Research Stage (M2)

Title: Dissecting the impact of natural genetic variation on chromatin conformation and gene regulation

Where: Quantitative regulatory genomics team, LBMC
(http://www.ens-lyon.fr/LBMC/equipes/quantitative-regulatory-genomics)
ENS de Lyon, 46, allée d'Italie, 69364 LYON CEDEX 07, France
When: Beginning of 2020 (flexible)
Duration: 6 months (M2)
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Keywords: Big data, integrative genomics, machine learning, regulation of gene expression, chromosome conformation.

Description of the project:
In the team we are interested in both genetic- and non-genetic influences gene regulation and phenotypes[1-4]. Chromosomes adopt a complex spatial conformation inside the nucleus, which plays an important role in gene regulation[5]. Yet surprisingly few studies have explored the genetic architecture of chromosome conformation, and how genetic variation in chromosome conformation contributes to gene regulation and phenotypic variation in evolution. Many disease-associated genetic variants alter the expression of genes located very far in the linear sequence but close in space. One of the possible underlying mechanisms for this might be a change in chromatin conformation. Thus, understanding how genetic variation impacts chromatin conformation will help us to predict causal variants in common diseases and to understand and their mechanism of action[6].

We have now collected data on chromatin conformation and gene expression during embryogenesis in two genetically different fly lines. By integrating these data together with available functional genomics data, we aim at understanding how genetic variation impact chromatin conformation and gene expression.

You will learn how to manage, integrate and analyse big gene expression and genomic data using state-of-the-art machine learning tools, to address fundamental biological questions.
A good level of English is absolutely required, such as good computational skills. Scripting skills in a programming language among R, Matlab or Python and good statistical skills are highly desirable. Database management is also desirable.

In short, if you have good computational and data analysis skills and you want to crack the secrets of the regulation of gene expression, join the "Quantitative Regulatory Genomics" team at the LBMC!

Contact me at Mirko.francesconi@ens-lyon.fr to ask for further information and apply (CV and a motivation letter).

References

1. Francesconi, M. & Lehner, B. The effects of genetic variation on gene expression dynamics during development. *Nature* **505**, 208-211, doi:10.1038/nature12772. Epub 2013 Nov 24. (2013).
2. Perez, M. F., Francesconi, M., Hidalgo-Carcedo, C. & Lehner, B. Maternal age generates phenotypic variation in Caenorhabditis elegans. *Nature* **552**, 106-109, doi:10.1038/nature25012 (2017).
3. Francesconi, M. *et al.* Single cell RNA-seq identifies the origins of heterogeneity in efficient cell transdifferentiation and reprogramming eLife 8:e41627 (2019).
4. Francesconi, M. & Lehner, B. Reconstructing and analysing cellular states, space and time from gene expression profiles of many cells and single cells. *Mol Biosyst* **11**, 2690-2698, doi:10.1039/c5mb00339c (2015).
5. Schoenfelder S. & Fraser P., Long-range enhancer–promoter contacts in gene expression control, Nature Reviews Genetics 20, 437–455 (2019)

6. Lodewijk Krijger PH & de Laat W., Regulation of disease-associated gene expression in the 3D genome, Nature Reviews Molecular Cell Biology 17, 771–782 (2016).