Subject: Environmental exposure, health and epigenetic mechanisms

6 months internship

Context:

Adverse pregnancy outcomes carry a considerable public health burden of morbidity and mortality, both in pregnant women and their offspring throughout their lifespan (Kramer, 2003). Preterm birth is the leading cause of neonatal mortality and morbidity. In the long term, preterm birth and lower birth weight are associated with increased risks of neurodevelopmental disorders, cardiac and metabolic diseases, and impaired respiratory health during childhood and adulthood (Barker, 2004; Lawlor et al., 2005). It is increasingly recognized that *in utero* environmental exposures can affect the health of the baby at birth and later on during childhood and adulthood.

Maternal exposure during pregnancy to tobacco smoking, endocrine disruptors, air pollution, or climate conditions are potential risk factors of neonatal morbidity (Stieb et al 2012, Strand et al 2011), but also of neurodevelopmental disorders, impaired respiratory health, cardiac and metabolic diseases, in childhood and adulthood (Schultz et al 2012, Clifford et al 2016).

The mechanisms that could explain such associations between early exposures and later health outcomes are not completely understood. Among relevant mechanisms, it is being increasingly recognized that epigenetic mechanisms are potential molecular mediators of early life programming (Waterland et Michels 2007). DNA methylation is the best understood and the most cost-effective epigenetic mark to investigate in epidemiological studies. DNA methylation modifications have been shown after exposure to air pollution (Baccarelli et al 2009, Abraham et al 2018). These modifications are reversible, but they can also persist even in the absence of the cause that established them, which makes them relevant candidates for biomarkers of exposure and / or health effects. However, the large dimension of this type of data measured over the genome (-omics datasets) poses statistical and epidemiological challenges (Chadeau-Hyam et al 2013).

Aim:

Several internships are proposed. They aim at identifying the effects of environmental exposures (tobacco smoking, air pollution, climate) on the health of the mother and fetus (gestational duration, fetal and postnatal growth, cognitive and motor development, respiratory health) and on the respiratory health of adults.

The role of epigenetic mechanisms in these associations is investigated by studying the relationship between placental DNA methylation on one hand and environmental exposures (Abraham et al 2018) and health outcomes on the other hand; the objective here is to identify potential biomarkers of exposure and / or health outcomes and potential mediators / mechanisms that could explain the association between environment and health.

Environmental exposure, health data, epigenetic data and potential confounders are available. These data rely on several mother-child cohorts : EDEN (http://eden.vjf.inserm.fr/index.php/fr/), PELAGIE (http://www.pelagie-inserm.fr), and SEPAGES (http://sepages.inserm.fr/fr/accueil/), and on the EGEA study (http://egeanet.vjf.inserm.fr).

Candidate:

A candidate with a Master degree or Engineer degree with substantial background in statistics is required. Knowledge in R (and / or SAS / Stata) and English reading is needed. For internships relying on epigenetic data, a good practice and manipulation of large (omics) datasets with R is required. Candidates are expected to show professional behavior, scientific rigor and some autonomy. Applicants should have some interest and motivation for public health and environmental epidemiology. The candidates will have the opportunity to pursue with a PhD in epigenetic epidemiology.

Location:

Supervisors will depend on the topic of the internship

Location: Institute For Advanced Biosciences, INSERM U1209, Team 12 environmental epidemiology applied to reproduction and respiratory health

To apply send a CV and cover letter to Johanna Lepeule johanna.lepeule@univ-grenoble-alpes.fr