Current Topics

Bacterial Amyloids Appear To Play Role in Biofilms, Perhaps other Diseases

Because many types of bacteria depend on amyloid-rich curli to stick to host surfaces, disrupting these structures might open a new avenue for combating biofilms. Amyloid structures, which consist of aggregated fibers of insoluble protein in web-like sheets, are a substantial part of what makes curli so good at this task. Moreover, in addition to enhancing how well cells stick to surfaces, the aggregated fibers within curli help them to resist heat and chemical damage. More and more microbiologists admit to being intrigued by amyloid structures.

Whereas for human diseases “amyloid formation is a biological mistake, in Escherichia coli there’s a set of genes that encode the formation of these fibers,” says microbiologist Scott Hultgren of Washington University (WU) School of Medicine in St. Louis, who calls them “highly conserved machines.” Hultgren, Jeffrey Henderson, and their collaborators recently identified and patented a set of proprietary small molecules that can inhibit amyloid formation in E. coli, thus blocking the genesis of biofilms. Their report appears in the December 5, 2009, Nature Chemical Biology (5:913–919).

The amyloid structure of curli was revealed nearly a decade ago by Matthew Chapman, then a postdoc at WU School of Medicine and now at the University of Michigan in Ann Arbor. Finding functional amyloids in bacteria was then quite a surprise. Before that, amyloid structures, found in the central nervous system, were associated with patients having Alzheimer’s disease and a variety of other neurodegenerative diseases. Nobody expected to find the scourge of old age serving an important role in bacteria from an entirely different domain of life. “I think it’s probably something that most bugs have the capability to do,” Chapman says, referring to bacteria. “Biofilms in nature are chock full of amyloids.” Adds Henderson, “There’s some value in having an organism that intentionally makes them.”

Observing microbial amyloids may reveal insights about dysfunctional amyloids from other organisms, including humans, he points out.

During the past decade, researchers continued to identify functional amyloids in both bacteria and eukaryotes, including in human skin, fungi, and silkworms. Recently, for example, a research group led by Roberto Kolter at Harvard Medical School in Boston identified the protein TasA as a major functional amyloid in Bacillus subtilis biofilms. “Amyloid formation may be a common mechanism to attain architectural complexity in biofilms,” note Kolter and his collaborators in their report, published in the February 2, 2010, Proceedings of the National Academy of Sciences (107:2230–2234).

Interrupting the actions of amyloids could help to keep pathogens from forming biofilms, one way by which they become persistent and also resistant to antibiotics, according to Hultgren and Henderson. For instance, urinary tract infections typically become chronic after E. coli form biofilms there. The small molecules that they are evaluating obstruct colonization and thus prevent biofilms from forming without killing the bacteria. Thus, this approach is expected to minimize virulence and could also impede the likelihood that the bacteria develop resistance to antibiotics used for therapy, Hultgren says.

In terms of human health, one fascinating—and possibly sinister—quality of functional amyloids is their ability to self-assemble after a seed, or template, is established on a host cell or other surface. Could this be how amyloids instigate neurodegenerative diseases? Could bacterial amyloid templates trigger those diseases? One researcher in this field professes to being “very excited” by this question, which he adds is discussed only “behind closed doors.” However, there is no evidence for this mechanism being at work in neurodegenerative diseases, he adds.

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Bacterial Cells Engineered to Blink in Synch

Fluorescence-tagged Escherichia coli cells can be made to “blink” in unison by means of a constructed network of genes and proteins that coordinates oscillations within the growing cell population, according to Jeff Hasty and colleagues from the University of California, San Diego (UCSD) in La Jolla. In 2008 the team produced “flashing” microbial cells, but now they endowed those flashing bacteria with the capacity to synchronize their colony-building efforts.

This new form of a “molecular clock” was assembled in E. coli from