European School of Molecular Medicine

2025 summer call PhD selections

AVAILABLE POSITIONS

Principal Investigator	Marta Kovatcheva
Affiliation	IFOM ETS - The AIRC Institute of Molecular Oncology
Title of the proposed project:	Maladaptive cell plasticity in the progression from tissue injury to tumorigenesis.
Short description of the project	Recent work has illuminated that cell plasticity – long thought to be progressively restricted during development – is induced in many adult mammalian tissues as part of a conserved injury response. This involves the dedifferentiation of mature cells to more primitive states, allowing for regeneration of damaged tissue. However, cell plasticity also underpins tumorigenesis, yet the molecular details that distinguish beneficial, reparative cell plasticity from pathologic plasticity in cancer remain poorly understood. Our recent work has shown that 1-carbon (1C) metabolism plays a critical role in controlling cell plasticity by altering the methylation potential and epigenetic state of cells undergoing plasticity transitions. In this project, we will use 1C manipulation as a tool to study the epigenetic dynamics that underpin injury-induced intestinal cell plasticity and the consequences for homeostatic tissue function and the contribution of injury-induced plasticity to colorectal cancer. We will use a novel lineage tracing mouse model we have developed, which allows or the tracing of injury-induced epithelial cell plasticity. We will combine this system with murine models of ulcerative colitis and colorectal cancer, murine and patient-derived organoid systems, and state-of-the-art sequencing and proteomic technologies. Our results will significantly advance our understanding of injury-induced cell plasticity and have the potential to revolutionize therapeutic strategies for enhancing regenerative medicine.
Main research area for the project	Cancer Biology
Second research area for the project	Molecular and Cellular Biology
3 key words for project	cell plasticity, epigenetics, transformation
Main topic/s of the lab	Cell plasticity & Aging
Short description of the lab activity	The concept of "cell plasticity" refers to the capacity of a cell to adopt different identities without any genetic mutations. A classic example of cell plasticity occurs during development, when embryonic stem cells differentiate into the immense diversity of cell types we see in the adult body. It is now appreciated that cell plasticity also plays an important role in adult tissues, particularly in the context of injury and regeneration, where it is indispensable for tissue repair. However, cell plasticity is also a salient feature of cancer and can contribute to tumorigenesis, resistance to therapy, and metastasis. Our lab is interested in understanding and manipulating these dichotomous roles of cell plasticity. Our ultimate goal is to find

	ways to harness cell plasticity programs for enhanced tissue regeneration, and to control them in order to limit tumorigenesis, cancer progression, and relapse. To approach this, we use a combination of molecular and cell biology, and organoid models in vitro, in vivo mouse models, and next-generation sequencing technologies.
Recent bibliography	• DOI: 10.1038/s41418-024-01417-z • DOI: 10.1158/0008-5472.CAN-24-0529 • DOI: 10.1038/s44318-024-00259-2 • DOI: 10.1038/s41467-024-51363-0 • DOI: 10.1038/s42255-023-00916-6
Group composition	2 postdocs, 1 PhD student, 2 temp Fellows
Institutional page link	https://www.ifom.eu/en/cancer-research/programs/cell-plasticity-aging.php