PROJECT

Supervisor:	Prof. Marco E. Bianchi
Title:	*Origin and role of Cancer Associated Fibroblasts in Malignant Mesothelioma*
Curriculum:	BAIO
Link to the personal page of the University or relevant hospital site website:	https://www.unisr.it/docenti/b/bianchi-marco-emilio

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Malignant mesothelioma (MM) is a rare but aggressive cancer of body cavities; despite recent improvements, most patients survive < 2 yrs from diagnosis. New therapeutic opportunities are sorely needed, and research is focusing on targeting the MM microenvironment.

Cancer Associated Fibroblats (CAFs) are fibroblast-like cells that occur within many different tumors and contribute to their development. CAFs are abundant in MM and correlate with resistance to therapy and poor outcome. CAFs are generally considered to be non-tumor cells that are recruited from nearby tissues or bone marrow.

Rationale and hypothesis

Our central hypothesis is that tumor cells can transdifferentiate into Cancer-Derived Fibroblasts, which have the gene expression profile of fibroblasts but the genomic changes of tumor cells. Our preliminary data convincingly prove the existence of CDFs in MM patients.

Objectives and specific aims

- Aim 1, basic: consolidate the characterization of CDFs

- Aim 2, basic: understand the mechanism of CDF transdifferentiation and its generality in other tumors

- Aim 3, translational: understand the functional relevance of CDFs on patient outcome and therapeutic response.

Expected outcomes

We expect to understand:

1. whether CDFs contribute differently from "standard" CAFs to the development of MM, and therefore may represent both a disease marker and an additional therapeutic target,

2. how CDFs derive from tumor cells.

Skills that the student should acquire (max. 600 characters including spaces):

The student will acquire a set of project-specici skills and develop a set of soft skills.

Among project-specific skills:

- The ability to plan, execute, record and interpret results that answer specific questions

- Advanced cell culture techniques, including 3D cell cultures and organoids

- Advanced analytical techniques, including single-cell RNA sequencing and spatial transcriptomics

- Advanced statistical techniques

Among oft skills:

- Project management

- The ability to present scientific results to widely different audiences, from world leaders to the lay public, and in different formats, from elevator pitches to scientific papers, new projects and reports.

- The ability to effectively lead and educate more junior associates

References (max. 15)

Garcia-Manteiga JM, Rrapaj E, Caprioglio F, De Marchis F, Lamarca A, Colley LS, Carretta A, Finocchiaro D, Mercalli F, Molinario A, Arrigoni G, Boldorini R, Crippa MP, Mezzapelle R* and Bianchi ME* (*equal contribution) (2025) Fibroblast-like cells in mesothelioma can derive from tumor cells. Cell Death Diff, published online. doi: 10.1038/s41418-025-01639-9 PMID: 41402607