RESEARCH TOPIC DASME15
Multi omics approaches for the development of predictive risk scores for common disorders

Curriculum DASME standard

Research Area
Neuro

Laboratory name and address
Lab of Medical Genetics & RNA biology
Via Rita Levi Montalcini, 4
20072, Pieve Emanuele (Milano), Italy

Datascience Supervisor
Letizia Straniero letizia.straniero@humanitasresearch.it

Research Supervisor
Rosanna Asselta rosanna.asselta@hunimed.eu

Abstract
Multi-omics approaches have the potential to revolutionize the study of complex diseases. By integrating data from different omics platforms, such as genomics, transcriptomics, proteomics, and metabolomics, researchers can gain a more holistic view of disease processes and identify novel biomarkers and therapeutic targets.
Objective: This research aims to leverage multi-omics integrated approaches to investigate the molecular underpinnings of complex diseases such as Parkinson's disease, prostate cancer, multiple sclerosis, primary biliary cholangitis (PBC), unexplained bleeding disorders (UBD), and COVID-19. By integrating genomics, transcriptomics, and methylome profiles, we seek to elucidate the intricate molecular networks and pathways involved in disease pathogenesis. Our ultimate goal is to identify predictive disease profiles that can serve as valuable diagnostic and prognostic markers, enabling personalized medicine approaches and targeted interventions for improved patient outcomes. A particular emphasis will be placed in order to dissect possible sex-related factors behind these disorders.
Approach: Through comprehensive multi-omics profiling, we will analyze diverse biological samples including blood, tissue, and bodily fluids obtained from both diseased and healthy individuals. Advanced bioinformatics tools and machine learning algorithms will be employed to integrate and analyze large-scale omics datasets, allowing for the identification of disease-specific biomarkers and molecular signatures. Cross-omics correlation analyses will provide insights into the complex interactions between different molecular layers and their contributions to disease susceptibility and progression.
Understanding the molecular heterogeneity and complexity of diseases like Parkinson's, prostate cancer, multiple sclerosis, PBC, UBD and COVID-19 is crucial for developing effective diagnostic

strategies and therapeutic interventions. By uncovering predictive disease profiles, this research has the potential to revolutionize clinical practice by enabling early detection, accurate risk assessment, and tailored treatment strategies. Moreover, the insights gained from multi-omics integration may uncover novel therapeutic targets and pathways for the development of precision medicine approaches in the fight against these debilitating diseases.

Main technical approaches

It is preferable, but not mandatory, that the candidate has already acquired experience in bioinformatics (use of bioinformatics pipelines for analysis of omics data).

Scientific references

Straniero L, Rimoldi V, Monfrini E, Bonvegna S, Melistaccio G, Lake J, Soldà G, Aureli M, Shankaracharya, Keagle P, Foroud T, Landers JE, Blauwendraat C, Zecchinelli A, Cilia R, Di Fonzo A, Pezzoli G, Duga S, Asselta R. Role of Lysosomal Gene Variants in Modulating GBA-Associated Parkinson's Disease Risk. Mov Disord. 2022 Jun;37(6):1202-1210. doi: 10.1002/mds.28987.

Severe Covid-19 GWAS Group. Genomewide Association Study of Severe Covid-19 with Respiratory Failure. N Engl J Med. 2020 Oct 15;383(16):1522-1534.

Paraboschi EM, et al. Rare variants lowering the levels of coagulation factor X are protective against ischemic heart disease. Haematologica. 2020 Jul;105(7):e365-e369.

Asselta R, Paraboschi EM, Gerussi A, Cordell HJ, Mells GF, Sandford RN, Jones DE, Nakamura M, Ueno K, Hitomi Y, Kawashima M, Nishida N, Tokunaga K, Nagasaki M, Tanaka A, Tang R, Li Z, Shi Y, Liu X, Xiong M, Hirschfield G, Siminovitch KA; Canadian-US PBC Consortium; Italian PBC Genetics Study Group; UK-PBC Consortium; Japan PBC-GWAS Consortium; Carbone M, Cardamone G, Duga S, Gershwin ME, Seldin MF, Invernizzi P. X Chromosome Contribution to the Genetic Architecture of Primary Biliary Cholangitis. Gastroenterology. 2021 Jun;160(7):2483-2495.e26. MS

Cardamone G, Paraboschi EM, Soldà G, Liberatore G, Rimoldi V, Cibella J, Airi F, Tisato V, Cantoni C, Gallia F, Gemmati D, Piccio L, Duga S, Nobile-Orazio E, Asselta R. The circular RNA landscape in multiple sclerosis: Disease-specific associated variants and exon methylation shape circular RNA expression profile. Mult Scler Relat Disord. 2023 Jan;69:104426.

Brief description of the coherence of the project in relation to the PNRR objectives

Our project proposal will be in line with the major objectives of the 2021-2027 National Research Programme, including:

Consequences and challenges of ageing. Genetic variation/methylome and transcriptome profiles contribute to individual risk for many complex diseases and is increasingly being used for predictive patient stratification. Our project will examine omics data on many different pathologies, including some that represent a socio-economic burden.

Advanced diagnostics and precision medicine. The P4 medicine (personalized, predictive, preventive, participatory) implies a deep understanding of inter-individual differences in health/disease that are due to genetic, epigenetic, and environmental factors. We aim to dissect molecular mechanisms behind different disorders, to reach the ultimate goal of changing treatment paradigms also by taking into account sex-related factors. Thus, it belongs to the field of gender medicine, defined by WHO as the study of how sex-based biological and gender-based socioeconomic and cultural differences influence people health.

In compliance with the principles of open science and FAIR data policy, all the data produced with this project will be deposited in ad-hoc data repository with dedicated accession numbers and associated with detailed metadata. The results of this project will be presented at national/international congresses and published in peer-reviewed open-access journals.
In addition, the proximity and full integration among Humanitas University, Humanitas Hospital and Humanitas Research Center, with access to state-of-the -art technologies (e.g. omics and bioinformatics), will provide the ideal environment for the successful completion of the PhD program.
All participants to this project will completely endorse and will be fully committed to PNRR priorities.

N. of months abroad
6 months, at Institute for Molecular Medicine Finland, University of Helsinki, Helsinki, Finland

N. of months of internship
6 months, at Bristol Myers Squibb, P.le dell'Industria, 40-46, 00144 - Roma

Type of contract
PhD scholarship of € 21.000 gross per year awarded by Humanitas University on PNRR funds under M.D.M. D.D. N. 630/2024 and cofounded by Bristol Myers Squibb.
This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

Borsa di dottorato pari a € 21.000 annui lordi erogata da Humanitas University su fondi da D.M. 630/2024 e cofinanziata da Bristol Myers Squibb.
Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.

This contract cannot be awarded to holders of a medical specialisation scholarship.