

NAME: **DOVIZIO, MELANIA**

POSITION TITLE: **Assistant Professor of Pharmacology**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
University Alma Mater Studiorum of Bologna, Italy	Bachelor's Degree in Biotechnology	10/2002	10/2005	Biology and Biotechnology
University Alma Mater Studiorum of Bologna, Italy	Master Degree in Medical Biotechnology	10/2005	12/2007	Biology and Biotechnology
"G. d'Annunzio" University of Chieti-Pescara, Italy	PhD in Medical-Surgical Sciences, Clinical and Experimental Science	01/2009	03/2012	Pharmacology
"G. d'Annunzio" University of Chieti-Pescara, Italy	Post-doctoral Research Fellow	10/2012	06/2017	Pharmacology

A. Personal Statement

Senior researcher in pharmacology at the Department of Innovative Technologies in Medicine & Dentistry, University "G. d' Annunzio" of Chieti-Pescara. Over 15 years of documented scientific research, I have developed advanced pharmacological research expertise, focusing on the biological mechanisms underlying tumor progression and metastasis. I concentrated my work on the interaction between platelets and tumor cells, exploring how platelet-derived molecules influence inflammation, invasiveness, and epithelial-mesenchymal transition (EMT) in cancer, with the final objective of developing biomarkers for tumorigenesis. I have collaborated with national and international universities and research institutions, producing over 80 peer-reviewed publications.

My professional journey has encompassed various academic and extra-academic roles, including my current position as a Research Assistant at "G. d'Annunzio" University of Chieti-Pescara, where I am also a member of the PhD program in Molecular Oncology and Tumor Immunology. My career has been enriched by numerous research projects funded by national and international organizations, including the Italian Association for Cancer Research (AIRC), the Italian Ministry of Education, University and Research (MIUR), and Cancer Research UK.

A key aspect of my expertise lies in precision medicine, which has been a central theme in my research. By identifying biomarkers linked to tumor progression and therapeutic response, I aim to personalize treatment strategies to individual patients. My research has explored the relationship between platelet-derived extracellular vesicles (EVs) and inflammatory conditions and cancer, providing insights into how these biomarkers can guide targeted therapies. Additionally, I have contributed to pharmacoepidemiology, leveraging real-world evidence to optimize drug therapies based on patient-specific factors such as genetics, environmental exposures, and medical history. In recent years, I have also directed my research towards environmental health hazards, studying the effects of micro and nanoplastics on human health, with a focus on toxicity mechanisms in the lungs and intestines. My research activity has been complemented by my commitment to education, where I have had the opportunity to mentor and guide young researchers and PhD students. I am also a reviewer for several international scientific journals, contributing to the quality and dissemination of academic research.

My career goal is to continue developing innovative cancer treatment and prevention approaches, with a particular emphasis on personalized medicine, leveraging biomarkers to improve therapeutic strategies and optimize pharmacological treatments.

B. Positions, Scientific Appointments and Honors

Positions

- **2024 – Present** Senior Research Assistant of Pharmacology, "G. d'Annunzio" University of Chieti- Pescara, Italy
- **2024 – Present** Member of Teaching and research staff of PhD program in Molecular Oncology and Tumor Immunology, "G. d'Annunzio" University of Chieti- Pescara, Italy
- **2021 – 2024** Project Manager at CliCon Società Benefit - Health, Economics & Outcomes Research, Bologna, Italy
- **2019 - 2020** Member of Teaching and research staff of PhD program in Medical Biotechnology "G. d'Annunzio" University of Chieti- Pescara, Italy
- **2017 – 2021** Young Research Assistant of Pharmacology, "G. d'Annunzio" University of Chieti-Pescara, Italy
- **2012 – 2017** Post-doctoral Research Fellow, "G. d'Annunzio" University of Chieti-Pescara, Italy
- **2009 - 2011 (11 months)** Visiting Scientist at the Institute of Pharmaceutical Chemistry, University of Frankfurt, Germany
- **2009 – 2012** PhD Student in Medical-Surgical Sciences, Clinical and Experimental Science, "G. d'Annunzio" University of Chieti-Pescara, Italy
- **2009 – Present** Member of Italian Society of Pharmacology
- **2008 - 2009** Pre-doctoral Research Fellow, "G. d'Annunzio" University of Chieti-Pescara, Italy
- **2007 (3 months)** Visiting Scientist at the Center for Molecular Biology and Neuroscience (Norwegian Centre of Excellence), University of Oslo, Oslo

