European School of Molecular Medicine

2026 summer call PhD selections

AVAILABLE POSITIONS

Principal Investigator	DAVIDE PRADELLA
Institute of Affiliation	Italian Institute for Genomic Medicine

PROJECT INFO	
Title of the proposed project:	Novel tools to model chromothripsis and cancer genome evolution
Short description of the project	The development of models to faithfully recapitulate human cancer has provided the ground for a better understanding of the molecular mechanisms regulating tumor initiation and progression. Among the different classes of chromosomal abnormalities, extrachromosomal circular DNAs (ecDNAs) are associated with tumor heterogeneity, genomic evolution, and therapeutic resistance. Notably, ecDNAs found in patients frequently arise following chromothripsis events and are often characterized by complex rearrangements. Currently, there is no model system that faithfully recapitulates their formation and contribution to tumorigenesis. This lack of models is relevant because chromothripsis and the presence of complex ecDNA are pan-cancer phenomena and associated with poor prognosis in adult and pediatric patients. The project focuses on the design of next-generation cancer models that recapitulate the complexity of the cancer genome and, in particular, on how catastrophic events like chromothripsis can promote tumorigenesis, tumor progression, and therapeutic resistance.
Main research area for the project	Cancer Biology; Genome engineering
Second research area for the project	Molecular and cellular biology
3 key words for the project	ecDNA; chromothripsis; cancer modeling

LAB INFO	
Main topic/s of the lab	Cancer genome evolution and dynamics
Short description of the lab activity	The lab has recently been established at the Italian Institute for Genomic Medicine and aims at developing novel tools and models to recapitulate the genomic complexity of cancer cells. We are particularly interested in how catastrophic processes, like chromothripsis, can shape the evolution of the cancer genome during the different steps of tumorigenesis. The lab takes advantages of CRISPR engineering tools to design innovative model systems to crack the biology of the functional products of chromothripsis events, including the formation of complex heavily rearranged extrachromosomal DNAs (ecDNAs). Our long-term goal is to identify novel vulnerabilities associated with these chromosomal aberrations and translate this knowledge to the development of more effective therapies for patients with aggressive ecDNA- and chomothripsis-driven tumors.

Recent bibliography	Pradella D, Zhang M, Gao R, Yao MA, Gluchowska KM, Cendon-Florez Y, Mishra T, La Rocca G, Weigl M, Jiao Z, Nguyen HHM, Lisi M, Ozimek MM, Mastroleo C, Chen K, Grimm F, Luebeck J, Zhang S, Zolli AA, Sun EG, Dameracharla B, Zhao Z, Pritykin Y, Sigel C, Chang HY, Mischel PS, Bafna V, Antonescu CR, Ventura A. Engineered extrachromosomal oncogene amplifications promote tumorigenesis. Nature. 2025;637:955-964. doi:10.1038/s41586-024-08318-8. Noorani I, Haughey M, Luebeck J, Rowan A, Grönroos E, Terenzi F, Wong IT, Pradella D, Lisi M, Kittel J, Sharma N, Bailey C, Weeden CE, Bell DM, Joo E, Barbè V, Jones MG, Hung KL, Nye EL, Green M, Meader L, Norton EJ, Fabian M, Kanu N, Jamal-Hanjani M, Santarius T, Ventura A, Nicoll JAR, Boche D, Chang HY, Bafna V, Huang W, Mischel PS, Swanton C, Werner B. Extrachromosomal DNA-Driven Oncogene Spatial Heterogeneity and Evolution in Glioblastoma. Cancer Discov. 2025;15:2078-2095. doi: 10.1158/2159-8290.CD-24-1555. Brückner L, Xu R, Tang J, Herrmann A, Wong IT, Zhang S, Tu F, Pilon M, Kukalev A, Pardon K, Sidorova O, Atta J, Yu Q, Pradella D, Ilić M, Marco-Novais-Cruz, Kaltenbach S, Treue D, Giurgiu M, Herzog S, Hollinger AS, Fernandez M, Becker F, Louma VR, Schmargon R, Dörr J, Gamlin D, Lehmann A, Gürgen D, Richter M, Dubois F, Simeoni F, Pennycook BR, Hamilton A, Lindemann RK, Fischer M, Bafna V, Wahl G, Koche RP, Chang HY, Papathanasiou S, Medema R, Spanjaard B, Ventura A, Pombo A, Huang W, Werner B, Mischel PS, Henssen AG. Oncogene Silencing via ecDNA Micronucleation. bioRxiv. 2025:2025.04.15.648906. doi: 10.1101/2025.04.15.648906.
Institutional page link	https://www.iigm.it/?lang=en
Lab website link	https://www.pradellab.it