UNIVERSITÀ DEGLI STUDI DI MILANO-BICOCCA

DOTTORATO DI RICERCA IN Tecnologie Convergenti per i Sistemi Biomolecolari – XLII CICLO

Research Topic ID: XLII – 1.1

Project Tutor: Prof. Daniela Besozzi

Project Supervisor/s: Dr. Loris De Cecco (Fondazione IRCCS Istituto Nazionale dei Tumori di Milano), Prof. Fabio Stella (DISCo, Università di Milano-Bicocca)

Project Title: Development of computational methods for the identification of multi-exposure signatures in pediatric and AYA neoplasms

Scientific background & Objectives

Pediatric and adolescent and young adult (AYA) cancers, including brain tumours, neuroblastoma and colorectal cancer, are rare but increasing and represent a major cause of morbidity and mortality. Evidence suggests that only a minority of cases are explained by genetic predisposition, highlighting the potential role of environmental exposures such as air pollution, radiation, endocrine disruptors and socio-environmental factors. The objective of this project is to investigate how environmental exposures interact with genetic susceptibility across the life course, integrating epidemiological, multi-omic and socio-economic data to identify causal pathways and inform prevention strategies.

To this aim, we will exploit methods from computational systems biology and artificial intelligence to identify exposome-driven biomarkers across different cancer types and understand how multiple exposures contribute to cancer risk. The outcome of this project may lead to actionable strategies for personalized risk assessment and translational applications for precision interventions in pediatric and AYA cancer patients.

Project's Networks, Sustainability & Mobility

- Prof. Besozzi is PI of the "Computational Systems Biology" lab and has a longstanding expertise in the development of mathematical models, bioinformatics tools and artificial intelligence methods for the analysis of complex diseases and biomedical data. Dr. De Cecco is senior researcher at Istituto Nazionale dei Tumori, his research mainly focuses on the analysis of multi-omics data related to rare tumors (head-and-neck cancers and pediatric central-nervous-system neoplasms); his expertise includes the management and processing of bulk, single-cell and spatially resolved transcriptomics data.

Prof. Fabio Stella is PI of the "Models and Algorithms for Data and Text Mining" lab and has a longstanding expertise in the development of causal networks and Bayesian networks through the combination of domain knowledge and observational data.

The project will be carried out in collaboration with the "Integrated Biology of Rare Tumors Unit" of Istituto Nazionale dei Tumori, which will provide the biological and clinical data of pediatric and AYA patients, and will contribute to genomic, epigenomic and metagenomic analysis. The collaboration between Prof. Besozzi and Prof. Stella will support the

development of decision-making methods through expert knowledge modeling in clinical scenarios.

- Research articles by the proposers:

- Iannó, et al. A microRNA prognostic signature in patients with Diffuse Intrinsic Pontine Gliomas through non-invasive liquid biopsy. *Cancers* 14(17):4307, 2022.
- Cazzaniga P, et al. Fuzzy logic for knowledge-driven and data-driven modeling in biomedical sciences. In: Big Data Analysis and Artificial Intelligence for Medical Sciences (Carpentieri B, Lecca P. Eds.), Wiley, 17-41, 2024.
- Locatelli M, et al. Reinforcement learning and fuzzy logic modelling for personalized dynamic treatment. Proceedings of the 3rd AIxIA Workshop on Artificial Intelligence For Healthcare (HC@AIxIA 2024), CEUR WS 3880, 116-129, 2024.

- Putative foreign institution for ordinary mobility: Prof. Kristel Van Steen, University of Liège (Belgium) and Center for Human Genetics at KU Leuven (Belgium)