Chemical Biology Approaches for Biofilm Eradication

Date: 09 Sep 2016 Friday
Time: 4pm
Venue: Classroom 1, SBS

Abstract

A bacterial biofilm is a surface attached community of microorganisms embedded in and protected by an extracellular matrix of self-made biomolecules. The US National Institute of Health (NIH) has estimated that 65-80% of all microbial infections involve bacterial biofilms. Biofilm-based bacteria can evade the otherwise detrimental actions of immune responses and develop into chronic infections. Because the present day’s armory of conventional antimicrobials cannot efficiently eradicate biofilms, there is an urgent need to understand the fundamental mechanism of antibiotic resistance by biofilms. One major obstacle to study biofilm physiology is the heterogeneity in biofilms, which often confounds our efforts to target specific aspects of biofilm biology. Bis-(3’-5’)-cyclic dimeric GMP (c-di-GMP) is a global, intracellular secondary messenger that controls biofilm differentiation. High intracellular levels of c-di-GMP stimulate bacteria to form biofilms by enhancing synthesis of adhesive structures and biofilm matrix components while low intracellular levels facilitate motility and chemotaxis. The heterogeneity in biofilms often hinders the application of systems biology tools (e.g. transcriptomics and proteomics) in studying biofilm physiology. Here, we applied stable isotope labeling by amino acids in cell culture (SILAC) technology to selectively label the proteome from different subpopulations of biofilms. We found that type IV pili and quorum sensing (QS) are essential for the development of colistin-tolerant cells within P. aeruginosa biofilms. Applying dispersal agents that can reduce intracellular c-di-GMP content significantly reduces the development of colistin-tolerant cells in P. aeruginosa biofilms. We discovered a P. aeruginosa self-produced glycosyl hydrolase, PslG, which is able to trigger biofilm disassembly by disrupting exopolysaccharide matrix.