Fiche de poste CPJ2021 MMG -EN

Institution/organisation: INSERM

Name of the head of establishment/organisation: Gilles BLOCH

Site : Aix-Marseille University - Faculty of Medical and Paramedical Sciences

Academic region: Aix Marseille

Partner institutions/organisations: if applicable

Research unit: MMG - U1251

Project name: Diagnostic Deadlocks in Genetic Diseases

Possible acronym: **DDGD**

Keywords: give 5 keywords characterising the scientific project

Rare diseases, genetics, -omics, bioinformatics, stem cells, therapy

Target duration: 6 years

Scientific theme : Life Science, Health, genetic diseases

Corresponding CNU/CoNRS/CSS section(s) :

Institutional strategy: describe how the recruitment is in line with the strategy of the institution (15 lines maximum)

INSERM participates in numerous national and European initiatives and supports various research programmes to develop all the resources necessary to improve the diagnosis, understanding and treatment of rare genetic diseases.

Furthermore, as part of the Aix-Marseille site policy, AMU set-up 18 institutes with its IDEx partners, including INSERM. The goal is to gather the site's strong scientific skills towards solving societal challenges through interdisciplinary approaches and by strengthening the training-research link. The DDGD project is fully in line with the strategy of the Aix Marseille University "Marseille Maladies Rares" (MarMaRa) institute, which brings together the expertise of 11 research units in physics, biology, mathematics, social sciences and medicine.

Strategy of the host laboratory: describe how the recruitment is in line with the strategy of the host laboratory (15 lines maximum)

The Marseille Medical Genetics laboratory (MMG, INSERM-AMU U1251) is mainly focused on the study of rare genetic diseases. The work carried out in the laboratory ranges from the identification of new genes, in close collaboration with clinical services and reference centres, to the development of models for the study of pathophysiology and to the development of innovative therapies. The laboratory has developed deep expertise and cutting-edge strategies (e.g., core facility for the production and differentiation of induced pluripotent stem cells) for modelling and studying pathophysiological mechanisms, validating genomic variants, and therapeutic developments (from screening of bioactive molecules to gene or cell therapy).

In rare diseases, the identification and understanding of causative genomic variations is currently a major objective in order to reduce the number of patients without a clear diagnosis and who are in diagnostic wandering or deadlock. This requires integrative and interdisciplinary approaches merging genetics analysis and the development of relevant disease models. The candidate will oversee the development of innovative and cutting-edge approaches for the modelling of rare diseases and/or the development of therapeutic approaches.

Summary of the scientific project: 15 lines maximum

Our project aims to identify new mutations and explore molecular mechanisms for patients in diagnostic deadlock and to establish proofs-of-concept for the classification of undiagnosed rare diseases. This aim might be achieved by combining different strategies, including (but not limited to) the exploration and integration of descriptive clinical diagnosis, genomics and omics analyses, stem cell-based disease modelling and computational/numeric approaches. This project, in collaboration with rare disease reference centres, is in line with the perspectives of the National Plan for Rare Diseases (PMRIII) and responds to the European directives of personalised medicine and the perspective of "a diagnosis for all". Through an integrated multidisciplinary approach, we hope to develop and federate new skills and propose innovative approaches to the diagnosis and treatment of debilitating diseases whose genetic cause is unknown, with the longer-term goal of identifying the cause(s) of undiagnosed rare diseases and defining adapted treatments for each patient. The project will focus on the exploration of rare genetic diseases within the field of disciplines explored in the MMG laboratory.

Summary of the teaching project: 15 lines maximum

The candidate will participate in the teaching of the "Biology and Health" Master's degree. We expect the candidate to take responsibilities, and in particular lead teaching modules based on his/her expertise. The candidate will also be involved in the missions of the "Marseille Maladies Rares" Institute for the implementation of an interdisciplinary master's degree focused on rare diseases, including genetics, genomics, bioinformatics but also more transversal themes such as human and social sciences. The candidate will also participate in teaching in other structures (Medical Sciences, Polytech...).

Scientific dissemination: specify the expected results in terms of scientific dissemination (publications, communications, etc.)

Our ambition is to create a solid scientific environment as a first step to promote scientific sharing. We want to achieve this objective through our involvement in national rare diseases networks and to offer an environment that allows research training for students and young scientists. A large amount of data will be made available through publication and deposited in public databases. The knowledge derived from this project will benefit academic researchers in various research fields, including rare genetic diseases, genomics, bioinformatics. As such, we will target journals relevant to these communities to publish our results, giving priority to open access journals. We will also disseminate our results by participating in international scientific meetings and workshops. In addition, this project will make a strong contribution to higher education, training students through interdisciplinary approaches who will become the next generation of researchers and clinicians.

Open Science: Is the project part of an open science approach? If so, describe its implementation.

The MMG unit is committed to open science. The full text of the unit’s publications are available in HAL and we are giving priority to Open Access journals. The large amount of data produced in the unit are available through publications and dedicated public databases, and the code of our methods is available in GitHub. The candidate’s project will be included in the MMG unit open science framework.

Science and society: does the project envisage communication with the general public? If yes: specify how and when

Thanks to our close links with various clinical services and the involvement of clinicians at each stage of the project, part of this research will be directly transferable to the hospital. The immediate impact on patients is therefore high, with an impact on health management and care. The transfer of information to clinicians and the wider public will be greatly facilitated by the interactions already in place within the host structure. Dissemination to the general public is the very culture of the MMG laboratory, which has always been involved in communication actions with patients or in the dissemination of research to the general public (Fête de la Sciences, Journée des familles, 1000 chercheurs dans les écoles).

The general public will also be informed of our discoveries through national or international publicity via our institutions (AMU, INSERM) and via the Marseille Rare Diseases Thematic Institute, which will raise public awareness.

Indicators: specify the indicators for monitoring the deployment of the project and the methodology for monitoring them

Financial summary: using the attached financial form, describe the financial needs and their distribution to carry out the scientific project (doctoral student, post-doctoral student, IT, equipment, etc.)

ANR funding package	200 000 €