IMG

Institute of Molecular Genetics
of the Czech Academy of Sciences

Lecture

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"DNA topology perturbation and epigenetic modification impact gene expression and intracellular survival of M. tuberculosis"

The bacterial genome is supercoiled, compacted, and condensed into a nucleoid by the combined action of topoisomerases and nucleoid associated proteins (NAPs). We have used a combination of approaches to study the function of both topoisomerases and NAPs in M.tuberculosis. To understand their cellular role, and to target them, we have developed inhibitors and constructed conditional knock down strains disturbing their cellular function and down regulate the expression, respectively. The genetic and chemical perturbation of the DNA topology of the organism has provided insights on new intervention strategies against the pathogen. By structure based design we have developed small molecule inhibitors of HU, an essential protein of M. tuberculosis. The inhibitors bind to the DNA binding cleft in the protein and displace DNA, de-compact the nucleoid and inhibit M.tuberculosis growth. Chemical probing using the inhibitors reveal the importance of HU regulon to the organism. HU is modified extensively by post- translational modifications, that include acetylation, phosphorylation, succinylation and methylation, influencing the bacterial gene expression. Some of these epigenetic modifiers impact the host genome dynamics and intracellular survival of the pathogen. I will describe the function of one such bacterial effector- a methyl transferase that intercepts and reprograms host epigenetics and downstream signaling to ensure better survival of the pathogen in the hostile intracellular environment.

The seminar will be held

on Thursday 1st June 2023 at 14:00

in the Lecture room 0.195 at IMG

(Institute of Molecular Genetics of the Czech Academy of Sciences, Vídeňská 1083, Prague 4)