Sept. 18th, 2012

Title of the project: **Multi-scale analysis of chromatin dynamics during meiosis**

Name of the lab: **Spatial regulation of genomes**

Head of lab: **Romain Koszul**

PhD director or contact person: **Romain Koszul**
Email: **romain.koszul@pasteur.fr**

Web site address of the lab: **http://www.pasteur.fr/ip/easysite/pasteur/en/research/scientific-departments**

Doctoral school affiliation and University: **CdV** (Complexité du Vivant), Université Pierre et Marie Curie - Paris 6 (UPMC)

Summary of the project

Meiosis is the essential, highly regulated process by which a diploid cell gives rise to haploid gamete cells in sexually reproducing organisms. Dysfunctional progression of the central events of meiosis, i.e. pairing of homologs and accompanying recombination, is likely to generate important chromosomal mis-segregation and lead to infertility or genomic diseases in offspring. These processes take place during meiotic prophase concomitantly with important changes in nuclear organization and chromosome structure. However, the influence of this dynamic and changing physical environment on the progression of recombination is not well understood. Using complementary, multilevel approaches, we will investigate the influence of the highly organized chromosome fiber and chromatin dynamics onto meiotic recombination in budding yeast. In addition, the advent of the genomic era has revealed the extent to which genomes from natural eukaryotic populations are polymorphic. Such polymorphisms range from single nucleotide polymorphisms to insertions/deletions of various sizes up to structural variations of hundreds of kb. We will analyze the influence of both polymorphisms on pairing and recombination in *S. cerevisiae* in light of meiotic specific features. This work will impact our understanding of meiosis taking place in heterozygous diploids, which is the common situation in nature, and should also shed light on the mechanisms at the basis of reproductive isolation.
The student will work in the group “spatial regulation of genomes”, in the “genomes and genetics” department. The team, also funded by the European Research Council (ERC), aims at studying the interplay between the organization and dynamics of eukaryotic chromosomes with several biological processes. There, the candidate will use complementary, multilevel approaches to achieve his goals, relying both on the expertise already present in the laboratory (genomic derivatives of chromosome conformation capture technique [Cournac *et al.*, in press; Marbouty *et al.*, in prep], high-resolution gene mapping and chromatin dynamics quantitative analysis [Wong *et al*., in press; Koszul *et al.*, 2008]) and on the development of innovative assays. One original tool currently under development in the lab consists in the design and *de novo* assembly of large chromosomal regions of interest, aiming at replacing their natural counterpart. This approach, at the forefront of the synthetic biology field, will be of tremendous help to increase the resolution of the assays, and will allow us to monitor at an unprecedented resolution large regions of the genome. Ongoing and well-established collaborations with physicists and mathematicians will also be beneficial to the project as well, and candidates with such backgrounds are welcome to apply if committed to turn to (at least part-time) biologists during their PhD!

1. Cournac, Marie-Nelly, Marbouty, Koszul[&], Mozziconacci[&], BMC Genomics, 2012 *in press*
2. Wong, Marie-Nelly, Herbert, Carrivain, Blanc, Koszul, Fabre, Zimmer, Current Biology, 2012 *in press*
3. Koszul, Kim, Prentiss, Kleckner, Kameoka, *Cell*, 133 Jun 2008