biochemistry and Molecular Biology (Tutor: Prof. Eva Batanero Cremades) during my PhD program to acquire technical skills in air-liquid interface (ALI) 3D-cellular models.

Main Scientific Interests:

During my PhD in *Earthquake and Environmental Hazards* at the "G. d'Annunzio" University of Chieti-Pescara, Italy, I conducted research at the Laboratory of Molecular Pharmacology and Pharmacogenetics (MPP-Lab), led by Prof. Patrizia Ballerini. My PhD project focused on investigating the toxic effects of micro- and nanoplastics (MNPLs) on the respiratory system.

The key findings of my research demonstrated that polystyrene nanoplastics (PS-NPs), which constitute over 5% of global plastic demand, can penetrate the cytoplasm of human lung adenocarcinoma cells (A549), leading to reduced cell viability, oxidative stress, cellular senescence, and apoptosis (*Milillo et al., Front Public Health. 2024; 12:1385387*). While this study provided valuable insights into the mechanisms of PS-NP toxicity in the respiratory tract, its reliance on submerged cell cultures posed limitations. To address this, I collaborated with the Complutense University of Madrid, where I spent a four-month training period to investigate the toxic effects of PS-NPs on bronchial adenocarcinoma cells (Calu-3) cultured at the air-liquid interface (ALI). This advanced 3D cellular model closely mimics the impaired airway epithelium. During this period, I also developed experimental

protocols for functionalizing nanoparticles with environmental biomolecules and assessing their toxic effects in a 3D bronchial cell culture model. My study revealed that PS-NP exposure reduced cell viability and disrupted epithelial integrity, suggesting that MNPL exposure may exacerbate pre-existing pulmonary conditions in compromised bronchial epithelium. These effects were associated with increased biogenesis and release of extracellular vesicles (EVs) from Calu-3 cells exposed to PS-NPs, indicating that MNPL-induced toxicity may be further modulated by EV biogenesis and release.

Furthermore, I contributed to the development of a rapid and efficient flow cytometry-based method for detecting MNPLs in various biological samples, including cell culture media, blood, and urine. This approach will be particularly valuable for testing the hypothesis that EVs derived from Calu-3 cells may act as carriers for MNPL transport and play a role in amplifying cellular signaling pathways.

My expertise in cellular and molecular biology—particularly in 3D cellular models that simulate impaired airway epithelium—along with my extensive experience in studying MNPL toxicity, will be instrumental in achieving the objectives of this research project.

Chieti, July 02nd, 2026