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Whole Genome DNA Methylation (Methylome) Analysis and Role of Dam DNA Methyltransferase in the life-cycle of an Entomopathogenic Bacterium

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Background: DNA methylation is an epigenetic mechanism involved in the pathogenicity of several major bacterial pathogens. It can decrease the affinity of some transcriptional regulators to their binding site, leading to sub-populations expressing or not various genes, depending on the DNA methylation state. Dam DNA methyltransferase is widespread in *Gammaproteobacteria* and methylates the adenine of GATC sites.

Objectives: The role of Dam was investigated in *Photorhabdus luminescens* during its symbiosis with a soil nematode and during its pathogenic stage in insects.

Methods: SMRT sequencing (PacBio), which allows identification of the DNA methylation of the whole genome (methylome), RNAseq and phenotypic analysis were performed in a *P. luminescens* strain overexpressing Dam.

Results: Dam overexpression caused a decrease in motility whereas it increased biofilm formation. While symbiosis ability of the Dam overexpressing strain was not significantly different from that of a control strain, the nemato-bacterial complex displayed an impaired pathogenicity in insect, as also observed after direct insect injection of the bacteria alone. Transcriptomic analysis revealed that the observed phenotypes were related to differences at the transcriptional level. More than 99% of the GATC sites of the genome were found methylated and DNA methylation levels did not change over growth kinetics. However, the Dam-overexpressing strain displayed more methylated GATC sites than the control and most of these sites were located in promoter regions. These sites may be involved in the observed differences in phenotypes and gene expression and provide clues to understand the involvement of Dam DNA methylation in *P. luminescens* life-cycle.

Key words: Epigenetics, DNA methylation ; Gene regulation