Scientific Appointments and Honors

- **2009** Awarded for the best poster presented at the "XIII Seminar of PhD Students in Pharmacology and Related Sciences," Certosa di Pontignano, Siena, Italy, granted by the Italian Society of Pharmacology
- **2010** Winner of a research grant funded by the Abruzzo Region, P.O. F.S.E. Abruzzo 2007-2013
- **2010** Travel Award for participation in the "WorldPharma 2010" conference, Copenhagen, Denmark, granted by the Italian Society of Pharmacology
- **2011** Winner of a research grant funded by the Abruzzo Region, P.O. F.S.E. Abruzzo 2007-2013
- **2012** Travel Award obtained during the "14th Winter Eicosanoid Conference, Eicosanoid Research Association," Baltimore, USA
- **2013** Award for the best poster presented at the "Novel Drugs and Drug Targets to Treat Inflammation" meeting, Finnish Pharmacological Society, Ylläs, Lapland, Finland
- **2016** Winner of the "Gianesini Fund" Research Grant in Medical Sciences, funded by the Unicredit Foundation, Verona, Italy
- **2017** Winner of a "Research Grant for Individual Annual Funding of Basic Research Activities" funded by MIUR – Italian Ministry of Education, Italy
- **2018** Obtained the National Scientific Qualification (ASN) as Associate Professor in Pharmacology, awarded Italy by MIUR – Italian Ministry of Education, Italy
- **2018** Awarded with "Fondi di Ateneo ex 60%" Research Grant for the project "Identification of new eicosanoids-esterified in membrane phospholipids in the interaction between platelets and tumor cells: effect on epithelial-mesenchymal transition" funded by MIUR – Italian Ministry of Education, Italy

C. Contributions to Science

My scientific production is documented by:

- 92 publications in Peer-Reviewed Journals
- Complete List of Published Work in:
<https://pubmed.ncbi.nlm.nih.gov/?term=dovizio+m&sort=pubdate>

Bibliometric indicators (from Scopus):

- Total citations: **2594**
- H-index: **29**

Main Scientific interests:

My research has primarily focused on uncovering novel mechanisms of platelet-mediated tumorigenesis and metastatic spread. Specifically, I have explored how platelets interact with inflammatory and cancer cells, releasing molecules and extracellular vesicles (EVs) that induce phenotypic alterations in target cells. My work spans in vitro, in vivo, and ex vivo models, aiming to develop predictive biomarkers for disease progression and drug response in human patients. These efforts align with the goals of precision medicine, which seeks to tailor treatments based on individual molecular and cellular interactions driving disease. By identifying platelet-derived biomarkers and their role in tumor progression, my research contributes to the development of targeted therapies and personalized cancer treatments.

Over the past three years, I have also been involved in real-world evidence (RWE) studies, leveraging data from electronic health records, claims databases, and patient registries to assess drug effectiveness and safety beyond controlled clinical trials. My work in pharmacoepidemiology has provided critical insights into drug utilization and outcomes in large populations. Integrating these population-level findings with molecular pharmacology, which examines drug mechanisms at the cellular level, enhances our understanding of therapeutic effects and individual variability, further supporting precision medicine approaches.

