

Master of Science in BIOMEDICAL SCIENCES
UNIVERSITÀ DEGLI STUDI DELL'INSUBRIA
Academic Year 2025/26

THESIS PROJECTS (I)

LABORATORIO DI FISILOGIA CELLULARE E MOLECOLARE

Prof.ssa Elena Bossi - Prof.ssa Cristina Roseti

JOIN US



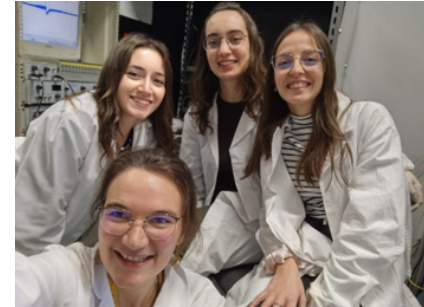
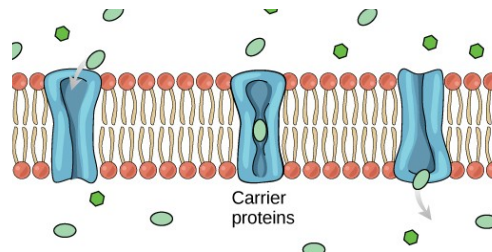
Main techniques

- Electrophysiology
- Molecular Biology
- Immunochemistry
- LC-MS/MS and HPLC

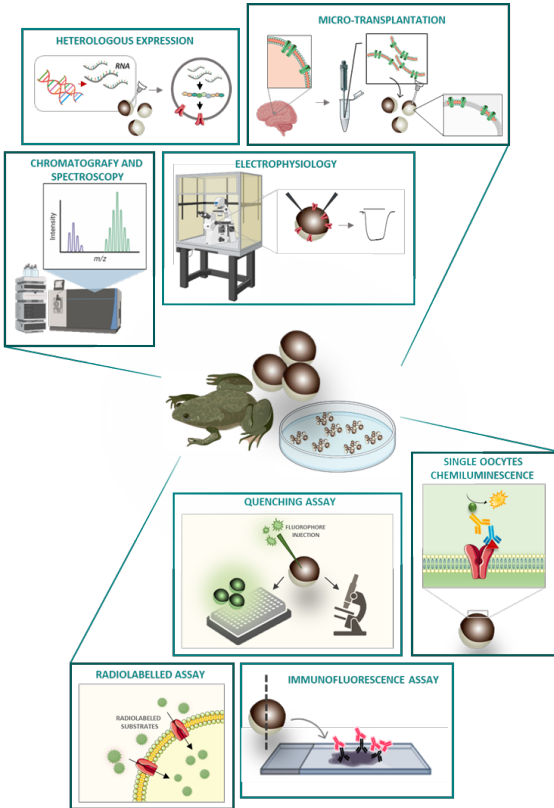
PROTEIN HETEROLOGOUS EXPRESSION IN *XENOPUS LAEVIS* OOCYTES

Biophysical study of
**Neurotransmitters
Transporters (NTTs)**

Analysis of **GAT1**
mutants linked to
**Neurodevelopmental
Disorders**



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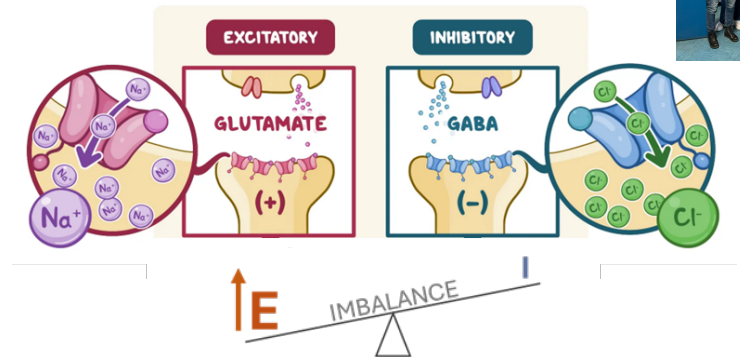
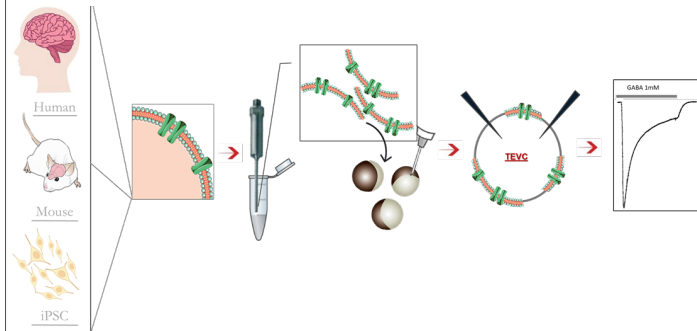


LABORATORIO DI FISILOGIA CELLULARE E MOLECOLARE

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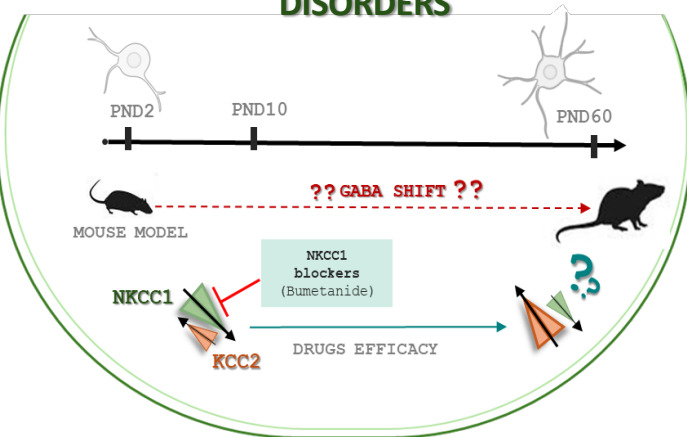


