COMMUNIQUÉ

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De/From
Clotilde Roussille
clotilde.roussille@univ-angers.fr

Discovery of a novel gene responsible for a severe form of epilepsy in children

A team from the French laboratory of Integrated Neurovascular and Mitochondrial Biology (University of Angers/ Inserm/ CNRS) from the Mitochondrial Medicine Research Centre (MMRC), gathering researchers and physicians from the University and Hospital of Angers, has recentlydiscovered a new gene (*UBA5*) responsible for severe epilepsy associated with intellectual deficiency in children. The study has been published in the *American Journal of Human Genetics*.

Main investigator :
Pr. Dominique Bonneau, Angers, France

Epileptic encephalopathies are very severe neurological disorders, which appear in children in the very first years of life. They manifest by severe epilepsy associated with intellectual deficiency. It is a very heterogeneous group of diseases which have most often a genetic cause. Although about 15 genes have been identified, the real cause of the disease remains often unknown.

In collaboration with French, German, American and Spanish research groups, the MitoLab team from the French laboratory of Integrated Neurovascular and Mitochondrial Biology (University of Angers/ Inserm/ CNRS) has very recently discovered a novel gene responsible for this disease.

This study, which has been published on August 17th in the *American Journal of Human Genetics*, has discovered mutations in the *UBA5* gene in 5 children with pharmacoresistant epilepsy associated with mental retardation.

A new method of analysis of the human genome, the high throughput sequencing, was used to screen the 20,000 genes present in the whole genome of each children and their parents.

The analysis of this huge amount of data has been made possible by the collaboration with the « French Exome Project » (FREX), located in Nantes and Brest (France).

It is the first time that *UBA5* is incriminated in a human pathology. *UBA5* is involved in a new mechanism of protein modification and the severity of the disease appears to be inversely correlated to its residual activity.

This discovery contributes to the understanding of complex mechanisms leading to brain dysfunctions, which is a mandatory step prior to the development of therapy.

As for now, this discovery enables geneticists and neuro-pediatricians to make an earlier diagnosis in children affected with severe epilepsy, hence improving their management.

About MMRC/ PREMMi

The Mitochondrial Medicine Research Centre (MMRC/PREMMi), based in Angers, France gathers all local laboratories involved in mitochondrial investigations, hence creating a scientific dynamic for emergence of a unique, international-sized, mitochondrial medicine consortium.

The MMRC/PREMMi strategy consists in transferring the knowledge and skills acquired on mitochondrial inherited rare diseases to common diseases involving mitochondrial dysfunction (Alzheimer, Parkinson, cancer, diabetes, cardio-vascular diseases, aging).

One of the main challenges in mitochondrial medicine is to identify therapeutic pathways targeting mitochondria in many diseases for which there is no treatment available yet.

The MMRC/PREMMi program favors the reinforcement of collaborations between plant and metazoan life sciences research axes. From this alliance, new therapeutic molecules should be identified to generating tomorrow medicine for common diseases involving mitochondria

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