

Innov4-ePiK: Innovative diagnostic and therapeutic approaches in potassium channel developmental and epileptic encephalopathies (K-DEEs) using 4P for medicine.

Ten major stakeholders of the French healthcare sector are committed to accelerate the development of **personalised, predictive, preventive, and participatory medicine** for patients suffering from drug-resistant developmental and epileptic encephalopathies.

Institut *Imagine*, Servier, NAOX Technologies, AP-HP, Inserm, Université de Rennes, CNRS, Hospices civils de Lyon, Hôpitaux Universitaires de Strasbourg and CentraleSupélec announce the signature of a funding agreement as part of the France 2030 Program. The aim of this project is to develop new innovative diagnostic and therapeutic approaches for epileptic and developmental encephalopathies.

Coordinated by the Institut *Imagine* and funded of €9.9 million over 5 years, the Innov4-ePiK program is one of the 19 winners of the sixth call for projects for "University Hospital Research in Health" under the France 2030 program. This project is a chance to get together a consortium of 10 academic and industrial partners who have joined forces to develop disruptive and transformative approaches to the diagnosis, prognosis and treatment of developmental and epileptic encephalopathies linked to genes coding for potassium channels.

Developmental and epileptic encephalopathies (DEEs) are characterized by drug-resistant epileptic seizures and significant neurodevelopmental disorders. These are due to the combined effect of epileptic seizures and electroencephalogram (EEG) abnormalities, associated with the effect of the etiology of DEEs, which is often genetic. The genes most frequently involved in DEEs, and especially early-onset childhood DEEs, are those encoding ion channels.

Deciphering these diseases, from the genetic to the pathophysiological level, and understanding the underlying molecular and cellular mechanisms, could lead to precision healthcare and personalised therapies for patients.

The Innov4-ePiK project aims to trigger a paradigm shift in the understanding, diagnosis, and treatment of DEEs linked to the genes encoding the KCNT1, KCNB1 and KCNA2 potassium channels, known as K-DEEs, through the development of clinical, EEG and



biological biomarkers focused on patient needs and natural history. Based on personalised, predictive, preventive, and participatory medicine (4P), the project also aims to develop cellular, animal, or virtual models and innovative methodologies for clinical trials.

Coordinated by Pr Rima Nabbout, University Professor and Hospital Practitioner at Necker Enfants-Malades Hospital (AP-HP) and head of the epilepsy program at Institut *Imagine* in the Translational Research in Neurological Diseases unit headed by Dr Edor Kabashi (Inserm, research director), Innov4-ePiK benefits from a unique multidisciplinary and translational environment that brings together academic experts from different scientific fields (neuroscience, signal analysis, physiology, data science, artificial intelligence, multi-omics analysis), physicians and industrial partners.

"The strength and originality of our Innov4-ePiK program is that; It brings together the largest cohorts of patients with K-DEEs with in-depth phenotyping and follow-up, and brings together internationally renowned French experts in the field of clinical, electrophysiology, preclinical modelling, biomarkers and data science, as well as partners from the medical device sector and the pharmaceutical industry, to provide methodological advances and the knowledge to lead to innovative global therapies for patients", announced Pr Rima Nabbout. Innov4-ePiK paves the way for much more personalised medicine as well as new diagnostic and therapeutic solutions, based on new molecules or the repurposing of known molecules.

Innov4-ePiK aims to change the care pathway for K-DEEs patients: "The fundamental objectives of the project are to offer an application to support healthcare professionals in their diagnostic and therapeutic decisions, and to develop new therapeutic strategies".

This program demonstrates the interest of the public and private sectors in deciphering K-DEEs by using multi-omics investigations coupled with analyses based on artificial intelligence. The quality of the expertise of the partners involved, in the creation of a customised program, makes Innov4-ePiK a unique project in its field.

Innov4-ePiK is based on the Geen-DS Chair held by Pr Rima Nabbout and supported by the FAMA Fund represented by the Swiss Philanthropy Foundation. The programme is also supported by the patient association KCNB1 France (www.kcnb1-france.org/), a long-standing partner of the Institut *Imagine*, which puts families of diagnosed patients in touch with each other.