MICROTRANSPLANTATION TECHNIQUE



OVERVIEW OF CURRENT PROJECTS

1. GABA RECEPTORS IN NEURODEVELOPMENTAL DISORDERS



Investigate GABA immaturity across different developmental stages and brain regions

Test compounds that can rescue GABAergic defect.

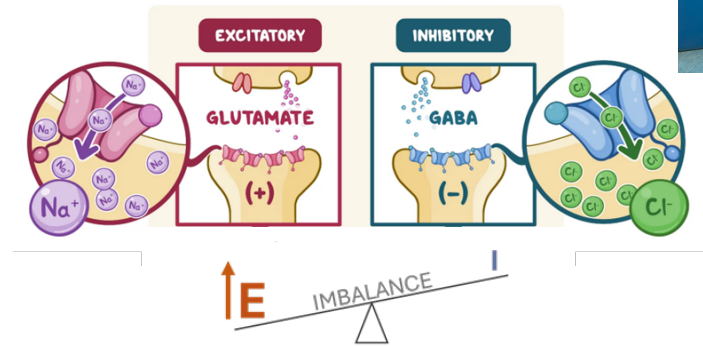
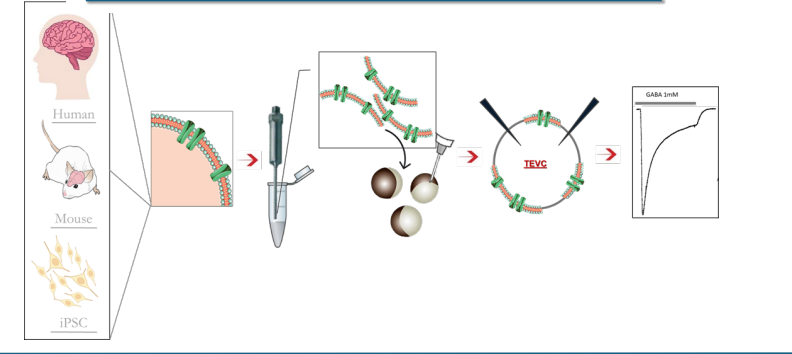
Contact: cristina.roseti@uninsubria.it

LABORATORIO DI FISILOGIA CELLULARE E MOLECOLARE

Prof.ssa Cristina Roseti – Prof.ssa Elena Bossi

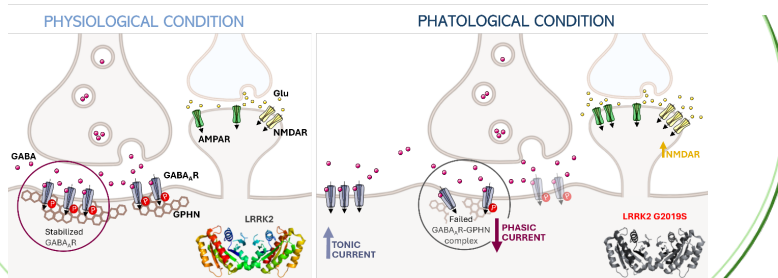


MICROTRANSPLANTATION TECHNIQUE



OVERVIEW OF CURRENT PROJECTS

2. GABA RECEPTORS IN LRRK2 G2019S –PARKINSON'S DISEASE



How does the LRRK2 G2019S mutation alter GABAergic inhibitory neurotransmission?

What is the link between LRRK2 and GABA_A receptor?

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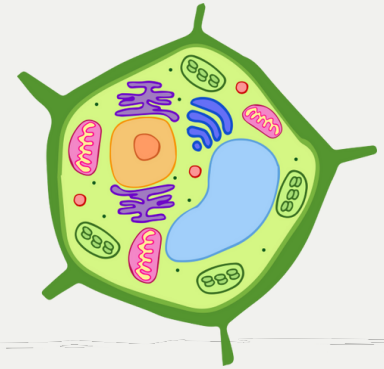
SEDE DI VIA J.H. DUNANT, VARESE

1 piano verde

Lab. BIOLOGIA CELLULARE

Rosalba Gornati, Roberto Papait, Christina Pagiatakis

- Studi sulla tossicità di nanoparticelle (nanotossicologia) utilizzando come modello cellule staminali mesenchimali. (Gornati)
- Studi sull'utilizzo di cellule staminali mesenchimali e dei loro derivati (secretoma e extracellular vesicles) in medicina rigenerativa. (Gornati)
- Il ruolo dell'epigenetica nell'invecchiamento. (Papait e Pagiatakis)



Tecniche utilizzate:

Tecniche di biologia cellulare e molecolare: estrazioni di cellule da tessuti, mantenimento di colture cellulari, estrazione di DNA e RNA, valutazione della citotossicità, retrotrascrizione, real-time PCR, western blot, clonaggi.

