Universität Basel

Research Project

Cyclic Di-GMP signaling in cell behavior and reproduction (Bonus of excellence)

Project funded by own resources

Project title Cyclic Di-GMP signaling in cell behavior and reproduction (Bonus of excellence)
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Organisation / Research unit
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Project start 01.04.2013
Probable end 31.03.2016
Status Completed
Lay summary:ăPathogenic and non-pathogenic bacteria exist in two fundamentally different life styles, a single cell, free-living, so-called planktonic state and a multicellular, surface adherent and matrix embedded state, which is generally referred to as biofilms. In pathogens, biofilms are generally associated with reduced virulence and increased persistence mechanisms, which allow bacteria to counter and survive the attacks by the host immune system and by antimicrobial agents during chronic infections. Bacterial biofilms are the primary cause of chronic infections and of resulting infection relapses. To be able to interfere with bacterial persistence it is vital to understand the molecular details of biofilm formation and to define how motile planktonic cells transit into surface-grown communities. The nucleotide second messenger cyclic di-guanosinemonophosphate (c-di-GMP) has emerged as a central regulatory factor governing bacterial surface adaptation and biofilm formation. Although c-di-GMP signaling may well represent the Achilles heel of bacterial communities, c-di-GMP networks in bacterial pathogens are exquisitely complex and an integrated cellular system to uncover the details of cdGMP dynamics is missing. To quantitatively describe cdGMP signaling we propose to exploit Caulobacter crescentus, an organism with a simple bimodal life-style that integrates the sessile-motile switch into its asymmetric division cycle. We aim to: 1) identify the role and regulation of all diguanylate cyclases and phosphodiesterases that contribute to the asymmetric cellular program with the goal to model the temporal and spatial distribution of cdGMP during development; 2) identify and characterize c-di-GMP effectors, their downstream targets and cellular pathways; 3) elucidate how c-di-GMP coordinates cell differentiation with cell growth and propagation; 4) unravel the role of c-di-GMP as an allosteric regulator in mechanosensation and in rapid adaptation of bacteria to growth on surfaces. We propose a multidisciplinary research program at the forefront of bacterial signal transduction that will provide the molecular and conceptual framework for a rapidly growing research field of second messenger signaling in pathogenic bacteria.
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2291915	Jenal, Urs	Pfohl, Thomas, Professor	Departement Chemie, University of Basel	01.04.2013	31.03.2016
2291919	Jenal, Urs	Schirmer, Tilman, Professor	Biozentrum, University of Basel	01.04.2013	31.03.2016