Cytochrome bd is required for uropathogenic Escherichia coli pathogenesis and biofilm development

Biofilm formation is a common bacterial survival strategy
- Bacteria form multicellular communities known as biofilms in the natural environment and during infection
- Bacteria in biofilms are highly resistant to antibiotics and immune systems
- Biofilms are a major contributor to chronic bacterial infection and treatment failure

Oxygen is a regulator of UPEC biofilms
- Uropathogenic Escherichia coli (UPEC) encounters oxygen gradients during its infectious cycle
- UPEC requires aerobic respiration to infect the urinary tract
- Biofilm formation is a critical aspect of virulence in the urinary tract
- Oxygen availability regulates UPEC biofilm formation

Quinol oxidases are expressed in spatially distinct subpopulations
- Cytochrome bd and cd are inversely organized along the oxygen gradient
- UPEC organizes into differentially respiring subpopulations in biofilms

Hypothesis
Differentially respiring subpopulations regulate biofilm development and stress tolerance
Loss of cytochrome bd disrupts biofilm formation and UTI pathogenesis

Loss of cytochrome bd increases biofilm sensitivity to antibiotics

Conclusions
- Quinol oxidases are spatially organized along biofilm oxygen gradients
- Cytochrome bd is a central regulator of biofilm development
- Loss of cytochrome bd increases biofilm sensitivity to antibiotics by influencing the accumulation of antibacterials and other chemical signals
- Inhibition of cytochrome bd is a potential therapeutic strategy

Future Directions
- Identify mechanisms by which cytochrome bd promotes host colonization
- Define mechanisms by which cytochrome bd influences ECM production
- Investigate inhibition of cytochrome bd as a potential anti-biofilm therapeutic approach

Funding: NIH R01AI137322, P2000121957, T25MI007347, and F30AI150077.