Preparazione di campioni per analisi epigenetiche (RNA-Seq, ChIP-seq-Chromatin Immunoprecipitation followed by Sequencing), microscopia ottica ed elettronica.

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christina.pagiatakis@uninsubria.it





Laboratory of Biochemistry and Functional Proteomics

Department of Science and High Technology (DiSAT)
via Manara 7 - Busto Arsizio (VA)



Prof. Tiziana Alberio
tiziana.alberio@uninsubria.it



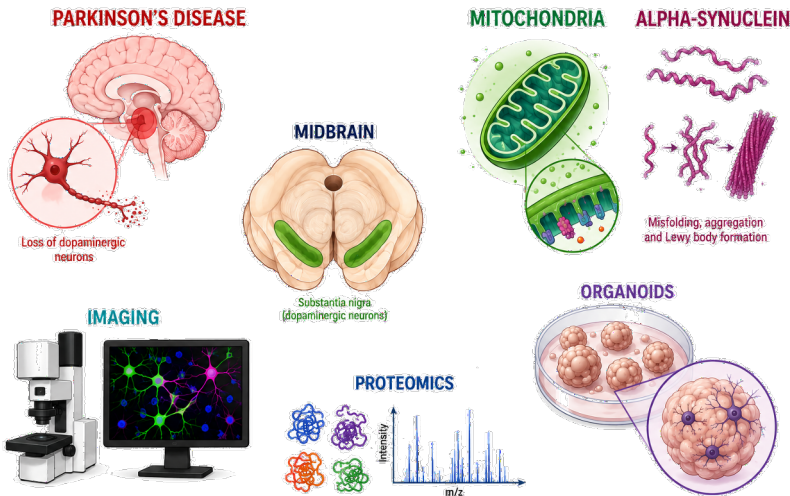
Dr. Marta Lualdi
marta.lualdi@uninsubria.it

Research Areas: Neurodegeneration, Mitochondrial Biology, Toxic Protein Aggregates, Vesicle Trafficking.

Methodologies: Biochemistry, Cellular and Molecular Biology, 3D Cultures, Proteomics, Systems Biology.

Thesis Project Opportunity:

Proteomics profiling of midbrain organoids to study Parkinson's disease (PD) pathways.



Midbrain organoids (**MOs**) represent an advanced, human-specific *in vitro* system that recapitulates the cellular architecture of the midbrain and allows for long-term modeling of disease processes.

The project aims to investigate PD-related pathogenic mechanisms by applying quantitative proteomics to human MOs derived from iPSCs of patients carrying α -synuclein (*SNCA*) mutations.

The work plan includes:

- i) generation of MOs;
- ii) morphological and molecular characterization of MOs by imaging and biochemical assays;
- iii) proteomics profiling of MOs;
- iv) functional analysis to identify dysregulated pathways.



Prof. Mauro Fasano
mauro.fasano@uninsubria.it

Research Areas: Neurodevelopmental Disorders (NDDs), Network Science

Methodologies: Systems Biology, Bioinformatics, Data Science, Machine Learning, Biostatistics, Coding

Thesis Project Opportunity:

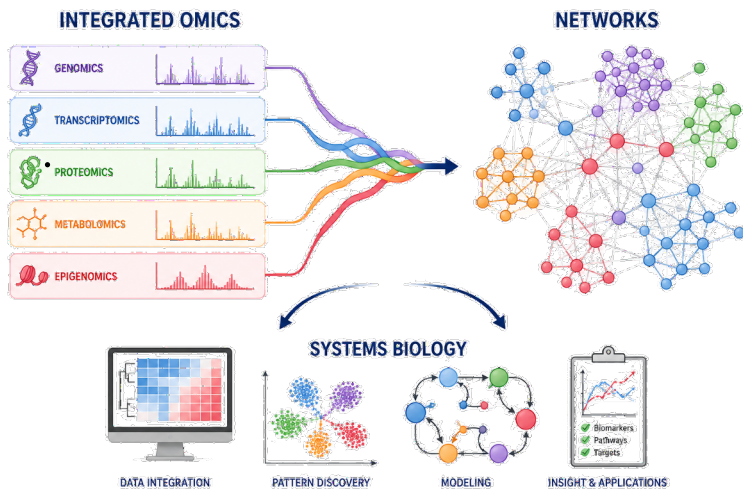
Neudig project

NDDs affect >3% of children worldwide, sharing overlapping phenotypes rooted in compromised brain development. With a genetic architecture spanning from highly penetrant rare/de novo monogenic variants and CNVs to common SNPs with small effects.

Despite advances in genome sequencing, many NDDs still lack an identified genetic cause, a gap this study addresses by discovering oligogenic patterns in NDD etiology.

What will you learn?

- Multi-omics data integration
- Network medicine approach
- Data analysis



Warm suggestion: attend the “Systems Biology” course! 😊

ZBTB18: a master tumor suppressor in glioblastoma

Background:

Glioblastoma (GBM) is the most malignant type of brain tumor characterized by a high recurrence rate and therapy resistance. GBM exists in 4 cellular states that are reminiscent of canonical neurodevelopmental cell types. In particular, the mesenchymal-like (MES-like) state has been associated with aggressive properties such as invasion, therapy resistance, and immune suppression.

