*Al collegio docenti del Dottorato in Medicina Molecolare*

**Dr.ssa**: Ester Cifaldi

**Ciclo**: XXXVII

**Tutor**: Prof. Alberto Magi

**Scientific report (1st year of PhD Fellowship), academic year 2021/2022**

***Introduction***

Epilepsy accounts for a significant proportion of the world's disease burden, affecting around 50 million people worldwide. Focal epilepsy (FE), characterized by seizures initiating in spatially limited cortical networks, accounts for 2/3 of epilepsy cases. More than 1/3 of FE patients are drug-resistant. FE is often caused by structural brain lesions, particularly Focal Cortical Dysplasias (FCDs) type I and II. The origin of epilectic crises is largery unexplained and epilepsy surgery is the best option to achieve seizure freedom. However, post-surgical lesion remnants are significant risk factors for seizure recurrence. The identification of early genetic markers is still unknown but it can have implication in the diagnostic and theraupetic management of these patients. With the advent of next generation sequencing (NGS), new genetic causes have been implicated in FE patients but with poor long-term real impact of FE-related genes. To date, the genetic diagnostics are still not routinely performed and exhaustive reports on genetic cases undergoing epilepsy surgery are limited, sometimes without follow-up data. The spectrum of germline and somatic variants related to phenotypic and histopathological differences between genetic patients remains something to be explored. In particular, the role of somatic variants seems crucial to determine the severity of phenotype, histology and surgical outcome.

***Methods and results***

We aim to perform NGS gene panels on various tissues of drug resistant FE patients: we extracted genomic DNA from blood, fresh frozen brain specimens, formalin-fixed paraffin-embedded tissues. Using the tool MIPgen, we designed 960 single-molecule molecular inversion probes (smMIPs) to target genes and mutational hotspots in matched tissues of our cohort of patients. Preliminary experiments made it possible to optimize some specific parameters relating to the target, the quality scores and the position on the strands. smMIPs technique has proved to have high sensitivity (>83%) also in the identification of low frequency variants (1%). We examined 150 samples from different groups: indeed, the cohort of patients enrolled in the study includes cases with a histological diagnosis of FCDs, brain tumors, gliotic scars and cryptogenics and so we included a NGS tumor panel which involves mutations also tested in cases of gliotic scars while as to cryptogenics patients the mutations will be detected through Whole Exome Sequencing. We constructed the library and sequenced on Illumina machine; currently we are performing bioinformatic analysis.

***Courses***

Silvia Aurigi e Cristina Mencarelli: "Ricerche bibliografiche e open access & science". 19 May 2022
Alessandro Palmieri: "Diritto dei brevetti". 27 May 2022
Francesco Maria Senatore: "Spin Off e Start up della ricerca: L'ecosistema di innovazione a supporto delle start up". 7 June 2022
Laura Neri: "Creating value from large archive and big data". 13 June 2022

Agnes Allansdottir: “I rapporti tra scienza e società: tra persistenze e cambiamenti”. 15 June 2022
Elena Meli: “Comunicare in ricerca”. 20 June 2022
Alessandro Mongatti: “Lavoro editoriale per l'editoria scolastica e universitaria (scienze e lettere)”. 1 July 2022
Gennaro Prota: “Possibili percorsi formativi post PhD”. 5 September 2022
Gianluca Murgia e Carlo Carobbi: “Il ruolo della standardizzazione nei processi di innovazione”. 7 e 8 September 2022

***Congress and seminars***
Clinical Genomics and NGS. Bertinoro, 8-13 May 2022
“Exploring the genomic and epigenomic landscape of Acute Myeloid Leukemia with Nanopore sequencing”, Prof. Alberto Magi. Firenze, 20 April 2022

• Visit to other italian laboratories:

U.O.C. Genetica Medica, IRCCS Azienda Ospedaliero-Universitaria di Bologna (Policlinico di Sant'Orsola).