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 : institut Curie
Région académique : Paris

Établissements/organismes partenaires envisagés : *le cas échéant*

Nom du projet :
Développement de nouvelles méthodes statistiques pour étudier la composante génétique des maladies complexes au-delà des études d'association

Development of new statistical methods to study the genetic component of complex diseases beyond association studies

Mots-clés : maladie complexe, facteur génétique, facteur environnemental, style de vie, prédisposition génétique

Durée visée : 5 years

Scientific domain : Genetic statistics - genetic epidemiology

Section (s) CNU/CoNRS/CSS correspondante (s) :

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

The Genetic Epidemiology of Cancer team (GEC) is located at the Institut Curie (http://www.curie.fr), which is a world-class Comprehensive Cancer Center with a hospital group treating more than 13,000 patients per year, and a multidisciplinary research center combining research in biology, genetics, computational biology, soft matter physics, organic and medicinal chemistry. It is part of the Inserm Unit "Cancer and Genome: Bioinformatics, Biostatistics and Epidemiology of Complex Systems" (U900). U900 staff is studying several aspects of cancer pathology and treatments and focusing on the underlying molecular and cellular mechanisms: initiation (estimation of cancer risks, including genetic and non-genetic factors, optimization of patient follow-up strategies), tumor development and progression, and improvement of therapeutic strategies. The research projects are carried out by interdisciplinary teams comprised of biologists and clinicians, epidemiologists, mathematicians, statisticians, physicists and computer scientists. U900 staff scientists are experts in high-dimensional data analysis and modeling. Their activity combine experimental and theoretical approaches, cycling in iterative manner from experimental biology and clinics to mathematical models and back. The final results are validated explicative and predictive models.

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

Projects developed by GEC aim at characterizing genetic variants involved in predisposition to cancers by considering effects of other genetic or non-genetic factors. In addition to variants involved in monogenic transmission, common variants are also studied, as well as their interactions with lifestyle and environmental exposures.

Studied populations are populations at high risk of cancer, such as Hereditary Breast and Ovary Cancer families, or populations having a cancer risk *a priori* similar to that of the general population. Within the team, the Platform of Investigation in Genetics and Epidemiology was established to support epidemiology- and genomics-related activities. This platform is involved in the setting up, collection and centralization of epidemiological, familial and clinical data of the national studies that the team coordinates. The team also aims to adapt laboratory, pathology and bioinformatics-related genomic techniques to suit the projects' particular needs and is endowed with a wet lab activity.
Results from this research will *in fine* allow to improve risk prediction models and therefore to more precisely estimate tumor risks, which in turn will help elaborating personalized screening, follow up and new prevention strategies.

Summary of the scientific project : *15 lignes maximum*

Classical methodologies and analytical strategies used to study the genetic component of complex diseases as cancer have reached their limit to discover new susceptibility variants. So far, methods such as the genotype-restricted likelihood method, maximum likelihood parametric methods or other modified segregation-analysis approaches allow estimation of penetrances of variants (or cumulative risks of developing the disease) in a high risk family context under simplistic transmission models. For more common variants, conferring either a moderate- or low-risk of diseases, strategies such as genome-wide association studies (GWAS) have also reached their limit.
The scientific project will consist in proposing new analytical methods and strategies to consider the complexity of multifactorial diseases. As example, adequate consideration of environmental and lifestyle factors, such as their variation over time, should make it possible to highlight genetic factors acting differently throughout life and influencing the onset of the disease. This work should not only be based on simulated data but above all on real-life data. Data from studies coordinated by GEC and international data of the consortia to which GEC belongs will be available to develop and validate the methods.

Summary of the teaching project : *15 lignes maximum*

The teaching will consist in presenting the methods in genetic epidemiology for complex diseases both for family data and for so-called general population data. This teaching should be generously illustrated with examples of real-life data to raise awareness of the advantages and limitations of these methods.
Reminders of the fundamentals of genetics (transmission models, classification of variants....) and epidemiology (concept of risk: relative, cumulative, absolute...; choice of control populations: unaffected relatives, population-based controls; biases related to ascertainment, anamneses, genetic testing ...) should be considered according to the background of the students.

Funding :

ANR package	200k€
Co-funding*	€
Total project	200k€

*source et montant

Scientific communication and dissemination :
The policy of the U900 lab is to publish in the best journals and conferences in our discipline. The recruited researcher is expected to publish regularly as principal author but also as co-author.

Open Science :
In view of the industrial potential for this work, major innovations will systematically combine patent filling followed by scientific publications, in open access. All the published articles will be on HAL in their integral version. As for the data collected and prepared for research, they will be made available to the community as soon as possible, after a possible embargo period. Participation in the creation of challenges in the field will allow further enhancing the value of the proposed developments and their recognition in the wider international community.

Science and society :
The U900 lab participates every year in the Fête de la Science and the Nuit des Chercheurs. The recruited researcher will be expected to actively participate in these events and communicate with the general public. Depending on his or her current situation, he or she may also be interviewed by journalists from the general or popular science press.

Indicators :

Teaching

Research

Knowledge transfer