Appel à manifestation d'intérêt - Chaire Inserm
Fiche projet type

Établissement/organisme porteur: Inserm
Nom du chef d'établissement/d'organisme : Gilles Bloch
Site concerné: INSERM1231 – GAD team (https://www.gad-bfc.org/)
Région académique: INSERM GRAND EST

Établissements/organismes partenaires envisagés : *le cas échéant*
FHU TRANSLAD (http://www.translad.org/presentation.html).
Filière de santé maladies rares AnDDI-prenatome (http://anddi-rares.org/)
ERN ITHACA (https://ern-ithaca.eu/)

Nom du projet : De la modélisation cellulaire des maladies rares neurodéveloppementales vers la médecine personnalisée
From cellular modeling of rare neurodevelopmental diseases to personalized medicine

Mots-clés: rare diseases, single cell, OMICS, human iPSCs, brain organoids

Durée visée: 3 years

Scientific domain: genetic rare diseases

Section (s) CNU/CoNRS/CSS correspondante (s) :
CNU:
Section 64 - Biochimie et biologie moléculaire
Section 65 - Biologie cellulaire
CoNRS:
Section 22 - Biologie cellulaire, développement, évolution-développement - Institut des sciences biologiques (INSB)
Section 25 - Neurobiologie moléculaire et cellulaire, neurophysiologie - Institut des sciences biologiques (INSB)
CSS:
CSS1 - Biologie cellulaire, moléculaire et structurale
CSS2 - Cancérologie, maladies génétiques
CSS4 - Neurosciences

Strategy of the host institution: *(15 lignes maximum)*

For many years, Inserm has invested in research on rare diseases (RD) by coordinating major national and international research programs, *i.e.* the European Joint Program on Rare Diseases (EJP RD) and the "*Programme Prioritaire de Recherche Maladies Rares* (PPR-RD)". Inserm also coordinates the "*Plan France Médecine Génomique 2025"* in a care-research continuum that will allow the reanalysis in research of the genomic data from hundreds of thousands of RD patients in the national "*Collecteur Analyseur de Données" (CAD*). Through the EJP RD, Inserm has put in place a governance system that aligns France's strategy with the national strategies of the 35 countries involved, that of the European Commission and

other major players such as industry partners. All of these actions have led Inserm to be recognized as a major European player in the field of rare diseases. In Dijon, the UMR1231 joint center of the Inserm institution and the University of Burgundy (9 teams, more than 270 people) has a long experience in multidisciplinary research, combining fundamental and clinical research, with major capabilities for high-level international publications and rapid translation into the clinic. This also translates into an excellent fundraising record and the ability to grow, with the recruitment of permanent positions as CRCN and DR levels.

Strategy of the host laboratory:*(15 lignes maximum)*

Within the UMR1231, the GAD team is developing an innovative translational research project with the objectives to identify new gene-phenotype associations responsible for rare neurodevelopmental disorders (NDDs) and to implement genomic medicine, by focusing on new technologies, reducing diagnostic odyssey, understanding the physiopathology of NDDs, developing its expertise in coordinating therapeutic trials, and participating in emblematic European projects.

The GAD team is thus part of a very dynamic framework dedicated to personalized medicine and rare diseases, in particular due to the close relationship with the FHU TRANSLAD, the national French “Rare Disease Healthcare Network” AnDDI-rares and the “Grand Campus BIOME” bioinformatics platform of Burgundy University. The GAD team also hosts the NeuroGeMM emerging team directed at understanding the neurobiology and the genetics of mammalian brain development in health and disease. Therefore, one of the four scientific axes of the GAD team is devoted to functional genomics and physiopathology, based on mouse and innovative cellular models such as human iPSCs and brain organoids. In this context, the team leads the PPR-RD MultiOmixCare project, with one full-time engineer and one technician, who will work full time with the candidate, already recruited. This chair aims to support and intensify this work, while consolidating the existing dynamic.

