European School of Molecular Medicine

2025 summer call PhD selections

AVAILABLE POSITIONS

| Principal Investigator | Nicole Soranzo |
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| **Affiliation** | Human Technopole |
| **Title of the proposed project:** | Discovery and functional dissection of genetic targets of chronic human diseases through the lens of immunology |
| **Short description of the project** | Anchoring detailed molecular knowledge of disease processes to the diagnosis of chronic diseases using 'real-world' biomedical data remains an open challenge. This PhD fellowship is part of our ERC Advanced Grant-funded project IMPACT (Charting Immunological Maps of Populations through Complex Trait and Disease Trajectories). The main goal of this proposal is to study how aging of the human immune system contributes to the accumulation of chronic disorders in human populations. The project combines statistical modelling of single-cell genomic traits from diverse human populations with health data to define new models that can accelerate the early detection, prognosis, and treatment of chronic conditions.<br>Our group leverages the power of single-cell technologies alongside rich health records and large-scale population genomics to derive a list of germline variants associated with the deterioration of immune function throughout the human life course.<br>The student will be involved in designing and executing large-scale in vitro and ex vivo experiments with the following objectives:<br>(i) to systematically test the identity and function of genes associated with gene regulatory programmes relevant to human ageing and immune cell function using high-throughput CRISPR/Cas9-based screens in human embryonic stem cells (ideally targeting hundreds of genes);<br>(ii) to validate the primary identity of causal genetic variants through targeted variant engineering and tailored cellular functional assays in primary human haematopoietic stem cells. These assays may include cell differentiation and activation studies, chemotaxis assays cell cycle and apoptosis analysis, and colony formation assays, to evaluate the effects of gene knockouts on cell proliferation and self-renewal.<br>The outcome will be the development of a functional validation and characterization pipeline to assess the impact of genomic perturbations on immune functions. The project will involve training in a variety of techniques spanning cell culture, immunology, gene editing, and single-cell multiomic technologies. The student will benefit from close supervision by experienced senior scientists with expertise in genetics and genomics, CRISPR/Cas9, molecular haematology, and functional genomics. If desired, there will also be opportunities for training in computational biology. |
| **Main research area for the project** | Genomic Medicine |
| **Second research area for the project** | Molecular and Cellular Biology |

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| **3 key words for project** | Single cell genomics, immunity, ageing |
| **Main topic/s of the lab** | Investigating the impact of germline variation on complex phenotypes and diseases |
| **Short description of the lab activity** | Our group conducts large-scale genetic and genomic analyses to investigate how human genetic variation shapes complex traits, particularly those related to cardiometabolic, immune, inflammatory, and blood-associated conditions.<br>We use population-scale genomic and multi-omic approaches—including whole-genome sequencing, transcriptomics, epigenomics, metabolomics, and single-cell RNA sequencing—to map how genetic variation influences human phenotypes across molecular, cellular, and organismal levels.<br>Through our ERC Advanced Grant project *IMPACT*, we will undertake the largest exploration to date of how genetic, biological (e.g., age and population), and environmental factors interact to affect immune cell function. Our goal is to identify critical molecular signatures that distinguish healthy ageing from disease trajectories.<br>The overarching aim of our research is to uncover how genetic and environmental factors converge to predispose individuals to chronic conditions, and to develop predictive models using machine learning and AI to stratify disease risk and inform preventive strategies. This proposal will leverage and further develop new datasets integrating genomics with transcriptomics and epigenomics—at both bulk and single-cell resolution—to conclusively determine how genetic variants exert their effects across tissues and cell types, with a particular focus on blood and immune cells.<br>The research group combines cutting-edge computational analyses with state-of-the-art experimental capabilities. We are seeking a motivated and self-reliant student with prior expertise in one of the following areas: immunology, cancer biology, or haematology.<br>Previous experience with core experimental techniques in tissue culture and molecular biology is required. |
| **Recent bibliography** | • Guo J, Walter K, Quiros PM, Gu M, Baxter EJ, Danesh J, et al. Inherited polygenic effects on common hematological traits influence clonal selection on JAK2V617F and the development of myeloproliferative neoplasms. Nature Genetics. 2024;56(2):273-80.<br>• Tardaguila M, Von Schiller D, Colombo M, Gori I, et al. Integrating Natural and Engineered Genetic Variation to Decode Regulatory Influence on Blood Traits. bioRxiv 2024.08.05.606572.<br>• Kundu K, Tardaguila M, Mann AL, Watt S, et al. Genetic associations at regulatory phenotypes improve fine-mapping of causal variants for 12 immune-mediated diseases. Nat Genet. 2022 Mar;54(3):251-262.<br>• Bomba L , Walter K, Guo Q, Surendran P, et al. Whole-exome sequencing identifies rare genetic variants associated with human plasma metabolites. Am J Hum Genet 2022 Jun 2;109(6):1038-1054. |

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| | • Vuckovic D, Bao EL, Akbari P, Lareau CA, Mousas A, Jiang T, et al. The Polygenic and Monogenic Basis of Blood Traits and Diseases. Cell. 2020;182(5):1214-31.e11. |
| **Group composition** | 4 PhD students, 4 post docs, 1 senior bioinformatician, 1 senior research tech, 1 staff scientist + centre-wide scientific support units in genome analysis, cell screens and biostatistics. |
| **Institutional page link** | https://humantechnopole.it/it/gruppi-di-ricerca/soranzo-group/ |
| **Lab website link** | |
| **Social media links** | |
| **Video link** | |