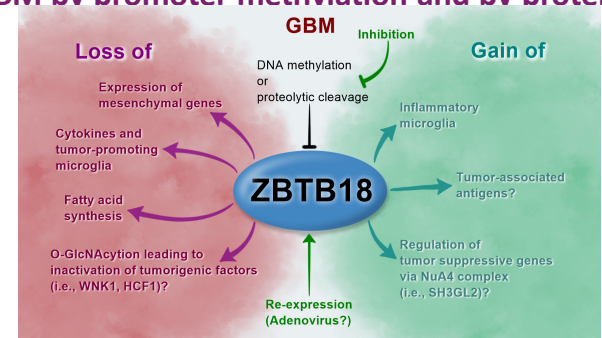
Research in my group focuses on the characterization of deregulated gene expression mechanisms in GBM, mainly associated with the upregulation of MES genes. We have previously pinpointed ZBTB18 as a transcriptional repressor of MES genes and a tumor suppressor in GBM. We discovered that ZBTB18 is negatively regulated in GBM by promoter methylation and by protein cleavage.

Ongoing projects of the group:

- *Role and significance of ZBTB18 interaction with the NuA4/TIP60 complex*
- *Regulation of ZBTB18 by protein cleavage and function of ZBTB18 cleaved fragments (Nte and Cte)*
- *Role of ZBTB18 in protein O-GlcNAcylation*
- *Role of ZBTB18 in antigen presentation and immune response*

Maria Stella Carro, PhD
Assistant Professor
Laboratory of General Pathology and Immunology "Giovanna Tosi"
Department of Medicine and Technological Innovation (DIMIT)
School of Medicine
University of Insubria

Email: mariastella.carro@uninsubria.it



Key publications:

- <https://www.nature.com/articles/s42003-024-07144-y>
- <https://www.life-science-alliance.org/content/lsa/6/1/e202201400.full.pdf>
- <https://www.sciencedirect.com/science/article/pii/S2589004222008975>
- <https://aacrjournals.org/mcr/article/15/8/998/267245/Epigenetic-Regulation-of-ZBTB18-Promotes>
- <https://www.nature.com/articles/nature08712>

MAIN RESEARCH TOPICS

1. Biology of Natural Killer (NK) cells and innate lymphoid cells (ILCs) in solid tumors (prostate, pancreas, colorectal, lung, kidney).
2. Stromal-immune cell interactions in solid cancers
3. Innate immunity and inflammation in cardiovascular diseases (atherosclerosis, diabetes).
4. Investigation of the tumor microenvironment and tumor angiogenesis as targets for therapy and prevention.
5. Role of pollutants in tumor insurgence, progression and response to therapies
6. Alarmins as immune-targets in cancer.
7. Cancer stem cells (CSCs).

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LABORATORY TECHNIQUES (Bruno-lab.)

Students joining in our lab. will have the possibility to acquire advanced theoretical and technical skills in the following experimental procedures:

- *Standard techniques in cell biology, molecular biology, biochemistry*
- *Isolation and maintenance of immune cells from peripheral blood and tissues (human and murine samples)*
- *Advanced multicolor flow cytometry (up to 18 parameters), cell sorting, and complex flow data analysis*
- *2D and 3D (spheroids, organoids, PDOTs) cell culture systems*
- *Murine models in oncology and immune oncology*

Students will have **full access** to our advanced flow cytometry facility, at IRCCS MultiMedica, under the supervision of the Facility manager and/or a researcher, equipped with:

- *BD FACS Canto II cell analyzer (3 lasers, 12 colors)*
- *BD FACS Fortessa x20 cell analyzer (5 lasers, 18 colors)*
- *BD FACS Aria Fusion cell sorter (3 lasers, 12 colors)*

N.B: Projects will be carried out at the Lab. of Innate Immunity IRCCS MultiMedica, Italy and Lab. of Translational Immunology (ongoing), University of Insubria, Busto Arsizio, Italy.

Hypothesis

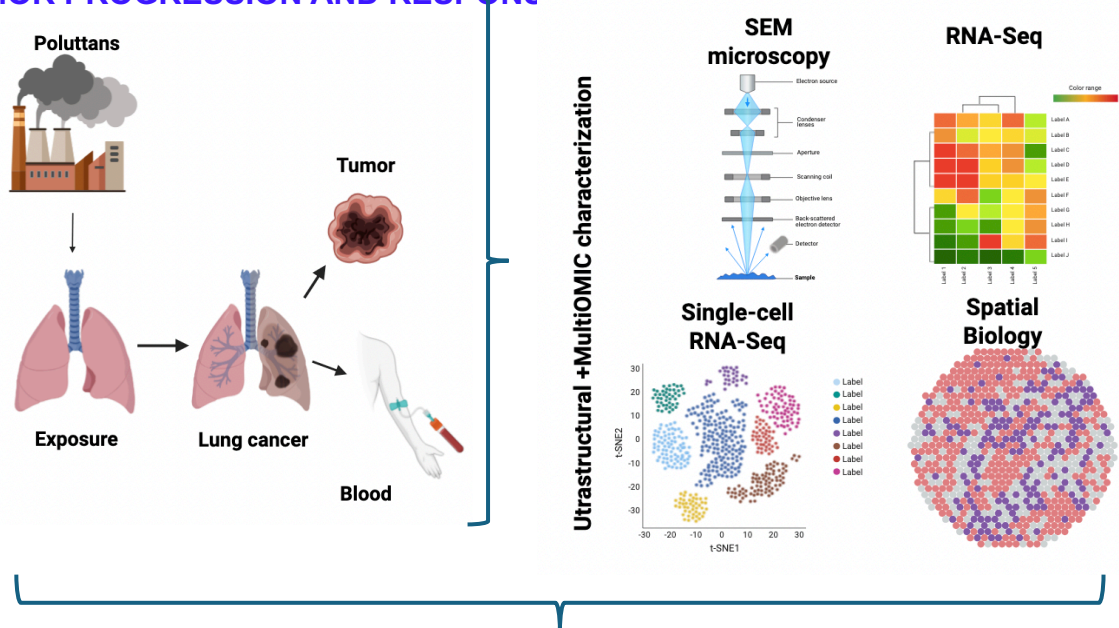
Exposure to air pollutants can generate an immune tumor microenvironment (TIME) potentially contributing to metastasis and response to (immuno)therapies

