European School of Molecular Medicine

2025 summer call PhD selections

AVAILABLE POSITIONS

Principal Investigator	Edoardo Scarpa
Affiliation	National Institute of Molecular Genetics (INGM)
Title of the proposed project:	A senescence-conditional therapy to precisely resect infected cells
Short description of the project	Pathogens represent one of the most significant selective pressures in human evolution. The co-adaptation between human hosts and their invading pathogens is reflected in the nowadays escalating emergency of antibiotic resistance (AMR), where the extensive abuse of antimicrobials has created a strong selective environment accelerating microbial resistance to antibiotics. There is indeed an urgent need to decipher the molecular basis of the host-pathogens interactions governing the AMR, with the perspective of finding definitive solutions to such dramatic problem. This project aims to understand how the presence of intracellular pathogens drives host cells towards a senescent phenotype, and how this is reflected in terms of infection spreading and AMR development. The molecular mechanistic involved will be methodically dissected by dual CRISPR wide genome screening on both the host cells and their invading pathogens. These will be coupled with trascriptomics (bulk and single-cell RNAseq) and metabolomics profiling to generate a detailed ATLAS of key proteins involved pathogens-induced cell senescence. Once validated, these targets will be used to guide the synthesis of infection-conditional PROTACs, namely molecules with activity restricted only to senescent cells harboring intracellular pathogens, thus minimizing off-target effects on healthy or uninfected cells. Advanced microscopy and cell-based assays will be employed to test the efficacy and specificity of these compounds in vitro, with the ultimate aim of demonstrating selective clearance of senescent, infected cells. By exploiting this precision degradation strategy, the project will open a new therapeutic avenue that targets bacterial pathogens indirectly by disrupting their intracellular niche, but that also contributes to the broader fight against AMR. This innovative PROTAC-based approach could represent a paradigm shift in antibiotic development, thus moving away from conventional broad-spectrum antimicrobials toward extremely highly targeted, context-specific, therapies.
Main research area for the project	Molecular Therapy
Second research area for the project	Molecular and Cellular Biology
3 key words for project	Cell senescence; infectious diseases; antimicrobial therapies
Main topic/s of the lab	Host-pathogens interactions; Precision therapies; antimicrobial resistance;
Short description of the lab activity	At the Infection Dynamics Lab, we study how pathogens cause disease by interacting with human cells at the molecular level. Our research explores all stages of infection, with a special focus

	on chronic infections. These are notoriously difficult to treat because the pathogens involved have evolved sophisticated strategies to evade the immune system and adapt to the host environment, making them resilient against conventional therapies. Our primary goal is to unravel the intricate mechanisms that allow pathogens to survive within the human body, bypass immune defences, and hijack normal cellular functions for their own benefit. To do this, we employ a broad spectrum of state-of-the-art experimental techniques that provide a detailed, multi-dimensional view of the infection process. For example, advanced microscopy enables us to observe the interactions between microbes and host cells in real time, at the single cell level. We use molecular biology tools to dissect the genetic and biochemical pathways involved in infection. Genomic approaches allow us to identify and manipulate key genes in both pathogens and host cells. This helps us pinpoint the molecular players critical for infection establishment and persistence. Additionally, biochemical assays provide detailed information about protein functions and interactions, shedding light on how pathogens alter host cell machinery to their advantage. By integrating data from these diverse methods, we can construct a comprehensive picture of the complex host-pathogen interplay. Our ultimate goal is not only to deepen scientific understanding, but also to translate these discoveries into practical solutions. By identifying crucial molecular interactions exploited by the pathogens, we aim to develop innovative therapies that specifically disrupt these processes. Such targeted interventions could be especially effective against persistent infections, which often resist current antibiotics and immune clearance. Our work could lead to the creation of novel treatment strategies that interfere with the pathogens ability to survive and replicate inside host cells. This approach represents a promising alternative to traditional broad-spectrum antibiotics, which can contribute to the development of antimicrobial resistance. Hence, we aim to minimize side effects and reduce the likelihood of resistance emerging by precisely targeting the molecular crosstalk between pathogen and host. In short, we are a team of scientists driven by curiosity and a commitment to innovation, working to understand the mechanisms behind infectious diseases and to turn that understanding into better, more effective treatments.
Recent bibliography	- Gazzaniga G. et al., Journal of Medicinal Chemistry (2025) - Degiacomi G. et al., International Journal of Antimicrobial Agents (2024) - Scarpa et al., bioRxiv (2024) - Griego et al., bioRxiv (2023) - Mori M. et al., Pharmaceutics (2023)
Group composition	11 members: 1 Associate Professor, 1 RTT, 1 RtdA, 2 postdoc, 2 PhD, 1 fellowship, 3 students

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Institutional page link	
Lab website link	https://infectiondynamics.unimi.it/