

Next-generation sequencing (NGS) has transformed genomic research providing an accurate and comprehensive way for the detection of molecular mutations. On the other hand, finding the most promising genes among large lists of candidate genes is a time consuming task and has been defined as the gene prioritization problem. It is also necessary to assess the potential impact of amino acid changes on gene functions to provide computational predictions of casual variants for disease phenotypes. Then confirm the selected candidates by familial segregation studies and functional analysis *in vitro* or *in vivo*.

Ciliopathies is a group of disorders associated with genetic mutations yielding defects in the cilia structures, the basal body or the ciliary function. The ciliopathies is a pleiotropic disorder with phenotypes that include retinal degeneration, renal diseases, cerebral anomalies, liver congenital fibrocystic disease, diabetes, obesity and skeletal deformities.

In this study, we aimed to propose candidate variants using data from whole exome NGS of five unrelated patients clinically diagnosed to be suffering from ciliopathies disorders. Blood samples were collected from patients and DNA extracted to be used for whole exome sequencing and variant calling. The variants have been filtered and prioritized by a manual approach and in parallel by using bioinformatics prioritization tools. These prioritized variants have been checked for their pathogenicity to exclude neutral effect variants and have been sequenced to exclude false positive variants. Segregation analysis was performed when possible. One of the prioritized variants *DOCK6* has been checked *in vitro* for its effect on cilia structure.

All variants have been found to be pathogenic *in silico* except *CCDC88B* associated variant and all are expected to be related to cilia and responsible for the phenotypes appeared on patients. Family v646 variants are coherent with the family phenotype pedigree. *DOCK6* variant in this family did not show observable effect on cilia structure and needs further investigations. Family v645 variants appeared as heterozygous in the male patient (57) supposing there are other variants responsible for the male patient phenotype. All family v633 variants have been confirmed in the patient. We did not find promising homozygous candidates in family v636 and family v647 suggesting other mechanisms of inheritance responsible for the disorder. In this research we characterize new *in silico* pathogenic variants as promising candidates for ciliopathies disorders.