Aims

1-Assessment and evaluation of lung cancer (LC) risk biomarkers: impact of environmental pollutants on clinical parameters and immune system dynamics

2-Evaluation of differences in treatment response (e.g., immunotherapy) between patients exposed and not exposed to high levels of pollutants, to investigate the role of pollutants in treatment resistance

3-Deciphering immune cellular and molecular mechanisms of the metastatic lung cancer target organ(s) as permissive soil and in supporting resistance to immunotherapy in pre-clinical models



Response to

Chemotherapy

Immunotherapy

Chemotherapy + Immunotherapy



HYPOTHESIS

We hypothesized that **dissecting** the **tumor immune microenvironment**, both at **tissue** and **peripheral** levels, of lung **neuroendocrine** tumors, would impact on the **identification** of **immune-oriented mechanisms/targets** possibly involved in the induction and/or exacerbation of a neuroendocrine phenotype and tumor aggressiveness.

Type of study: Observational, prospective, multicentric (IRCCS MultiMedica, IRCCS Humanitas, ASST Settelaghi)

Population of interest:

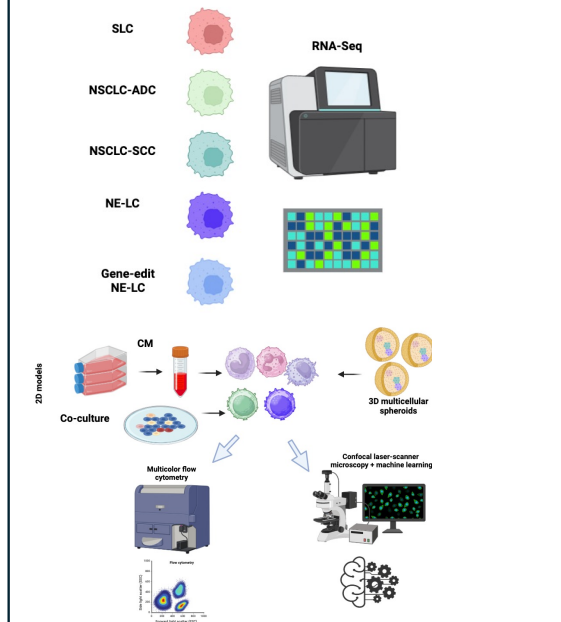
Patients with SLC, NSCLC (SCC and ADC), lung neuroendocrine carcinoids, patients with non-oncologic pulmonary inflammation (IPF or COPD)

Primary outcome: differences in NE-LC TIME Vs other lung cancers

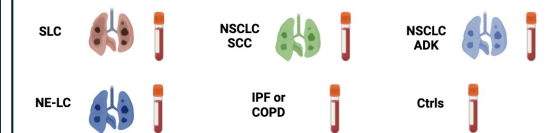
Secondary outcome: matching NE-LC circulating immune landscape with tissue NE-LC TIME

 Ministero della Salute Direzione generale della ricerca e dell'innovazione in sanità PNRR: M6/C2, CALL 2023 Full Proposal Project Code: PNRR-TR1-2023-12377350	 Finanziato dall'Unione europea NextGenerationEU Call section: Tumori Rari
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AIM1: Generation of in vitro models (2D and 3D) to investigate the mutual interactions between neuroendocrine lung neoplasms cell lines with different immune cells.



AIM2: Dissecting the immune landscape of the macro (tissue local) and micro (peripheral blood) environments in patients with lung neuroendocrine neoplasms.



Multimic integration analysis

- FACS (up to 20 parameters, simultaneously)
- Single cell RNA-sequencing
- Metabolomics
- Spatial Digital Transcriptomics (for tissue samples).

