INSERM U1141 Neurodiderot PROTECT
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Post-doctoral position in computational and statistical genetics

Identification of key regulators of a gene network associated to epilepsies

Context:

Located in Paris, the **Neurodiderot PROTECT INSERM research unit** is a Neuroscience lab gathering five research teams working on understanding the mechanisms that alter the functioning of the developing brain. The laboratory is headed by Pierre Gressens, Research Director at Inserm and Professor of Fetal and Neonatal Neurology at King's College in London. Located in the **Robert Debré Hospital**, one of the largest pediatric hospitals in Europe, the Research Unit benefits from an optimal working environment to constantly promote exchanges between patients, the medical profession and researchers. This environment attracts bright and ambitious scientists from all over the world. Research in **the Integrative Genomics in Neurodevelopment group** centres around normal and diseased brain development. We are particularly interested in microcephaly, epilepsy and prematurity. Our research spans the areas of **gene networks-based approaches and systems genetics**, with a focus on applications in neurodevelopment to prioritize drug targets and new therapeutical strategies. Our main tools are **statistical and computational biology** approaches to integrate –omics data from patients, healthy individuals and animals or *in-vitro* models. We use simultaneously newly generated and open-source existing data. The group participates in unique collaboration with molecular and computational biologists, statistical geneticists and clinicians.

Project outline

The main objective of the **ANR[1] funded project "EpiReg"** is the **identification of genetic drivers for epilepsy** by integrating systems genetics approaches. A network of 320 co-expressed genes (termed M30), which is expressed widely throughout the human brain, was identified as a gene regulatory network on which converge rare and common epilepsies. The main scientific hypothesis of the EpiReg project is that **M30 might be targeted as a novel therapeutic strategy in epilepsy**. The purpose is to map key regulatory genes of M30 using existing and newly created methods. To this end, we will take advantage of the available transcriptional and genotype data in human brain from two consortiums: the United Kingdom Brain Expression Consortium (UKBEC) and the Gene Tissue Expression project (GTEx). For the most promising key regulators of the epilepsy-associated gene network M30, our collaborators will perform *in vivo* functional validation experiments

Founding article for the EpiReg project:

Delahaye-Duriez, Andree and others, 'Rare and Common Epilepsies Converge on a Shared Gene Regulatory Network Providing Opportunities for Novel Antiepileptic Drug Discovery', *Genome Biology*, 17 (2016), 245

Profile requirements:

- Highly motivated postdoc or PhD candidate
- Holding a degree in Statistical Genetics, Biostatistics, Computational Biology, Bioinformatics, Computer Science, or Mathematics
- Proficiency with at least one programming language (R and/or Python) and with bash/shell scripting
- Computational background to easily adapt to a UNIX environment in a high-computing cluster
- Experienced in analysing large-scale datasets
- Able to communicate effectively and to interact in interdisciplinary setting
- Flexibility to move between analytical and managerial work

Interested?

Please contact Prof Andrée Delahaye-Duriez to email: andree.delahaye@inserm.fr
When applying, please ensure you include a CV, a letter of interest (either in English or French), your list of publications and the names and addresses of at least two references. There is no strict deadline, but priority will be given to applications by Nov 1st. Starting date is also flexible, ideally by February 2019.

Other references (selection):

Johnson, Michael and others, 'Systems Genetics Identifies a Convergent Gene Network for Cognition and Neurodevelopmental Disease.', *Nature Neuroscience*, 19 (2015), 223–32
Krishnan, Michelle and others, 'Integrative Genomics of Microglia Implicates DLG4 (PSD95) in the White Matter Development of Preterm Infants.', *Nature Communications*, 8 (2017), 428
Srivastava, Prashant and others, 'A Systems-Level Framework for Drug Discovery Identifies Csf1R as an Anti-Epileptic Drug Target', *Nature Communications*, 9 (2018), 3561
Srivastava, Prashant and others, 'Genome-Wide Analysis of Differential RNA Editing in Epilepsy', *Genome Research*, 27 (2017), 440–50

[1] French national research agency