Additionally, environmental health introduces a crucial dimension by investigating how pollutants, endocrine disruptors, and micro/nanoplastics (MNPLs) influence disease susceptibility, drug metabolism, and treatment response. Environmental toxins can alter drug efficacy through epigenetic modifications, oxidative stress, and chronic inflammation, underscoring the need for individualized therapeutic strategies. By integrating molecular pharmacology, pharmacoepidemiology, and environmental health, precision medicine can refine risk stratification, optimize treatment selection, and develop targeted interventions that consider genetic, molecular, and environmental determinants at both personal and population levels.

The main scientific fields, documented by published works, are reported below.

Dissecting the mechanisms of cell-cell interactions in cancer progression and inflammation

- Extensive evidence now highlights the pivotal role of epithelial-mesenchymal transition (EMT) as a key invasive property of tumor cells, driven by the tumor-associated microenvironment. As a key component of the blood, platelets—beyond their established functions in hemostasis and thrombosis—are increasingly recognized as potent activators of EMT and other pro-tumorigenic phenotypic changes in cancer cells. In this context, a significant portion of my work has focused on the interaction between platelets and cancer cells. I demonstrated that platelets can upregulate the expression of cyclooxygenase (COX)-2 and promote EMT in tumor cells, two molecular events that enhance metastatic and invasive potential. Additionally, I investigated the effects of various anti-platelet agents, including low-dose aspirin, on mitigating the pro-tumorigenic impact of platelets on colon cancer cells, employing both in vitro and in vivo models (J Pharmacol Exp Ther. 2012;341:242-50; Mol Pharmacol 2013, 84: 25-40; Biochem Soc Trans. 2015;43:707-14; Oncotarget 2016; DOI: 10.18632/oncotarget.8655; J Lipid Res. 2021;62:100109; Cancers 2023, 15, 350).

- In addition to COX-2, another crucial enzyme in tumorigenesis is microsomal prostaglandin E synthase-1 (mPGES-1), which is responsible for the synthesis of prostaglandin E2. I collaborated with Prof. Dieter Steinhilber (University of Frankfurt) on a project investigating the role of miR-574-5p and the CUGBP1 protein in regulating mPGES-1 expression in human lung adenocarcinoma cells (FASEB J. 2019; 33:6933-6947).
- Beyond its role in cancer, platelets also play a significant part in inflammatory processes. To further explore this, I contributed to the development of a mouse model with platelet-specific COX-1 deletion, effectively mimicking the effects of low-dose aspirin. Using this model in the context of dextran sodium sulfate (DSS)-induced colitis, we demonstrated that inhibiting platelet function was sufficient to alleviate colitis symptoms and prevent chronic inflammation and intestinal fibrosis (J Pharmacol Exp Ther. 2019; 370:416–426).

Development of innovative approach for the detection of circulating biomarkers in human health and disease