BRUNO-LAB DISSECTING THE ROLE OF NEUTROPHILS IN ATHEROSCLEROSIS (ATS)

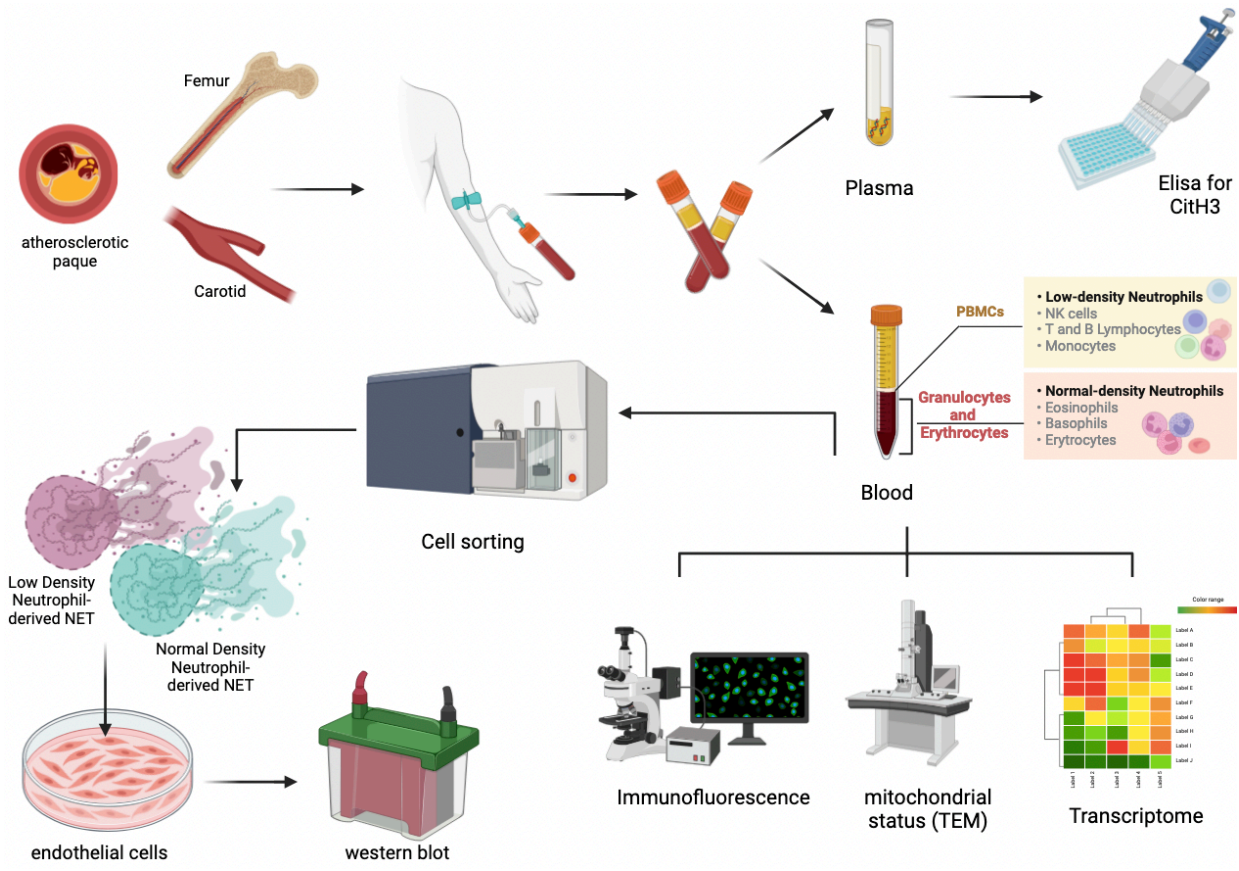


HYPOTHESIS

We hypothesized that based on the **phenotype** and **functional** alterations induced by the **ATS macro** (circulating) and **micro** (plaque) **environments**, neutrophils can participate to ATS progression and plaque outcomes

AIM

- Dissect the cellular, molecular and functional alterations governing neutrophil direct and indirect (via soluble factor) contribution to ATS progression
- Identify new neutrophils subsets as potential circulating biomarkers to trace ATS progression/evolution, by liquid biopsy approaches

