

Double strand break repair triggers genome plasticity in *Streptomyces*

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Introduction: Double strand breaks (DSB) are the most detrimental damage that bacteria have to cope with. Two main DSB repair pathways, namely homologous recombination (HR) and non-homologous end joining (NHEJ) are in charge with DSB repair. HR relies on an intact copy of the damaged DNA molecule as a template. NHEJ, for its part, which is present in only 20% to 25% of the bacteria, is considered as a mutagenic pathway. Hence, in the absence of template, NHEJ is an error-prone mechanism triggering nucleotide addition or deletion at DSB healing site.

Objectives: Although the high plasticity of the *Streptomyces* linear chromosome was reported until the first genetic studies, the relative contribution of HR [1] and NHEJ [2] to the stability and evolution of the chromosome of *Streptomyces* remains unknown.

Material and methods: DSBs were induced by heterologous expression of the meganuclease I-SceI targeting I-SceI sites inserted into different chromosomal locations and in different genetic backgrounds.

Results: DSB repair in the chromosomal arms is accompanied by the formation of large deletions. In contrast, DSB healing in the central region is associated to mutagenic repair without major rearrangement. This mutagenic repair is resulting from NHEJ as shown by DSB repair surveys in mutants deficient for putative NHEJ actors (Ku, ligases). Homologous recombination was shown to occur between duplicated loci distributed along the chromosome, leading to chromosomal arm replacement and intense DNA amplification. NHEJ repair induced chromosomal circularization and the formation of large deletions. Further, the involvement of NHEJ was concomitant with the integration of genetic material at the healing site.

Conclusion: These data support that DSB repair is driving genome plasticity in *Streptomyces* and that NHEJ may favor insertion of information from horizontal transfer. These recombination processes could confer the capacity to evolve in response to environmental adversity.

References

[1] Hoff G, Bertrand C, Piotrowski E, Thibessard A, Leblond P. Implication of RuvABC and RecG in homologous recombination in *Streptomyces ambofaciens*. Res Microbiol. 2017 Jan;168(1):26-35.

[2] Hoff G, Bertrand C, Zhang L, Piotrowski E, Chipot L, Bontemps C, Confalonieri F, McGovern S, Lecointe F, Thibessard A, Leblond P. Multiple and Variable NHEJ-Like Genes Are Involved in Resistance to DNA Damage in *Streptomyces ambofaciens*. Front Microbiol. 2016 Nov 28;7:1901.