European School of Molecular Medicine

2026 spring call PhD selections

AVAILABLE POSITIONS

Principal Investigator	FABIO GRASSI
Institute of Affiliation	INGM

PROJECT INFO	
Title of the proposed project:	Conditioning the gut ecosystem to enhance immune checkpoint blockade efficacy via enterotropic T cells
Short description of the project	The gut ecosystem conditions the outcome of cancer immunotherapy with checkpoint inhibitors (CPIs). Therefore, various approaches are exploited to condition it and improve the therapeutic efficacy of CPIs. We have shown that microbiota-derived extracellular ATP (eATP) limits the generation of secretory IgA (sIgA) in the ileum. We hypothesize that SIgA amplification by ileal eATP degradation beneficially conditions the gut ecosystem during treatment with CPIs and promote the generation of effective tumoricidal cytotoxic T cells that migrate to the tumor. The present project aims at: i) defining the TCR repertoire and functionality of tumor infiltrating enterotropic T cells. ii) defining bacterial species and metabolites responsible for the improved tumoricidal activity of tumor infiltrating T cells induced by SIgA amplification. iii) characterizing both phenotypically and functionally enterotropic CD8+CCR9+ CD8 T cells in oncologic patients treated with CPIs. iv) characterizing the transcriptional program and TCR clonality of patient-derived circulating CCR9+ T cells before and after immunotherapy. The PhD researcher will use mouse models of solid tumors to understand the impact of SIgA amplification within CPIs therapy on the intestinal ecosystem (e.g. microbiota composition and bacterial metabolites) and enterotropic T cells (e.g. phenotype, TCR repertoire and cell function) migrating to the tumor. The data will be correlated with circulating enterotropic T cells and fecal microbiota of patients treated with CPIs to identify intestinal mechanisms impinging on the therapeutic efficacy.
Main research area for the project	Cancer immunotherapy, mucosal immunity, microbiota
Second research area for the project	Transcriptomics and Metabolomics
3 key words for the project	Solid tumors, adaptive immunity, microbiota

LAB INFO	
Main topic/s of the lab	Immune system microbiota interaction
Recent bibliography	1. De Ponte Conti B. et al. Secretory IgA amplification during immune checkpoint blockade enhances the control of tumor growth by enterotropic T cells. *Science Advances,* 11: eaeb5308 (2025). 2. Perruzza L. et al. Protection from environmental enteric dysfunction and growth improvement in malnourished

	newborns by amplification of secretory IgA. *Cell Reports Medicine,* 5: 101639 (2024). 3. Perruzza L. et al. Postnatal supplementation with alarmins S100a8/a9 ameliorates malnutrition-induced neonate enteropathy in mice. *Nature Communications*, 15: 8623 (2024)
Institutional page link	https://ingm.org/en/
Lab website link	https://ingm.org/en/grassi-lab-2/