

<b>Principal Investigator</b> BIANCHI FABRIZIO	
<b>Institute of Affiliation</b>	Fondazione Casa Sollievo della Sofferenza - I.R.C.C.S.
<b>Title of the proposed project:</b>	The Role of Non-coding RNA in Lung Cancer Progression and Chemo-Immunotherapy Response
<b>Short description of the project</b>	Lung cancer remains the leading cause of cancer-related mortality worldwide, largely due to disease progression and variable responses to systemic therapies. In recent years, chemo-immunotherapy has become a standard of care for many patients with locally-advanced and advanced non-small cell lung cancer (NSCLC); however, primary and acquired resistance remain major clinical challenges. Emerging evidence indicates that non-coding RNAs (ncRNAs), including microRNAs, play a central role in regulating tumor cell plasticity, immune evasion, and therapeutic response. This work explores the contribution of ncRNAs to lung cancer progression and response to chemo-immunotherapy through their dynamic interaction with the lung cancer transcriptome and the tumor immune microenvironment. We highlight how ncRNAs modulate key oncogenic and immune-related pathways, including interferon signaling, antigen presentation, immune checkpoint regulation, and cancer cell plasticity. In particular, ncRNA-mediated regulation of immune checkpoint molecules such as PD-L1 and interferon- $\gamma$ -responsive programs emerges as a critical determinant of immunotherapy sensitivity. By integrating bulk and single-cell transcriptomics, spatial profiling, and functional validation, this study aims to identify ncRNA-driven regulatory networks that underlie tumor evolution and therapy resistance. Understanding these mechanisms will provide a framework for the development of ncRNA-based biomarkers to predict response to chemo-immunotherapy and may uncover novel therapeutic vulnerabilities to improve clinical outcomes for patients with lung cancer. All research activities will be carried out at the Unit of Cancer Biomarkers, Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG), Italy.
<b>Main research area for the project</b>	Cancer biology
<b>5 key words for the project</b>	Immunotherapy, Lung ca., MicroRNA, Response and/or resistance to therapy, Functional genomics

<b>LAB INFO</b>	
<b>Main topic/s of the lab</b>	Lung Cancer basic and translational research
<b>Short description of the lab activity</b>	Our lab employs genomic, computational, and functional methods to study the lung cancer transcriptome, focusing on both coding (mRNA) and non-coding (microRNA) regions. Our goal is to identify biomarkers that can improve diagnosis and guide the selection of optimal therapeutics. In the post-genomic era, we are now able to analyze the molecular profiles of various cancer types. Using multi-omics approaches, we have discovered

	<p>that seemingly identical lung tumors can be distinguished by specific molecular features, known as molecular subtypes. These subtypes influence how the tumor responds to treatment and its potential for metastasis. Additionally, we have explored the circulating miRNome in the blood of lung cancer patients and identified valuable biomarkers for early diagnosis. Our findings also suggest that circulating microRNAs act as molecular messengers, transferring information between tumor cells and the tumor microenvironment (or vice versa), which plays a key role in lung cancer progression. Understanding both the coding and non-coding transcriptomes in lung cancer will undoubtedly facilitate earlier detection of tumor lesions and the development of more effective treatment strategies.</p>
<b>Recent bibliography</b>	<ul style="list-style-type: none"> <li>- Unveiling the origin and functions of diagnostic circulating microRNAs in lung cancer. BRIT J CANCER 2025 Jun; 132: 947</li> <li>- A plasma 9-microRNA signature for lung cancer early detection: a multicenter analysis. BIOMARK RES 2025 May; 13: 74</li> <li>- Aggressive early-stage lung adenocarcinoma is characterized by epithelial cell plasticity with acquirement of stem-like traits and immune evasion phenotype. Oncogene 2021 Aug; 40: 4980</li> <li>- miRNome profiling of lung cancer metastases revealed a key role for miRNA-PD-L1 axis in the modulation of chemotherapy response. J Hematol Oncol 2022 Dec; 15: 178</li> <li>- Functional analysis of the human miRNome in non-small cell lung cancer unveils a novel miR-92b-3p/NOTCH3 axis that drives tumor progression. CELL DEATH DIS 2026 Apr; 17:</li> </ul>
<b>Group composition</b>	<p>Our lab team currently employed 2 postdoctoral foreign researchers, 1 PhD student (wet lab) and 1 PhD student (bioinformatician), and 1 remote scientist (MD).</p>
<b>Institutional page link</b>	<p><a href="https://operapadrepio.it/it/">https://operapadrepio.it/it/</a></p>
<b>Lab website link</b>	<p><a href="https://www.cancerbiolab.com">https://www.cancerbiolab.com</a></p>
<b>Social media links</b>	<p><a href="https://www.linkedin.com/feed/">https://www.linkedin.com/feed/</a></p>