Chromatin structure and DNA recombination along the linear chromosome of *Streptomyces*

***Streptomyces* are rhizosphere bacteria, involved in geochemical cycles and plant growth and health. Their complex development cycle is associated with a secondary metabolism exploited by biotechnologies (*e.g.* antibiotics, anticancer). They have a large linear chromosome, between 6 and 12 megabases, and an extreme percentage of G and C bases (72%). These bacteria are subject to a high genetic instability associated, under laboratory conditions, with large chromosomal rearrangements (deletions, amplifications, translocations, circularization).**
The plasticity of the linear chromosome results from the reorganization of the order of genomic sequences, to the loss and gain of sequences from horizontal transfer. In the DynAMic laboratory (StrAda team), we have shown that the repair of DNA double-strand breaks is at the origin of large-scale genomic rearrangements, inducing homologous recombination or illegitimate recombination. These rearrangements affect the terminal regions of the chromosome, called chromosome arms, more than the central region. This compartmentalization is correlated with a specific structuring in vivo: the central region is more strongly structured than the terminal regions, which are more "relaxed". Our working hypothesis is that the spatio-temporal dynamics of chromatin is at the origin of the characteristic compartmentalization of the *Streptomyces* chromosome. Our project aims to explore the link between chromatin composition (proteins associated with DNA), and molecular recombination processes.

The following questions will be addressed during the thesis:
- Are double-strand breaks handled equivalently by the two repair mechanisms identified in Streptomyces (i.e. homologous and illegitimate recombination) along the chromosome?
- Could differential chromatin composition influence the spatiotemporal pattern of recombination in this chromosome?
Molecular genetic approaches will be used (construction of a recombination monitoring cassette, introduction of targeted double-strand breaks by a CRISPR strategy). In addition, the composition of chromatin along the chromosome can be described by (i) ChIP-seq type chromatin immunoprecipitation experiments targeting proteins known to be associated with DNA (ii) a proximal labelling approach without a priori. Using these same approaches, the dynamics of chromatin composition following a double-strand break will be studied and put into perspective with the recombination profile observed along the chromosome.

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Recent publications of the team :

Lorenzi J.-N., Lespinet O., Leblond P., Thibessard A. . Subtelomeres are fast-evolving regions of the Streptomyces linear chromosome. *Microbial Genomics*. 2021. 7:525 DOI: https://doi.org/10.1099/mgen.0.00052

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Application: full CV + 2 referent names + M2 manuscript. To be sent to Pierre Leblond (pierre.leblond@univ-lorraine.fr), Annabelle Thibessard (annabelle.thibessard@univ-lorraine.fr), Claire Bertrand (claire.bertrand@univ-lorraine.fr).

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