Deoxycholate-Enhanced *Shigella* Virulence Is Regulated by a Rare $\pi$-Helix in the Type Three Secretion System Tip Protein IpaD

ABRAM BERNARD
Shigella

Pathogenicity

- Spread through the fecal oral route
- Up to 90 million cases of shigellosis per year with 100,000 deaths worldwide
- 10-100 organisms needed for infection

Image Credits: 1) David Goulding, Wellcome Trust Sanger Institute, Wellcome Images 2) Health Department, Laport County, IN (2016)
Virulence Requires the Type III Secretion System

Type III Secretion System (T3SS) utilizes the Type III Secretion Apparatus (T3SA)

- Forms a direct conduit between bacterial and host cytoplasm
- Required for bacterial virulence
- Requires activation and maturation for invasion
- Interruption would prevent infection

Schroeder, GN, Clinical Microbiology Reviews (2008)
DOC Sensitivity

IpaD

S. flexneri

HeLa

DOC

Invasion
Structure Function Investigation
Into IpaD Bile Salt Sensing
Mutations Restore Secretion Control and Pore Formation

Loss of secretion control
  ◦ Protein leakage
Loss of pore forming ability
Non-Invasive

Regains Secretion control
  ◦ Reduces leakage
  ◦ Inducible
Regains pore forming ability
Invasion near wild type ability
  ◦ Increase when exposed to DOC
Triple Mutation Alters DOC sensitivity
IpaB-IpaD binding is less sensitive to DOC
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