

Study of the role of the bacteriophage T4 protein, Ndd in the disorganization of the bacterial nucleoid in *E. coli*

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Introduction and objectives

In bacteria, chromosomes are packed in a sub-cellular compartment called the nucleoid, providing rapid access to genetic information for the molecular machineries operating on DNA. Bacteriophages, viruses of bacteria, have selected various mechanisms to specifically hijack key metabolic functions of their bacterial host. Our work focuses on the mechanism by which the T4 lytic phage disorganizes the nucleoid of its host, *Escherichia coli*. Studies have shown that the expression of a single gene in its genome, the Nucleoid Disorganization Deficient (nnd) gene, is necessary and sufficient to induce this disorganization phenotype and subsequent bacterial death of the bacteria within minutes. The high toxicity associated with Ndd expression prevented researchers in the 1990s from investigating the molecular mechanism behind this intriguing phenomenon. The aim of this project is to study the role of Ndd on bacterial nucleoid disorganization and its relevance for the phage lytic cycle.

Materials and methods

We have developed an easily manipulated inducible system enabling us to study changes in nucleoid organization upon Ndd production using advanced genomic technologies (ChIP-seq or, chromosome conformation capture, Hi-C) and cell biology (high-resolution microscopy) approaches.

Results, discussion and conclusion

These experiments confirmed some observations of previous work, but also showed that nnd expression a disruption of the nucleoid at different scale level. These observations led to the hypothesis that Ndd binding to the genome is at the origin of these perturbations. ChIP-seq experiments revealed a strong association of Ndd at several loci in the bacterial genome. High-resolution microscopy and Hi-C enabled us to characterize in detail the internal disorganization of the nucleoid, observing that the long-range organization and the gene organization of the *E. coli* genome into domains was impacted. Nucleoid of Ndd treated cells form small globules expelled from cell center and laying on the membrane. These results open the way to the study of Ndd function during lytic T4 phage cycle.

Mots clés : *E. coli* - Ndd - nucleoide - phage.

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