

BIOGRAPHICAL SKETCH

NAME: Giulia Bertolini

POSITION TITLE: Staff Scientist (Permanent position)

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Milan, School of Medicine and Surgery. Milan	Master degree in Medical Biotechnology	07/2005	Biology and Medical science
Open University PhD Course. Fondazione IRCCS Istituto Nazionale Tumori, Milan	PhD	06/2011	Translation Cancer Research/Cancer stem cells
Fondazione IRCCS Istituto Nazionale Tumori, Milan	Postdoctoral Fellow	12/2017	Cancer Stem Cell, Drug resistance, Circulating Tumor cells
Ministero dell'Università e della Ricerca. Italy	National Scientific Qualification for Blood diseases and oncology/General pathology and clinical pathology	09/2023	Oncology and Pathology

A. Personal Statement

My academic training and research experience have provided me with an excellent background in multiple biological disciplines including cellular biology, molecular biology and genetics. My main field of research study are Cancer stem cells (CSC) and Circulating Tumor Cells (CTC).

As an undergraduate, I conducted research in Prof Finocchiaro Lab (Neurological Institute C. Besta Milano where I got trained in main *in vitro* and *in vivo* techniques for the characterization of cancer stem cells (CSC). After receiving my Master's Degree in Medical Biotechnology in 2005 I joined the Unit of Epigenomics and Biomarkers of Solid Tumors at the Istituto Nazionale dei Tumori (INT), under the supervision of Dr Sozzi, where I started a new project aimed at characterizing lung CSC. My PhD project led for the first time to the identification of CD133+ chemoresistant CSC in human lung cancer (>600 citations) (1). My Postdoc project was mainly focused in the identification of possible new targets and therapy to specifically block the dissemination and metastasis initiation supported by CSC exploiting both clinical samples and patients derived xenografts models (2, 3). During the postdoc, I independently managed my work and obtained funding for my own salary by AIRC and Fondazione Veronesi, Cancer Research Foundations.

In 2014, I got trained in CTCs research at Prof. Caroline Dive's lab (Cancer Research UK Manchester), a world-renowned leader in CTCs field, supported by a travel fellowship from Accademia Nazionale dei Lincei. During my stay I was trained in forefront technologies for CTC isolation and single-cell NGS genomic profiling and I gave my contribution to the first study proving the tumorigenic potential of NSCLC-CTC (4). After the return at INT in 2015, I translated the acquired expertise into a novel research line aim at investigating CTCs heterogeneity in NSCLC. In 2018 I star my own group, funded by funded by "Roche per la Ricerca", with a project aim at studying the central role of the SDF-1/CXCR4 axis as mediator of chemotherapy-elicited metastasis (5, 6) and by Institutional funding that allows me to

optimize an innovative strategy for single-cell analysis of CTC(7). Data generated from these projects, were instrumental in winning “FRRB-Early career award” grant (2021-2024), aimed at monitoring circulating MICs in NSCLC patients receiving neo-adjuvant platinum-based chemotherapy for prognostic/therapeutic purpose.

Currently, I am also the Unit Coordinator of RF-2018 grant (PI Dr Vitale, San Martino-Genoa) focused on the study of the killing activity of NKs against lung MICs (8) and I was co-PI of RF-2016 (PI Dr Roz, INT-Milan), dissecting the cross-talk between MIC and tumor microenvironment, in particular cancer associated fibroblasts, in dictating lung cancer progression. During my career I supervised several young fellows and two ungraduated students, well as incoming PhD students from European research collaborators.

I am an Associate editor of the Journal of Translational Medicine and Advances in Cancer Biology and Metastasis. I am member of American, European and Italian association for cancer research and of Metastasis Research Society (MRI).

I am a member of the Communication Advisory Board at INT, whose goal is to improve and implement scientific communication between research groups, civil society and patients.

B. Positions, Scientific Appointments, and Honors

2024 Staff Scientist (Permanent position), IRCCS Istituto Nazionale dei Tumori, Milano

2018-Today Junior PI, IRCCS Istituto Nazionale dei Tumori, Milano

2017-2019 Postdoctoral Fellow of Fondazione Umberto Veronesi

2011-2013 Postdoctoral Fellow of AIRC-FIRC

Honors

Winner of ‘FRRB-Early career award 2020’

Recipient of Roche per la Ricerca’ 2018 grant

Recipient of Fondazione Umberto Veronesi Post-doctoral fellowship 2017 and 2018

Winner of 2nd prize ‘Marzia Galli Kienle-Associazione SOS- Solidarietà in Oncologia San Marco’ for the best papers published by young researchers in oncology field (October 2015).

