Project Proposal

(*Instructions: this proposal will appear on the PhD webpage https://cqb.dieti.unina.it/ and will be forwarded to specialized sites. Please give a synthetic background and two to four research objectives. Include some information about the expected background of the candidate and relevant references. Please fill the part regarding the funding source/grants of the research activity needed for equipment, reagents, travels, conferences, traineeships etc.*)

Project Title

Project Description (*max 500 words*)

The aim of our research is to understand the complex interaction between inherited genetic variation and that acquired at the tumor level and therefore to understand its effect on carcinogenesis, tumor progression and on the response to therapy. To this end, we use next generation sequencing, GWAS, epigenomic data to decode the tumor genome and identify cancer genes, followed by functional genomic studies. Computational analyses of large genome datasets are used to unravel novel genetic mechanisms underlying carcinogenesis.

The main objectives of our research are:

1. Identification of inherited genetic variation that predisposes to the development of neuroblastoma through large-scale genome analysis. We apply computational analyses of whole exome sequencing data from a large set of patients with cancers and healthy controls to study the burden of pathogenic variants in genes of clinical importance.
2. Explore the role of somatic noncoding mutations affecting binding sites of transcription factor that are key regulators of neuroblastoma core regulatory circuitry by computational analysis of data from whole genome sequencing data and from methods to identify functional DNA elements such as ATAC-seq and HiC assays, assays of DNA methylation, and immunoprecipitation (IP) of proteins that interact with DNA and RNA, i.e., modified histones, transcription factors, chromatin regulators, and RNA-binding proteins, followed by sequencing.
3. Decipher how single-cell gene expression, before and after chemotherapy, affects survival, proliferation and therapeutic treatment response of neuroblastoma cells. We will apply algorithms on single cells RNAseq data from neuroblastoma resistant-cell to identify "causal genes" liable of neuroblastoma resistant-cell selection and survival.

Final goal of this project is to develop individualized care for children with cancer using genomic biomarkers that allow a precise risk stratification and the development a personalized treatment.

Supervisor(s), Lab/Group details, other additional info. (*please provide information about the group and available facilities*)

The major interest of the Supervisor is to study the genetic basis of cancer. His research interests are focused on translational genomics in pediatric cancers. He has the expertise in

the analysis of genomic data obtained by diverse methodological approaches such as SNP array, Gene Expression array, Next Generation Sequencing. He also has competence in the application of statistical methods to a wide range of topics in biology. It encompasses the design of biological experiments, the collection and analysis of data from experiments and the interpretation of the results. The Supervisor is currently the Head of the Bioinformatic Service for NGS at CEINGE Biotecnologie Avanzate.

Supervisor's Laboratory is located at CEINGE Biotecnologie Avanzate and his Group is composed of 3 Post-docs whom 2 bioinformaticians, 5 PhD students whom 2 bioinformaticians, 1 fellow and 2 ungraduated students. The team members have competences in different disciplines such as bioinformatics, functional genomics, molecular biology, and cancer genetics. The candidate will find a multidisciplinary environment and qualified team members for his / her training growth in bioinformatics, in genetics and biology.

The candidate should be motivated to acquire competences for the computational analysis of next generation sequencing, microarray, GWAS and epigenomic data but also acquire knowledge related to genetics and biology in order to achieve a complete training that will enable him / her to be able to perform bioinformatic analyses but also to interpret the results.

Funding (*how the reagents, equipments, conference and travelrs will be supported)*
1. 2019-2023: NIH, ID: R01 CA124709-06, (USA), Budget: 29,000 euro, Co-Investigator, "The Genetic Basis of Neuroblastoma Tumorigenesis".
2. 2021-2023: OPEN the Association of Pediatric Oncology and Neuroblastoma, Budget: 285,000 €, Principal Investigator, " Five hundreds CHildren with cANCErs (CHANCE): Unravel the panorama of genetic inheritance in childhood cancer to facilitate the development of personalized treatments ".
3. 2018-2022: Ministry of Health, GR-2016-02364546 Budget: 82,500 €, Co-Investigator, "Advanced therapeutic medicinal product based on CD30-specific chimeric antigen receptor (CAR) T cells for treatment of patients with relapsed / refractory CD30 + lymphomas ".
4. 2022-2024: Italian Foundation for the Fight against Neuroblastoma, Budget: € 281,000, Principal Investigator, " Discover the genetic predisposition of neuroblastoma to improve diagnosis and treatment (GENEDREN)".
5. 2020/2023: PRIN, Budget: 110,000 €, Co-Investigator. "Morphological biomarkers for early diagnosis in oncology – MORFEO"
6. 2022/2026: AIRC (ID 25796), Budget: 485,000 €, Principal Investigator. "Noncoding regulatory mutations as driving event for the oncogenic core regulatory circuitries of neuroblastoma"

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7. Lasorsa VA, Formicola D, Pignataro P, Cimmino F, Calabrese FM, Mora J, Esposito MR, Pantile M, Zanon C, De Mariano M, Longo L, Hogarty MD, de Torres C, Tonini GP, Iolascon A, Capasso M. Exome and Deep Sequencing of Clinically Aggressive Neuroblastoma Reveal Somatic Mutations That Affect Key Pathways Involved in Cancer Progression. Oncotarget. 2016 Apr 19;7(16):21840-52.
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