48c Signaling in Biofilms: Regulation and Biofilm Inhibitors

Andres Barrios, Youngsoon Um, Moshe Herzberg, Joanna Domka, William E. Bentley, and Thomas K. Wood

Bacterial biofilms are sessile communities with high cell density that are ubiquitous in natural, medical, and engineering environments. Currently, there is an explosive amount of biofilm research, most of it with the ultimate aims of its prevention, control, or eradication. By studying the genes that are differentially expressed in biofilms as well as those that are regulated by plant-derived biofilm inhibitors, we have determined that the cross-species, quorum-sensing signal AI-2 induces biofilm formation 30-fold in E. coli K12 by increasing expression of 67 genes, primarily those associated with chemotaxis, motility, and flagellar synthesis including the specific motility loci qseBC and flhD. DNA microarrays also helped us to determine this induction of biofilms was via the completely uncharacterized protein B3022 and that this protein was the master regulator of QseB. Through microarrays, we also discovered the protein which exports AI-2 (YdgG) which has been theorized to exist but never found; deleting ydgG caused 31% of the bacterial chromosome to be differentially induced and 7.6% of the genes were repressed due to trapping AI-2 inside the cell. YdgG not only negatively modulates expression of flagella- and motility-related genes but also all the other known products essential for biofilm formation: 4 known operons for flagella synthesis and motility (flgABCDEFGHIJ, fliEFGHIJK, fliLMNOPQR, and motABcheAW), adhesion determinants (type 1 fimbriae and the autotransporter protein Ag43), curli production, colanic acid production, and production of _-1,6-N-acetyl-D-glucoseamine polysaccharide adhesin. These studies also led us to discover that both sulfur and tryptophan are important for biofilm formation and that a stationary-phase signal, indole, helps to regulate biofilm formation. There are few known natural compounds which inhibit biofilm formation while not affecting cell growth, but the quorum-sensing antagonist (5Z)-4-bromo-5-(bromomethylene)-3-butyl-2(5H)-furanone (furanone) from the marine alga Delisea pulchra inhibits biofilm formation in E. coli without inhibiting its growth. By screening 13,000 plant extracts, another three potent biofilm inhibitors have also been found, and the DNA microarrays have been used to gain insights into how these compounds function as well as to how biofilms may be controlled.