Session 5: Synthesis and Assembly and Function of the Biofilm Matrix

Tuesday, October 9, 2018, 10:50 am - 12:45 pm

Inhibition of Curli Assembly & Biofilm Formation in *E. coli* by Human Chaperone-Like Proteins

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Abstract Body:

*Escherichia coli* & related enteric bacteria form communities called biofilms that are resistant to host immune defenses & antibiotic treatment. Therefore, alternative approaches to conventional antibiotic therapy are urgently needed to treat biofilm related infections. The biofilm matrix is composed of exopolysaccharides, extracellular DNA & protein polymers commonly known as amyloid fibrils. Curli are amyloid fibrils produced in *E. coli*. The major subunit of the curli is CsgA protein that is capable of forming amyloid fibrils under *in vitro* conditions. An innovative strategy to prevent biofilm formation is to inhibit amyloid aggregation on the cell surface. The Chapman Lab has identified a periplasmic protein called CsgC that keeps CsgA in soluble form & assist its efficient secretion to the cell surface where it assembles into curli amyloid fibers. CsgC is structurally similar to the human amyloid precursor protein: transthyretin (TTR). TTR and CsgC are both stably-folded, β-sheet rich proteins. We hypothesized that TTR can prevent bacterial amyloid formation & thus could reduce amyloid-associated biofilm & bacterial colonization inside the human host. In the present study, found that human wild-type tetrameric TTR (WT-TTR) and an engineered monomer (F87M/L110M) [MTTR], can inhibit amyloid formation by CsgA. The biological significance of the TTR-CsgA interaction was demonstrated by the ability of TTR to inhibit amyloid-dependent biofilm formation by *E. coli* & *B. subtilis* with no apparent bactericidal or bacteriostatic effects (Jain et al *PNAS* 2017). These findings prompted us to investigate the anti-amyloid characteristics of other structural homologs of TTR & CsgC. We found that β2-microglobulin, a human protein & structural homolog of TTR, is also capable of inhibiting biofilms without killing the bacteria. The observations suggest that TTR & its homologs can act as a broad spectrum anti-amyloid agents & might be utilized to enhance antibiotic efficacy in infections associated with significant biofilm formation.