European School of Molecular Medicine

2026 spring call PhD selections

AVAILABLE POSITIONS

Principal Investigator	**MSSIMILIANO PAGANI**
Institute of Affiliation	IFOM-ETS

PROJECT 1 INFO	
Title of the proposed project:	Functional dissection of cerebral cavernous malformations epigenetic drivers using single-cell CRISPR screens.
Short description of the project	Cerebral cavernous malformation (CCM) is a rare genetic disease arising from loss of function mutations in any of the three CCM genes in endothelial cells, leading to the development of capillary-venous vascular abnormalities, primarily affecting the central nervous system. To date, no approved pharmacological therapies exist, and standard care involves surgical resection of accessible lesions and symptoms management. Our recent published and unpublished work has revealed that Polycomb factors play crucial roles in CCM pathogenesis, demonstrating that epigenetic factors may represent new vulnerabilities for CCM. In this project we plan to perform high-throughput CRISPR-based perturbation screens using mouse and human CCM disease-relevant models to systematically dissect the function of epigenetic regulators in cavernoma. Coupling CRISPR screen with single-cell RNA-seq will allow to link individual perturbations to transcriptional rewiring and cell state transitions, enabling the identification of epigenetic factors critical for CCM-associated phenotypic shifts.
Main research area for the project	Functional genomics
Second research area for the project	Epigenetics
3 key words for the project	Cerebral cavernous malformation; Epigenetics; Functional genomics

PROJECT 2 INFO	
Title of the proposed project:	Novel hypoxia-based regulatory T cell programs in tumor-immune communication
Short description of the project	Hypoxia responsiveness is conserved in principle, but nuanced in practice. The project involves the transcriptional and epigenetic characterization of the cell-type specific response of tumor-infiltrating regulatory lymphocytes to ubiquitous tumor hypoxia. Crucially, it aims to detail the mechanistic underpinnings of such response, which could provide a druggable alley to derail a tolerogenic axis crucial for tumor resistance to therapy.
Main research area for the project	Oncoimmunology
Second research area for the project	Epigenetics
3 key words for the project	Cancer, Immunosuppression, Hypoxia

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LAB INFO	
Main topic/s of the lab	Epigenetic and molecular characterization of the primary and metastatic tumor microenvironment
Short description of the lab activity	In recent years, the Pagani lab has leveraged single-cell and spatial omics technologies, alongside 3D organoid models, to investigate the tumor ecosystem and the molecular determinants of tumor dissemination. These approaches enabled high-resolution characterization of regulatory cell heterogeneity in tumors (Nat Immunology 2021), identification of a shared aberrant enhancerome sustaining cancer cell states (Nat Communications 2021), and contributions to mapping cell type–specific gene regulatory networks in human neuronal development (Science 2021). Ongoing studies on the enhancerome of tumor-infiltrating Tregs are revealing key regulatory nodes driving their hyperactivated phenotype (Dossena et al., under revision). More recently, the group has investigated cerebral cavernous malformations (CCM), identifying a role for Polycomb components BMI1 and EZH2 in reshaping the endothelial epigenetic landscape (Valentino et al., Circulation; Pham et al., EMBO Mol Med 2024). This research aligns with the lab's broader interest in epigenetic mechanisms underlying dysfunctional transcriptional programs in disease.
Recent bibliography	Caire R, Bordo R, … V, Pagani M*, Cordenonsi M, * Piccolo S*. A 3D morphogenetic blueprint for metastatic outgrowth in breast cancer. **Cell**. 2026 Mar 31:S0092-8674(26)00276-X. doi: 10.1016/j.cell.2026.03.009 * co-corresponding author M Valentino, Malinverno M, … Pagani M BMI1 inhibition improves lesion burden in cerebral cavernous malformations **Circulation** Doi: 10.1161/CIRCULATIONAHA.123.067438. Tonnelli M, Rossetti G, Pagani M Spatial profiling technologies connect topology to function in the tumor microenvironment **Trends in Cancer**, 2023 2023 Sep 4;S2405-8033(23)00164-4. Bonnal RJP, Rossetti G, Lugli E, De Simone M, … Abrignani S, Pagani M. Clonally expanded EOMES+ Tr1-like cells in primary and metastatic tumors associate with disease progression. **Nature Immunology**. 2021. https://doi.org/10.1038/s41590-021-00930-4 Della Chiara G, Gervasoni F, Fakiola M, Godano C, D'Oria C, Azzolin L, Bonnal RJP, Moreni G, Drufuca L, Rossetti G, … Piccolo S, Pagani M. Epigenomic landscape of human colorectal cancer unveils an aberrant core of pan-cancer enhancers orchestrated by YAP/TAZ. **Nature Communications**: 10.1038/s41467-021-22544-y. 2021.

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Group composition	The group comprises 18 members, including senior researchers, postdoctoral fellows, PhD and Master's students. PhD students receive day-to-day supervision from senior lab members and have regular opportunities to discuss their work during weekly meetings with the broader team and the PI.
Institutional page link	https://www.ifom.eu/it/
Lab website link	https://www.ifom.eu/it/ricerca-cancro/ricerca-lab/ricerca-lab-pagani.php