Winner of AACR-SIC Scholar-in-Training Award (April, 2014).

Winner of Royal Society Fellowship of Accademia Nazionale dei Lincei (2014)

C. Contributions to Science

During my PhD project, we first reported, in a highly cited PNAS paper, the existence of a population of chemoresistant lung CSCs exploiting primary tumors and PDX models (1). Next, my postdoctoral projects led to the identification and characterization of lung CSCs subset responsible for metastasis initiation (2), their single-cell profiling to identify novel therapeutic targets (9) and on the use of novel CXCR4 inhibitors to counteract metastatic dissemination and paradoxical pro-metastatic effect of cisplatin (6). After the revolutionary advent of immunotherapy in the treatment of NSCLC, my research has also focused on the immunomodulatory capacity of CSCs and in particular on their differential interaction with NK cells that determines metastatic success (8).

In 20214 during my stay at Prof Dive’s Lab as a visiting fellow, I contributed to the study that for the first time demonstrated the tumorigenic potential of NSCLC-CTC (4). Once returned to INT, I optimized an innovative protocol for characterization of CTC at the single cell level exploiting cryopreserved PBMC, paving the way for CTC-based retrospective/multicenter studies(7). I’m currently leading clinical studies at INT aimed at evaluating at the single cell level the modulation of the CSC subset in the blood of patients with NSCLC and other solid tumors as a new biomarker to improve therapeutic outcome

Main Reference

1. **G. Bertolini et al.**, Highly tumorigenic lung cancer CD133+ cells display stem-like features and are spared by cisplatin treatment. *Proc Natl Acad Sci U S A* **106**, 16281-16286 (2009).
2. **G. Bertolini et al.**, Microenvironment-Modulated Metastatic CD133+/CXCR4+/EpCAM- Lung Cancer-Initiating Cells Sustain Tumor Dissemination and Correlate with Poor Prognosis. *Cancer Res* **75**, 3636-3649 (2015).

3. M. Moro, G. **Bertolini**, U. Pastorino, L. Roz, G. Sozzi, Combination Treatment with All-Trans Retinoic Acid Prevents Cisplatin-Induced Enrichment of CD133+ Tumor-Initiating Cells and Reveals Heterogeneity of Cancer Stem Cell Compartment in Lung Cancer. *J Thorac Oncol* **10**, 1027-1036 (2015).
4. C. J. Morrow *et al.*, Tumourigenic non-small-cell lung cancer mesenchymal circulating tumour cells: A clinical case study. *Annals of Oncology* **27**, 1155-1160 (2016).
5. C. D'Alterio, S. Scala, G. Sozzi, L. Roz, G. **Bertolini**, Paradoxical effects of chemotherapy on tumor relapse and metastasis promotion. *Semin Cancer Biol* **60**, 351-361 (2020).
6. **G. Bertolini** *et al.*, A novel CXCR4 antagonist counteracts paradoxical generation of cisplatin-induced pro-metastatic niches in lung cancer. *Mol Ther* **29**, 2963-2978 (2021).
7. M. Vismara, **Bertolini** *et al.*, Single-Cell Phenotypic and Molecular Characterization of Circulating Tumor Cells Isolated from Cryopreserved Peripheral Blood Mononuclear Cells of Patients with Lung Cancer and Sarcoma. *Clin Chem* **68**, 691-701 (2022).
8. M. Parodi, **Bertolini** *et al.*, Hybrid epithelial-mesenchymal status of lung cancer dictates metastatic success through differential interaction with NK cells. *J Immunother Cancer* **12**, (2024).
9. D. G. Rothwell *et al.*, Evaluation and validation of a robust single cell RNA-amplification protocol through transcriptional profiling of enriched lung cancer initiating cells. *BMC Genomics* **15**, 1129 (2014).

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/collections/mybibliography/>

and Scopus

<https://www.scopus.com/authid/detail.uri?authorId=26532426700>