- One significant research focus I have pursued involves the development of biomarkers to predict the anti-tumor effects of low-dose aspirin, as demonstrated in clinical studies. In this context, I have contributed to the development of an analytical method utilizing liquid chromatography-mass spectrometry (LC-MS) to quantify COX-1 acetylation levels in platelets and other tissues. This method represents the sole direct biomarker of aspirin's mechanism of action (J Thromb Haemost 2014; 12:1320-30; Clin Pharmacol Ther. 2017; 102:52-61). The application of this biomarker in clinical studies will facilitate the elucidation of the relationship between aspirin use and its anti-tumor effects, thereby informing its potential role in cancer chemoprevention.
- Given that chronic administration of low-dose aspirin is associated with a reduced incidence and mortality of colorectal cancer, we hypothesized that aspirin may interfere with early stages of intestinal tumorigenesis through platelet inhibition. To explore this, I was involved in a clinical study on patients with familial adenomatous polyposis (FAP), where we found that colorectal adenomas are associated with increased platelet activation (J Pharmacol Exp Ther. 2012; 341:242-50). Furthermore, in a clinical study on individuals undergoing colorectal cancer screening while taking low-dose aspirin, my research contributed to demonstrating that the drug modulates phosphorylation of the S6 protein, a key regulator of protein synthesis and cell growth (Clin Pharmacol Ther. 2017; 102:52-61).
- Overall, these studies have reinforced the critical role of platelets in inflammation and tumorigenesis. In this setting, I have been involved in two research studies with the objectives of phenotyping platelet-derived EVs in obese individuals and colorectal cancer (CRC) patients. Since obesity is linked to platelet activation and a higher cancer risk, I investigated the potential contribution of platelet-derived EVs to this association. In a clinical study, I characterized platelet EVs isolated from obese and non-obese women, revealing that EVs from obese individuals exhibit more significant size heterogeneity; moreover, by performing a proteomic analysis, we found that platelet EVs from obese individuals carry proteins that promote both thrombosis and tumorigenesis. Notably, these EVs exhibited a stronger ability to induce EMT and endothelial-mesenchymal transition (EndMT) markers and COX-2 expression in tumor and endothelial cells. These findings suggest a possible mechanistic link between obesity, platelet activation, and increased cancer risk (Front Pharmacol 2019; 22,10:7). More recently, we tested the hypothesis that platelets can ingest circulating plasma molecules and, upon activation, release them in EV. Notably, EVs can transfer their molecular content to tumor cells, which acquire a migratory and, thus, pro-metastatic phenotype. By conducting clinical studies in CRC patients versus healthy controls, we found that the protein content of platelet thrombin-stimulated EVs is modulated in CRC. Its evaluation may represent a noninvasive tool for prognostic information on cancer patients, which could help develop an appropriate anticancer strategy (Cancers 2023, 15: 350).

Impacts of Micro- and Nanoplastics (MNPL) on Human Health

- During the last year, as a senior researcher, I worked on in vitro studies assessing the toxic effect of MNPLs on pulmonary human cells. Our research team recently demonstrated that polystyrene nanoparticles (PS-NPs) can penetrate human lung adenocarcinoma cells (A549), leading to reduced cell viability, oxidative stress, cellular senescence, and apoptosis (Front Public Health. 2024; 12:1385387). While this study clarified the mechanisms of PS-NP toxicity in the respiratory tract, it was limited by the use of submerged cultures. To address this, we assessed the toxic effects of PS-NPs on bronchial adenocarcinoma cells (Calu-3) grown at the air-liquid interface (ALI), a 3D-cellular model mimicking an impaired airway epithelium. Preliminary results showed that PS-NP exposure reduced cell viability and altered epithelium integrity, suggesting that MNPL exposure may exacerbate pre-existing pulmonary conditions. These effects were linked to increased biogenesis and extracellular vesicles (EVs) release from Calu-3 cells. Additionally, we developed a flow cytometry method to analyze MNPLs in biological samples, finding that Calu-3 cells in ALI conditions release EVs containing MNPLs, indicating that EVs may serve as MNPL carriers and amplify cellular signaling (preliminary unpublished data).
- Ingested MNPLs are toxic to the intestines and may increase CRC incidence by disrupting the colonic mucus layer, allowing MNPLs to enter the bloodstream and affect various organs. We recently reviewed the most updated literature to highlight the mechanisms of MNPL toxicity in both healthy individuals and those with compromised intestinal barriers, such as IBD and CRC patients (Cancers. 2024; 16:3079).

Pharmacoepidemiology and Real-World Evidence: analysing drug use and Outcomes in large-scale populations

- During my extra academic experience, I carried out pharmacoepidemiologic analysis and RWE studies across various therapeutic areas (i.e., oncology, cardiology, rheumatology). Pharmacoepidemiology leverages real-world evidence to study drug use and its effects in large-scale populations, providing critical insights into medication safety and effectiveness. By analyzing data from diverse sources such as electronic health records and patient registries, we identified patterns and outcomes that inform clinical practice (J Clin Med. 2022 Sep 30;11(19):5820; Nutrients 2023, 15, 336; Dig Liver Dis. 2023 Apr 24:S1590-8658(23)00568-6; Eur J Intern Med. 2023 May;111:90-96; Eur J Intern Med. 2024 Mar;121:88-94; Adv Ther. 2024 Jul 4; J Clin Med. 2024 Feb 27;13(5):1342). This approach is integral to precision medicine, as it helps tailor treatments to individual patient characteristics, improving therapeutic outcomes and minimizing adverse effects. Integrating real-world evidence with molecular data further enhances our understanding of drug mechanisms, paving the way for more personalized and effective healthcare solutions.

