PHYSICIAN SCIENTIST
LA MEDICINA INCONTRA LA RICERCA
promosso da: AIRC Fondazione CARIPLO | con il supporto di: SEMM European School of Molecular Medicine | UNIVERSITÀ DEGLI STUDI DI MILANO

2026 Physician Scientist Call

AVAILABLE POSITIONS

Principal Investigator	**CAZZANIGA GIOVANNI**
Institute of Affiliation	Fondazione M. Tettamanti M. De Marchi Onlus
Title of the proposed project:	Predisposition to childhood acute lymphoblastic leukemia: from genes to families and back
Short description of the project	Childhood acute lymphoblastic leukemia (ALL) is the most common pediatric cancer. Although cure rates are exceeding 90%, the causes of the disease remain largely unknown, many children with clinical features suggestive of cancer predisposition still lack molecular diagnosis, and the biological significance of many rare germline variants remains unresolved. The granted IG project aims to elucidate the genetic and biological basis of predisposition to childhood ALL through integrated approaches. Within this context, the PhD candidate will: 1) investigate large national cohorts of pediatric ALL by integrating germline sequencing and somatic data to identify novel susceptibility genes, characterize rare pathogenic variants, and define genotype-phenotype correlations, with particular attention to variants of uncertain significance in DNA repair, cohesin genes and other regulators of hematopoietic development. 2) Selected variants will undergo functional validation using cellular models, genome editing, transcriptomic analyses and assays of genome stability. 3) A major objective for the MD-PhD candidate is the translation of research findings into clinical practice. Starting from the questionnaire collected from 1500 patients, the candidate will actively contribute to the multidisciplinary Childhood Leukemia Predisposition Clinic, participating in patient recruitment, genetic counselling and implementation of standardized workflows for germline testing, variant interpretation and surveillance of individuals at increased cancer risk. The project will ultimately contribute to improving diagnosis, patient management and family counselling while laying the foundations for future strategies of early detection and leukemia prevention. Through close interaction between laboratory research and clinical activity, the candidate will acquire multidisciplinary expertise in pediatric hematology-oncology, human genetics, functional genomics and translational medicine, preparing for an independent career as a physician-scientist in pediatric cancer predisposition. Clinical duties for the MD-PhD (ideally a Pediatrician) can be carried out at the Pediatric Hematology-Oncology Unit of Fondazione IRCCS San Gerardo dei Tintori, Monza.
Main research area for the project	Cancer biology
5 key words for the project	Pediatric tumors, Hereditary tumors, Acute Lymphoblastic Leukemia (ALL), Precancerous lesions, Prevention and/or chemoprevention

LAB INFO	
Main topic/s of the lab	Pediatric Acute Lymphoblastic Leukemia: from genetic predisposition to causes of pre-leukemia and evolution to blown disease.
Short description of the lab activity	The laboratory of Fondazione Tettamanti is an internationally recognized center for the study of genetics of childhood acute lymphoblastic leukemia (ALL). The Tettamanti Center is in the same building and tightly linked to the Pediatric Unit of Fondazione IRCCS San Gerardo dei Tintori, the teaching hospital of University of Milano-Bicocca, next door in Monza. As the national reference laboratory for molecular diagnostics and monitoring of pediatric ALL within the AIEOP network, the laboratory combines large-scale genomic analyses, functional genomics, and translational research to identify inherited factors contributing to leukemia susceptibility and disease evolution as well as somatic variants, mainly fusion transcripts, with a prognostic value and targeting. Research activities focus on the discovery and characterization of germline variants predisposing to ALL through whole-exome and whole-genome sequencing, integrated analysis of germline and somatic alterations, and investigation of gene–environment interactions. Particular attention is devoted to the identification and interpretation of variants of uncertain significance (VUS), with a focus on cohesin genes variants, the study of familial leukemia syndromes, and the elucidation of biological mechanisms underlying inherited susceptibility and evolution from pre-leukemia to blown disease. The laboratory has contributed to the identification of novel predisposition genes and pathways, including alterations affecting hematopoietic development, genome stability, and chromatin organization. Functional studies are performed using advanced cellular, molecular and in vivo models, including CRISPR/Cas9 genome editing, transcriptomic profiling, DNA repair assays, and patient-derived experimental systems, to generate evidence supporting variant pathogenicity and clinical interpretation. These activities are integrated with national and international collaborative networks, enabling translation of research findings into genetic counseling, surveillance programs, and precision medicine approaches for children and families at risk of leukemia. Of relevance, the PI is a founding and board member of the European Study Group on Minimal Residual Disease (EuroMRD), a member of the EuroClonality-NGS consortium and member of the Biology&Diagnosis Committee of the International BFM Study Group (I-BFM-SG), of which he is Chair of the Committee on Genetic Variation, focused on predisposition to leukemia. It also participates in the Biology Working Group of AIEOP and consultant of the AIEOP ALL Working Group. Through its extensive biobank, state-of-the-art genomic and proteomic platforms (NextSeq2000 and MiSeq, CyTOF XT, Seahorse XF, Luminex and Spark platforms, FACSs and sorter), and leadership in international pediatric leukemia consortia, the laboratory provides a unique environment for advancing knowledge on ALL predisposition and improving

	clinical management of hereditary leukemia risk. Fondazione Tettamanti is the research branch of the Fondazione Maria Letizia Verga ETS, which are highly integrated also in the dissemination activities.
Recent bibliography	- Potential role of STAG1 mutations in genetic predisposition to childhood hematological malignancies. BLOOD CANCER J 2022 Jun; 12: 88 - Diverse mechanisms of leukemogenesis associated with PAX5 germline mutation. LEUKEMIA 2024 Nov; 38: 2479 - Cohesins: Crossroad Between Cornelia de Lange Spectrum and Cancer Predisposition. AM J MED GENET A 2025 Aug; 197: e64076 - Overt and covert genetic causes of pediatric acute lymphoblastic leukemia. - Challenges in identifying paediatric cancer predisposition syndromes: international SCOPE survey and SIOPE expert consensus recommendations. EUR J HUM GENET 2026 Mar;
Group composition	The PI, head of the Research Unit on Genetics of Leukemia, supervises a multidisciplinary team consisting of: - 3 Project Leaders (senior PhD) - 5 Post-Doc (4 biotechnologists, 1 MD, pediatrician); - 4 PhD students (enrolled in the DIMET PhD program, Unimib) - 2 Research Fellow (MS in Biotechnology)
Institutional page link	https://fondazionetettamanti.it/
Lab website link	https://fondazionetettamanti.it/centro-di-ricerca/
Social media links	https://www.linkedin.com/company/fondazione-tettamanti-onlus/posts/?feedView=all&viewAsMember=true