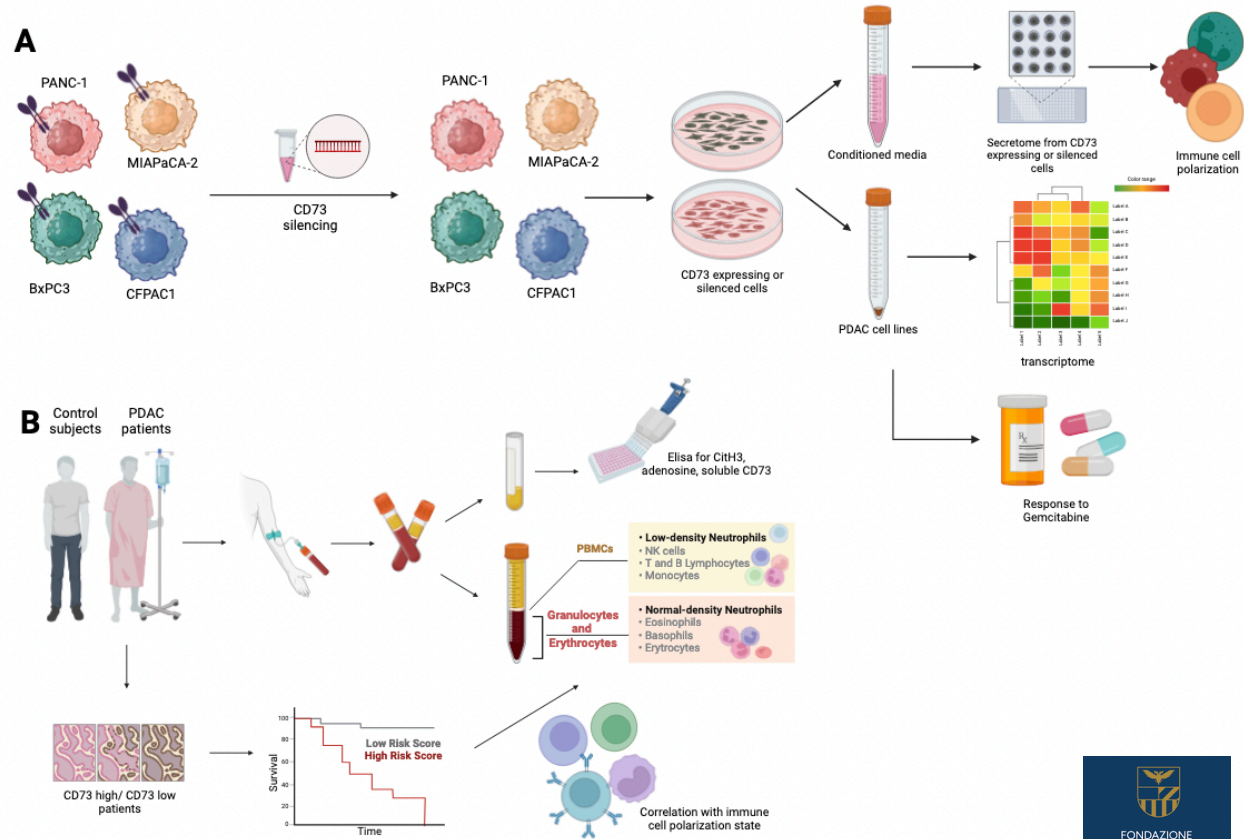


HYPOTHESIS

We hypothesized that **CD73 downregulation** on PDAC tumor cells could impact in reducing the generation of **pro-tumoral NK cells**, while **re-educating** NK cells to efficiently eliminate PDAC cells

AIMS

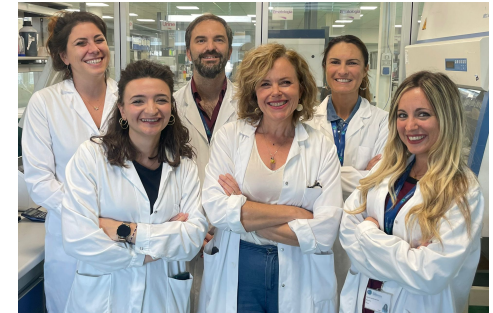
- Investigate how **CD73 KD** in PDAC cells **re-educate anti-tumor NK cells** via soluble factors or cell-to-cell contacts, by identifying the molecula drivers involved
- **Stratify PDAC patients** based on **CD73** circulating, tumor tissue levels, and **NK cell** anti-tumor/pro-tumor response.



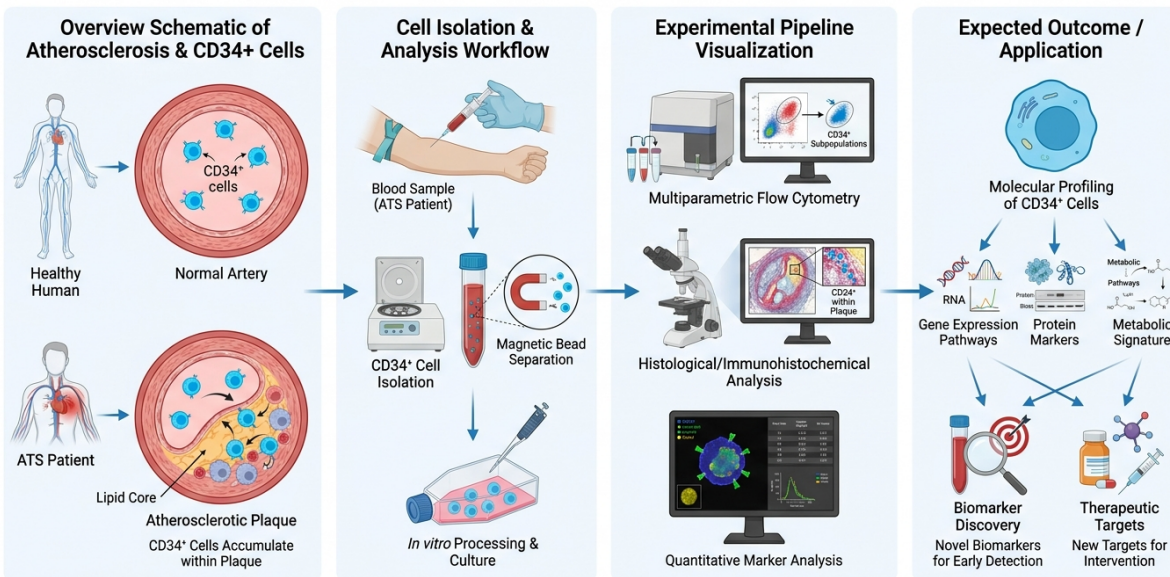
SPINETTI's LAB

Background. Atherosclerosis (ATS) is a chronic inflammatory disease. It is the major cause of myocardial infarction, stroke, and peripheral artery disease. CD34⁺ cells derived from the bone marrow are involved in ATS, in fact they are reduced in the blood of patients and found inside the atherosclerotic plaque. Despite their important role, an extensive characterization of these cells is still missing. Their molecular profiles would thus be the focus of this thesis.

