MASTER 2 BMC
PARCOURS GENOPATH
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Titre du sujet de stage :

A mechanical basis for recombination-dependent homolog pairing in meiosis

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Sujet de stage :

Meiosis is the specialized cell division at the basis of sexual reproduction. Homologous recombination is the molecular process that drives the recognition, pairing, and attachment of homologs during the first meiotic division. Ill-defined regulations of the meiotic recombination process underlie this major reorganization of chromatin. First, recombination takes place with the homolog rather than with the sister chromatid (homolog bias). Second, among the multiple recombination reaction taking place along each pair of homologs, at least one will be matured into an "obligatory" crossover. Finally, the designation of a crossover inhibits formation of other crossover at a typical distance nearby (crossover interference). These three phenomena of homolog bias, obligatory crossover, and crossover interference, known for decades to up to a century, have not yet been elucidated despite their centrality for sexual reproduction. Our goal is to crack these major enigmas in the field thanks to new hypothesis, ambitious synthetic biology approaches, novel high-throughput methodologies we developed, and polymer modelling.

We surmise that these three phenomena are the expression of a single property of the meiotic recombination machinery: that to sense mechanical stress. Using high-throughput Hi-C derivatives and molecular tools to track recombination intermediates and products, we aim at addressing this hypothesis by manipulating the dynamics and the physical properties of meiotic chromosomes. The student will participate in this endeavor by building strains, running synchronous meiotic time courses, and performing this suite of experiments uniquely available in our laboratory. His/her results will be compared to the output of polymer models of recombination. PhD positions will be available following the internship.

Technologies utilisées : Hi-C, Capture-C, Illumina sequencing, genome engineering

Mots clés : Meiosis, DNA repair, 3D genome

Publications d'intérêt :

1. Dumont A, Mendiboure N, Savocco J, Anani L, Moreau P, Thierry A, Modolo L, Jost D, Piazza A, Mechanism of homology search expansion during recombinational DNA break repair, bioRxiv, 2023, https://doi.org/10.1101/2023.12.01.569403 (Cell, in revision)
2. Reitz D, Djeghmoum Y, Watson AR, Rajput P, Argueso JL, Heyer WD*, Piazza A*, Delineation of two multi-invasion-induced rearrangement pathways that differently affect genome stability, Genes and Development, 2023 Aug 4. doi: 10.1101/gad.350618.123. *co-last authors
3. Piazza A*°, Bordelet H*, Dumont A, Thierry A, Savocco J, Girard F, Koszul K°, Cohesin regulates homology search during recombinational DNA repair, Nature Cell Biology, 2021 Nov;23(11):1176-1186 *co-first and °co-last authors
4. Piazza A, Shah SS, Wright WD, Gore SK, Koszul R, Heyer WD, Dynamic processing of displacement loops during recombinational DNA repair, Molecular Cell, 2019 Mar 21;73(6):1255-1266.e4
5. Piazza A, Wright WD, Heyer WD, Multi-invasions are recombination byproducts that induce chromosomal rearrangements, Cell, 2017 Aug 10; (4):760-773