





PhD Program in Molecular Biomedicine

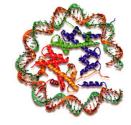
Thursday, March 7th 2019 - 4:00 pm

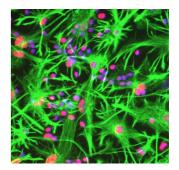
Seminar room, I floor, Q Building – Via Giorgieri 5

Prof. Tim Tolker-Nielsen

Costerton Biofilm Center Department of Immunology and Microbiology Faculty of Health and Medical Sciences University of Copenhagen, Denmark

Cyclic di-GMP signaling in Burkholderia cenocepacia





Abstract

Recent work indicates that the molecule cyclic diguanosine monophosphate (c-di-GMP) is a second messenger that regulates various cellular processes in bacteria, including biofilm formation, virulence, stress responses and motility. The c-di-GMP content in bacteria is determined by diguanylate cyclases (DGCs) that synthesize c-di-GMP and phosphodiesterases (PDEs) that degrade c-di-GMP. In addition to their catalytic domain the DGCs and PDEs often contain sensory domains that are thought to enable translation of diverse (by and large unknown) environmental cues into c-di-GMP levels. The c-di-GMP binds to effectors resulting in the activation or repression of specific cellular processes. Bacteria can typically synthesize dozens of different DGCs and PDEs, but it is unknown how they can deploy a given subset of them to produce a desired phenotypic outcome without undesired cross talk between c-di-GMP-dependent systems. A detailed understanding of the regulatory mechanisms that are involved in c-di-GMP signaling is essential for the development of measures to control bacteria in diverse settings. Using the opportunistic pathogen Burkholderia cenocepacia as model organism, we have found that the production of biofilm-stabilizing exopolysaccharide in this bacterium is regulated by c-di-GMP via the PDE RpfR, the sigma factor RpoN, and the two transcriptional regulators BerA and BerB. Furthermore, we have obtained evidence that virulence of *B. cenocepacia* is regulated by c-di-GMP via the phosphodiesterase activity of the Bcal2449 PDE/DGC protein.