The project will combine multiparametric flow cytometry with histological and immunoistochemical analysis of plaque features, to complete disease profiling through CD34⁺ cells characterization.



Molecular Characterization of CD34⁺ Cells in Atherosclerosis



Technologies:

- Primary Cell Isolation, processing and culture
- Multiparametric Flow Cytometry
- Histological and immunoistochemical analysis
- Tools for automated image analysis

Lab of Cardiovascular Pathophysiology-Regenerative Medicine

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PST MultiMedica

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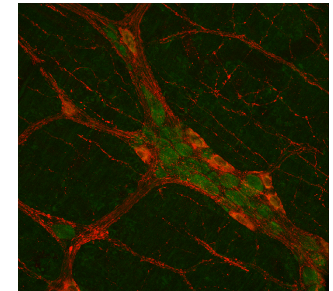
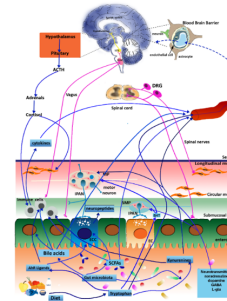


Ministero della Salute

UNIVERSITY OF INSUBRIA
DEPARTMENT OF MEDICINE AND TECHNOLOGICAL INNOVATION

DIGESTIVE SYSTEM PHARMACOLOGY
GROUP

Cristina Giaroni , Annalisa Bosi, Alessandra Ponti



The research activity of the group mainly focuses on the study of mechanisms regulating gastrointestinal function under physiological and pathophysiological conditions, with the aim of developing new pharmacological treatments or nutritional strategies. Our studies address the role of the enteric nervous system and its interactions with the different cellular components of the enteric microenvironment in the regulation of intestinal functions in preclinical disease models (e.g., inflammatory bowel injury, and irritable bowel syndrome). More recently, investigations have been expanded toward the study of the microbiota-gut-brain axis, including its impact on the central nervous system and its involvement in neuropsychiatric and oncological diseases. With this latter regard we are going to start a study on the role of diet in the development of early-onset breast cancer and the involvement of the microbiota-gut-breast-brain axis.

The applied methods consist in biomolecular approaches (qRT-PCR, Western blotting), ELISA assays, NGS sequencing, immunohistochemistry (HC on intestinal cross sections and IF on intestinal whole-mounts), pharmacological approaches (*in vitro* organ bath experiments on isolated intestinal segments and *in vivo* measurement of the efficiency of the intestinal transit), MRI imaging analysis of the gut wall (collaboration with the Department of Internal Medicine and Therapeutics of the University of Pavia), behavioural test (in collaboration with Prof Tiziana Rubino and Prof Erica Zamberletti)

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UNIVERSITÀ DEGLI STUDI DELL'INSUBRIA - DBSV
Lab. BIOLOGY OF INVERTEBRATES
Annalisa Grimaldi

<http://dipbsf.uninsubria.it/invertebrati/>; <https://www.ilfarm.it/>



Identification and characterization of inflammatory factors playing a key role in promoting a rapid tissue regeneration by establishing a functional cross-talk between inflammatory response and connective tissue remodelling process

Techniques used in the laboratory: optical microscopy, transmission and scanning electronics, immunohistochemistry, enzymatic histochemistry, Western blot, use of biopolymers for setting up cell cultures

Collaborations with:

Laboratory of human genetics, prof. Francesco Acquati, DBSV; Laboratory of microbiology, prof. Viviana Orlandi, DBSV; prof. Antonino Bruno, Lab. of Innate Immunity, IRCCS MultiMedica; Prof. Francesco Dondero, Department of Science and Technological Innovation, UNIUPO.

UNIVERSITÀ DEGLI STUDI DELL'INSUBRIA - DBSV

Laboratory of Molecular Neurobiology

Prof. Charlotte Kilstrup-Nielsen & Isabella Barbiero



Mutations in CDKL5 cause a severe neurodevelopmental disorder characterized by synaptic defects. In order to elucidate the underlying mechanisms and propose target-based therapies the focus of the laboratory is to study the role of CDKL5 in regulating mainly (but not only) inhibitory neurotransmission.

Project 1: Characterization of CDKL5 and InSyn1 interaction in Cdkl5-KO models.

CDKL5 has recently been shown to interact with InSyn1, which plays a key role in the formation of inhibitory connections through its association with the dystrophin-dystroglycan complex (DGC). The project aims to study the cross-talk between CDKL5 and InSyn1-DGC, thus shedding light on a critical aspect of inhibitory transmission. The student will use various biochemical approaches and immunofluorescent staining both in vitro (cellular and neuronal models) and ex vivo (mouse model) to characterize the interaction and the consequences of CDKL5 loss.

Project 2: Characterization of the overlap of networks belonging to CDKL5 and CDKL2.

CDKL2 is a poorly characterized kinase that has recently been shown to share at least one substrate with CDKL5. In this project, the student will use various biochemical and immunofluorescent approaches to 1) understand the functional overlap between the two kinases and 2) analyse how CDKL2 loss influences neuronal morphology and synaptic contacts. Proliferating cells, primary neurons and tissues from mouse models will be used.

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