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**Deciphering Cell Signaling in Bacterial Biofilms: The Role of Indole**

Bacterial biofilms are sessile communities with high cell density that are ubiquitous in natural, medical, and engineering environments; they are fascinating since they are primitive tissues with an advanced chemical communications network. Currently, there is an explosive amount of biofilm research, most of it with the ultimate aims of biofilm prevention, control, or eradication. Since the chromosome of the gut bacterium *E. coli* has been sequenced, we are able to discern which of its genes are turned on with various stimuli, including what genes are turned on in biofilms. By studying these 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 is the master regulator of what was considered the first protein in a regulon, 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 β-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 by binding to a receptor for homoserine lactones. From this we discovered that bacteria eavesdrop by listening to signals of other bacteria, and this helped us to develop more potent biofilm inhibitors of pathogenic bacteria based on indole. There are few known natural compounds which inhibit biofilm formation while not affecting cell growth, but the quorum-sensing antagonist (5*Z*)-4-bromo-5-(bromomethylene)-3-butyl-2(5*H*)-furanone (furanone) from the marine alga *Delisea pulchra* inhibits biofilm formation in *E. coli* without inhibiting its growth. Again, using the DNA microarrays to see how such inhibitors function, we have gained insights into controlling biofilm formation and have learned how bacteria are influenced from signals from their human hosts.