How to fold a linear chromosome of Streptomyces

3 September 2021

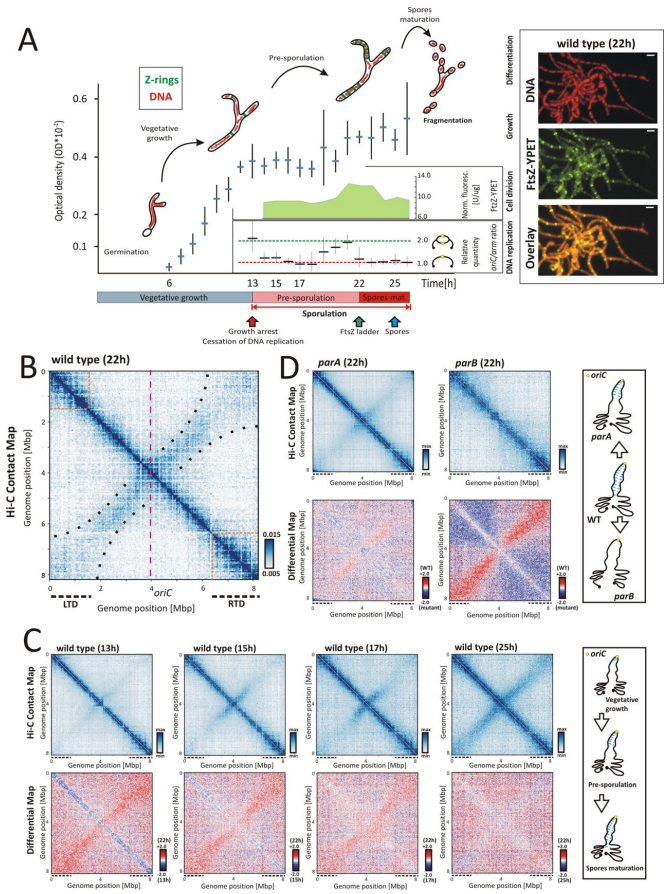

Fig. 1: Spatial organisation of the S. venezuelae linear chromosome during sporulation. A The S. venezuelae (wild-type ftsZ-ypet derivative, MD100) growth curve (in 5 ml culture), performed in n = 3 independent experiments. The mean optical density values and standard deviation (whiskers) are shown on the scheme. The critical time points of sporogenic development are marked with arrows: growth arrest and cessation of DNA replication (red), the appearance of FtsZ ladders (green) and the spore formation (blue). The normalised FtsZ-YPet fluorescence (a marker of a synchronous cell division) [U/µg] and the relative oriC/arm ratio (a marker of DNA replication; n = 3 independent experiments: mean oriC/arm values as well as calculated standard deviations (whiskers) are shown on the diagram) are shown as insets in the plot, with X axes corresponding to the main plot X axis. The oriC/arm ratio at the 26 h of growth was set as 1.0. The right panel shows the representative visualisation of condensing nucleoids (n = 250 analysed nucleoids per a single time point; DNA stained with 7-AAD) and FtsZ-YPet at 22 h of growth; scale bar 2 µm. B The normalised Hi-C contact map obtained for the wild-type (ftsZ-ypet derivative, MD100) after 22 h of growth (in 5 ml culture). The dotted pink lines mark the position of the oriC region. The dotted black lines mark the positions of the left (LTD) and right (RTD) terminal domains. The boundaries of the LTD and RTD are marked directly on the Hi-C contact map with the orange dotted lines. The contact range within the secondary diagonal axis is marked with black dots. C Top panel: the normalised Hi-C contact maps obtained for the wild-type (ftsZ-ypet derivative, MD100) strain growing for 13, 15, 17 and 25 h (in 5 ml culture). Bottom panel: the differential Hi-C maps in the logarithmic scale (log2) comparing the contact enrichment at 22 h of growth (red) versus 13, 15, 17 and 25 h of growth (blue). The X and Y axes indicate chromosomal coordinates binned in 30 kbp. The right panel shows the model of chromosome rearrangement in the course of sporulation. D Top panel: the normalised Hi-C contact maps generated for parA and parB mutants (ftsZ-ypet derivatives MD011 and MD021, respectively) growing for 22 h (in 5 ml culture). Bottom panel: the differential Hi-C maps in the logarithmic scale (log2) comparing the contact enrichment in the wild-type strain (red) versus the mutant strain (blue). The right panel shows the model of chromosome organisation in the parA and parB mutants.

Streptomycetes are the richest source of antibiotics, anticancer agents and immunosuppressants used in human and veterinary medicine.

The production of these important bioactive molecules is often intimately linked with the life cycle of this versatile genus of bacteria.

Unique among bacteria, Streptomyces has a very complex life cycle, and a linear chromosome instead of the usual circular chromosome found in most bacterial species.

How this unusual linear chromosome is folded in

three-dimensional space, and how folding might change during the life cycle of Streptomyces is not fully understood. To better understand the folding of the Streptomyces chromosome, researchers at the University of Wroc?aw (Poland) collaborated with the John Innes Centre.

The groups of Dr. Marcin Szafran and Professor Dagmara Jakimowicz at the University of Wroc?aw, with Dr. Tung Le, Group Leader, and Dr. Kim Findlay, Head of the Bioimaging platform at the John Innes Centre has led to a breakthrough in understanding how Streptomyces chromosomes fold which is published in *Nature Communications*.

Dr. Marcin Szafran and the team employed Hi-C technique (short for chromosome conformation capture with deep sequencing) to show that the arms of the Streptomyces venezuelae chromosome are separated from each other when the bacterium is in the early stage of its life cycle.

Upon sporulation, when spores are produced, chromosome arms are brought close together and the chromosomes become progressively more compacted. This is achieved by the action of a chromosome segregation protein ParB and a chromosome condensing protein SMC.

The research also showed that the ends of the linear chromosome are organized into distinct domains by a unique Streptomyces protein called HupS.

Dr. Tung Le said "This has been a fantastic collaboration, spearheaded by the Jakimowicz group, that reveals a key aspect of Streptomyces cell biology and development. It has been a pleasure to host Dr. Marcin Szafran at the John Innes Centre to transfer the Hi-C technique to him."

"It is exciting to see substantial changes in the folding of the chromosomes during the Streptomyces life cycle, from being open to becoming more closed and compacted in preparation for cell division. This is the norm in eukaryotes such as yeast, human, and plant cells but has not been demonstrated in other bacteria apart from Streptomyces."

This work is preceded by a long history of Streptomyces research at the John Innes Centre and with collaborators around the globe.

Three decades ago Professor Carton Chen's group of the National Yang-Ming University in Taiwan, and Sir David Hopwood's group at the John Innes Institute showed that the chromosome of Streptomyces lividans is linear. It is now clear that this is also true for most Streptomyces species.

"Spatial rearrangement of the Streptomyces venezuelae linear chromosome during sporogenic development" is published in *Nature Communications*.

More information: Marcin J. Szafran et al, Spatial rearrangement of the Streptomyces venezuelae linear chromosome during sporogenic development, *Nature Communications* (2021). DOI: 10.1038/s41467-021-25461-2

Provided by John Innes Centre