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Bioinformatic opportunities in periodontal pathogens' export machineries

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Aggregati bacteriactinomycetemcomitans is a Gram-negative bacterium that inhabits the mouths of one-third or more of the population. It has been linked to aggressive periodontitis, a disease that mostly affects the central incisors and first molars of African American adolescents. To colonize the oral cavity, cause disease, and persist in a host, this bacterium maintains an arsenal of virulence factors including exopolysaccharide, fimbriae and leukotoxin. The extracellular polysaccharide of A. actinomycetemcomitansis a major component of its biofilm and contributes to colonization, biofilm formation and maintenance, and pathogenesis. Among the toxins that have been described forA. actinomycetemcomitans, leukotoxin (LtxA).The primary role of LtxA is in immune evasion by targeting only certain WBCs, the cells that are most immunologically relevant. The Widespread Colonization Island discovered in 2001 consists of a 14 gene operon and was shown to contain the flp gene, whose product is responsible attachment to abiotic surfaces, aggregation, and tight adherence. Tooth adherence and biofilm persistence is a pre-requisite for survival in the oral domain and thus understanding the mechanism of export of these macromolecules to the extracellular milieu is of critical importance. This export could be carried out by simple or very complex export machineries whose structural architecture is undetermined. Three dimensional structures of a few members of the protein complex responsible for their export is currently known. Because of their complexity, it has become necessary to carry out a reductionist approach in the structure determinations. My laboratory and others' are actively pursuing the structure determination through crystallographic analysis. However, bioinformatics analyses on these structures are at their infancy. This area of research is prime for such an undertaking and in this presentation I will discuss the biological relevance of these export machineries. This research is partially supported by USPHS Grant DE027125.