

BCHM 421/422 Project Outline

Project #1: Many bacteria use long adhesion proteins (adhesins) to make initial contact with the surface on which they will bind, infect, and form biofilms. Attachment to the surface is through specific ligand-binding domains at the far end of the adhesin. We have shown in one system the potential to block infection/colonization with antibodies and small molecules that block the ligand-binding domains. We would like to extend this anti-microbial approach to other bacteria, including some human pathogens like *Vibrio cholera*, *Legionella pneumophila* and *Acinetobacter baumannii*. To do so we need to structurally characterize their ligand-binding domains and how to block them with specific ligands.

Supervisor: Peter L. Davies

Project Title: Antimicrobial strategies by blocking bacterial adhesion

Keywords (3-5):

1. Bioinformatics
2. DNA Cloning
3. Recombinant protein purification
4. X-ray crystallography
5. Ligand identification

Project Goals: Produce and purify adhesin ligand-binding domains. Characterize the proteins and identify their ligands. Place in crystallization trials and solve protein structures with and without ligands bound. Develop adhesion blocking strategies using antibodies and ligand competitors.

Experimental Approaches: Domain mapping using bioinformatics. Design of codon-optimized genes to produce recombinant ligand-binding domains in bacteria. Purification of recombinant proteins for crystallization. 3-D structure determination by X-ray crystallography. Identification of binding partners for the domains using microarrays. Design and test adhesion blocking strategies.

Reference: Guo, S., Stevens, C.A. Vance, T. D.R., Olijve, L.L.C., Graham, L.A., Campbell, R.L., Yazdi, S.R., Escobedo, C., Bar-Dolev, M. Yashunsky, V., Braslavsky, I., Langelaan, D.N., Smith, S.P., Allingham, J.S., Voets, I. K., Davies P.L. (2017) Structure of a 1.5-MDa adhesin that binds its Antarctic bacterium to diatoms and ice. *Sci Adv.* 2017 3(8):e1701440. doi: 10.1126/sciadv.1701440 [PubMed: 28808685](https://pubmed.ncbi.nlm.nih.gov/28808685/)