Participation in international and national conferences

I contributed as a speaker to 21 national and international conferences.

Participation in national and international research projects:

- **2008-2012:** *Staff Scientist* for a project funded by AIRC (Associazione Italiana per la Ricerca Sul Cancro) [Grant IG-1262, 2005-2007. **Project title:** "Determinants of colorectal adenoma recurrence in patients with FAP in response to celecoxib"].
- **2012-2014:** *Staff Scientist* for a project funded by AIRC (Associazione Italiana per la Ricerca Sul Cancro) [Grant IG-12111]. **Project title:** "Platelets in colorectal cancer development."
- **2013-2016:** *Staff Scientist* for a PRIN project, funded by Ministero dell'Istruzione, dell'Università e Della Ricerca (MIUR) [protocol number 2010FHH32M, 2010-2011, "G.d'Annunzio" University of Chieti-Pescara]. **Project title:** "A translational medicine research programme exploring early events in cancer development: the role of platelets in intestinal tumorigenesis."

- **2013:** *Staff Scientist* for a project funded by the pharmaceutical company Bayer Pharma AG. **Project title:** "Development of biomarkers of prostanoid inhibition using metabolomics and proteomics strategies"
- **2014:** *Staff Scientist* for a project funded by the pharmaceutical company Bayer Pharma AG. **Project title:** Aspirin and colorectal cancer prevention: exploring the platelet hypothesis of its mechanism of action"
- **2017-2020:** *Staff Scientist* for a project funded by AIRC, Associazione Italiana per la Ricerca Sul Cancro [Grant IG-20365]. **Project title:** "Extracellular vesicles in colorectal cancer: diagnostic and therapeutic implications."
- **2018-2020:** *Staff Scientist* for a project funded by Cancer Research UK Grant, AsCaP]. **Project title:** "Understanding the mechanisms of aspirin chemoprevention of cancer through population research".
- **2024-2025:** *Staff Scientist* for a project funded by "THE - TUSCANY HEALTH ECOSYSTEM", Piano Nazionale per la Ripresa e Resilienza (PNRR), emanato con D.D. n. 2004/2023 – Prot. 315887 del 22 dicembre 2023. SPOKE 3. Codice progetto ECS00000017. CUP B83C22003920001. PI: Rossella Grande, Co-PI Patrizia Ballerini, "G.d'Annunzio" University of Chieti-Pescara. **Project title:** "Microvescicole Batteriche: Implicazioni nella Fibrillazione Atriale" (MICROFIBRA)

Editorial Activity

Reviewer for the following peer-reviewed journals: Advances in Pharmacological Sciences, Annual Research & Review in Biology, Pharmacological Reports, Prostaglandins and Other Lipid Mediators, Molecules, Scandinavian Journal of Medicine and Science in Sports, Toxicology and Applied Pharmacology, Digestive and Liver Disease

2012: Co-author of the book chapter entitled "Mode of action of aspirin as a chemopreventive agent" book Prospects for Chemoprevention of Colorectal Neoplasia. Recent Results in Cancer Research, editori Chan A., Detering E, vol 191. Springer, Berlin, Heidelberg

2016: Co-author of the book chapter entitled "Acetylsalicylic acid as platelet aggregation inhibitor " book Pharmakon, editori Manfred Shubert-Zsilavec and Dieter Steinhilber

2017: Co-author of the book chapter entitled "La cascata dell'acido arachidonico" book Farmacologia Generale e Molecolare 5ed, editors Francesco Clementi e Guido Fumagalli.

Chieti, July 2nd, 2026

Rossella Grande