

PROPOSTA PROGETTUALE
DOTTORATO IN RNA THERAPEUTICS AND GENE THERAPY
CICLO XLI*

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TITOLO DEL PROGETTO: ENVIRONMENTAL POLLUTANTS AND LUNG DISEASE: THE EPIGENETIC ROLE OF MICRORNAS IN CHRONIC PULMONARY INJURY

Descrizione del progetto (max 300 parole)

Urban air pollution, particularly airborne particulate matter (PM), is a significant public health threat linked to the increasing incidence and severity of respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD), and idiopathic pulmonary fibrosis (IPF). Chronic exposure to pollutants like PM_{2.5}, cigarette smoke, heavy metals, and endocrine disruptors plays a critical role in the onset and progression of these diseases. While the epidemiological associations are well-established, the underlying molecular mechanisms remain insufficiently understood. Emerging evidence indicates that environmental pollutants can regulate gene expression via epigenetic mechanisms, particularly through the modulation of microRNA (miRNA) expression. miRNAs function as molecular sensors, translating pollutant exposure into persistent changes in gene expression. Dysregulation of specific miRNAs contributes to chronic inflammation, tissue remodeling, and the development of complex pulmonary diseases. This study aims to bridge environmental exposure data with biological insights by analyzing PM collected from urban districts with different pollution profiles. We will evaluate the chemical composition of the particles and their biological effects on respiratory epithelial cells, the primary interface between pollutants and host tissues. In vitro assays will assess cytotoxicity, inflammation, and miRNA expression changes, which may serve as early molecular markers for disease progression. Understanding how PM exposure alters miRNA regulation could reveal new insights into the molecular pathways driving chronic respiratory diseases. To establish a causal link between PM exposure, miRNA dysregulation, and disease, we will validate findings in experimental animal models of asthma and pulmonary fibrosis. These models will help determine whether miRNA modulation can mitigate PM-induced pathology, potentially leading to targeted therapeutic strategies. Ultimately, this research aims to uncover epigenetic mechanisms through which air pollution contributes to chronic lung diseases, offering insights that could inform future therapeutic approaches and public health policies to reduce the burden of urban pollution.

BIBLIOGRAFIA

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2. Sarah L O'Beirne, Sushila A Shenoy, Jacqueline Salit, Yael Strulovici-Barel, Robert J Kaner, Sudha Visvanathan, Jay S Fine, Jason G Mezey, Ronald G Crystal. Ambient Pollution-related Reprogramming of the Human Small Airway Epithelial Transcriptome. *Am J Respir Crit Care Med*. 2018 Dec 1;198(11):1413-1422.
3. Fabiana Furci, Alessandro Allegra, Alessandro Tonacci, Stefania Isola, Gianenrico Senna, Giovanni Pioggia, Sebastiano Gangemi. Air Pollution and microRNAs: The Role of Association in Airway Inflammation. *Life (Basel)*. 2023 Jun 12;13(6):1375.

FONDI

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***Per il dottorato in *RNA Therapeutics and gene therapy* selezionare anche una delle seguenti aree tematiche):**

- ☒ **Mechanisms of Diseases and Drug Target Identification**
- ☐ **Design and Delivery of New Gene Therapy and RNA-Based Medicines**
- ☐ **Validation and Safety In Preclinical and Clinical Studies**