CDKL5 Program of Excellence
2022 Pilot Grant Program

Project Title: "A functional genomics approach to dissect the molecular bases of CDKL5 Deficiency Disorder"

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The new era of genomics paves the way to a wide number of research and treatment opportunities for many diseases, by allowing researchers and clinicians to focus more deeply on the molecular bases of many diseases. Unfortunately, for rare and ultra-rare genetic syndromes, such as CDKL5 Deficiency Disorder (CDD), this process is still hampered by the limited number of patients, which means a limited knowledge of the determinant mechanisms that lead to disease. This, in turn, leads to a huge deficiency in the research of possible specific treatments. To solve these tasks, in recent years researchers tried to develop comprehensive tools that could generate information about a wide number of mutations in disease-driving genes like CDKL5. The main problem of these methods is the difficulty of finding a good balance between the amount of data generated, the cost-effectiveness and the easiness of application that could lead to the expansion to every possible disease driving gene. In my laboratory, we have developed the expertise to test, in a highly multiplexed but cost-effective manner, thousands of possible mutations of genes involved in common and rare genetic disorders. We implemented this tool in a way that the effect of each possible disease-driving mutation can be dissected at single-cell level. We have already successfully applied it to a gene whose mutations are drivers of ultra-rare diseases and now we want to expand this discovery to many other disorders. Due to our expertise in neurodevelopmental systems, we think that CDD is the perfect match for our purpose, because of the huge lack of knowledge that could be filled by our approach. This could definitely provide the scientific community with a comprehensive dataset of CDKL5 mutational effect and steer the research for actionable drugs. The research will be performed at the Telethon Institute of Genetics and Medicine, one of the European leaders for the research on the molecular basis of rare genetic disorders.