Summary of the scientific project : *15 lignes maximum*

Modelling NDDs *in vitro* is challenging due to the impossibility to get access to patient-derived relevant tissues. For this reason, our laboratory invested in the implementation of reprogrammed neurons and astrocytes, derived from patient-derived induced pluripotent stem cells (human iPSCs), as well as in the 3D cultures of brain organoids, to study the molecular mechanisms underlying pathophysiological changes. This approach opens the possibility to study cellular and molecular changes underlying pathogenic genetic variants in candidate genes of interest, such as neurons, astrocytes and brain organoids development and biological functions, electrophysiology (MEA technology), scRNA-seq and special transcriptomics, epigenomics.

Our current field of interest includes, but it is not limited to, the study of splicing factors involved in NDDs (i.e. PTBP1, SRSF1, CELF2, CELF4, etc…) and the phospohatidylinositol-3,4-biphosphate kinase PIK3CA. These personalized cellular models will also make it possible to carry out preclinical studies for the screening of molecules in ultra-rare diseases to open up perspectives in the therapeutic trials for patients suffering from NDDs. The recruited researcher will work within the mentioned framework and is also expected to develop his/her own research on NDDs.

Summary of the teaching project: *15 lignes maximum*

The recruited researcher will participate in the teaching within the doctoral school "*Environnnement et Santé*" (E2S - https://e2s.ubfc.fr/) of the University of Burgundy, particularly in the field of system biology and cellular models for neurodevelopmental disorders. The selected candidate will also participate in the teaching of master students within the UFR of Life Sciences and Health Sciences of the University of Burgundy

Funding :

ANR package	200k€
Co-funding* > a full-time engineer during 5 years > a full-time technician > laboratory consumables (PPR-RD MultiOmixCARE, FEDER PERSONALISE, MIND regional grant)	 300k€ 150k€ 550k€
Total project	1.200k€

*source et montant

Scientific communication and dissemination:

The recruited researcher will be encouraged to actively promote their results and define the target audience (representatives of patient organizations, healthcare professionals, researchers, industry, funding agencies). He/she will also publish his/her results in high-level international scientific journals and present them at international conferences (ASHG, ESHG, etc.).

Open Science:

The recruited researcher will comply with INSERM and University of Burgundy current policies about Open Science practices, in particular:

- Open access (OA) to scientific publications; OA to research data under the principle "as open as possible, as closed as necessary", including access to information about the research tools and instruments needed to validate or re-use our data; OA code for the CT designs and models that will be proposed and developed during this project;
- Responsible management of research data in line with the FAIR principles through the use of a data management plan (DMP).
- Deposit of all the scientific productions from the chair in the national HAL archive, like the productions of the host laboratories;
- Publication of "pre-print" (e.g., via biorxiv.org);
- Pre-registration of studies ("pre-registered reports");
- Data sharing with the whole community via OSF (Open Science Framework);
- Use of GITHUB type servers for the distribution and sharing of software and data analysis procedures

Science and society:

GAD team members are fully involved in sharing their research with the public through participation to national (i.e. The European Researchers' Night, Telethon, Rare disease Day), local events (e.g. Experimentarium program) and through special GAD's initiatives (e.g. lab open days, presentation in primary schools, etc…)

The team enhances the visibility of career paths in genetics (i.e. scientific and medical professions) among secondary school students through laboratory open days, developed several communication tools such as books and videos, and collaborates closely with the PEMR (Plateforme d'Expertise Maladies Rares) and its patient associations network.

Indicators:
Mentoring will be set up with the UMR1231 center to support and advise the recruited researcher on administrative, regulatory, human resources and financial aspects, and also to seek solutions in case of difficulties. During the pre-tenure phase, bimonthly progress reports an annual scientific and pedagogical reviews will be carried out with the GAD management team, to monitor the progress of the project (ongoing experiments/developments, publications plans and promotion of results), teaching organization, fundraising, and discuss about the difficulties encountered and any possible reorientations. The purpose of this follow-up is to ensure the recruited researcher the best conditions for site integration in prevision of his/her tenure at the end of the chair.