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Limiting Iron Acquisition of E. Coli With Anti-TonB1 and AntiTonB2

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Nova Southeastern University Protein Modelling Class

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Resolution

- 3.3 angstrom resolution of crystal structure of TonB carboxyl – terminal domain in complex with FhuA

Format: helix backbone

RP:

Description:

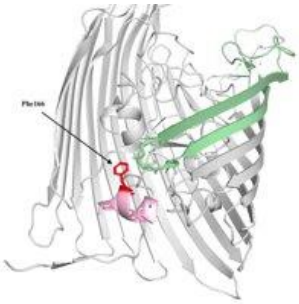
Iron is a prized commodity in the biological world. So much so that bacteria infect humans and other animals to obtain iron. In the human body, it can serve as a redox catalyst for a wide array of cellular processes as it cycles between two oxidation states, Ferrous (Fe^{2+}) and Ferric (Fe^{3+}). Acquiring iron is a central part of a bacteria's survival and bacteria have been found to secure iron from their hosts through many different mechanisms. In fact, iron acquisition is the purpose for infection and facilitates illness in humans. Here, the production of siderophores by *E.coli* is further explored. Siderophores, produced by gram-positive and gram-negative bacteria are small ferric iron chelators that have an incredibly high binding affinity to iron. Transferrin, the protein in the human body that binds and transports iron throughout the body has as association constant of 10^{36} while siderophores have an association constant of at least 10^{50}, easily outcompeting transferrin in the blood stream. FhuA is a ferrichrome protein located in the membrane of *E.Coli*, responsible for siderophore binding and completion of the iron transport into *E.coli*. For FhuA to successfully bring in iron from a siderophore, another protein, TonB, must attach to a region of FhuA that faces inside E.coli called the Ton Box. A protein model was designed to bind to the Ton Box region of FhuA with higher affinity by altering polar and charged residues to nonpolar or aliphatic residues that were present in the original TonB protein. Specifically, the regions 166-170 and 225-235 in TonB contained new changes in residues as they directly participated in

Commented [ESL1]: Nice attention-grabbing introduction – makes the reader see the significance of the molecular story right away

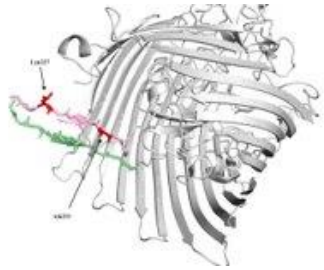
Commented [ESL2]: Explain what you mean by a "central part of pathogenesis better – do you mean this is important for bacteria being able to cause illness?"

binding with Ton Box of FhuA. Three mutations, R166F, N227L, K231A were made to create two new proteins, Anti-TonB1 and Anti-TonB2.

Specific Model Details:



Model 1: Anti-TonB1, residues 166-170 were manipulated with the mutation N166F. This region of TonB interacts with residues 588-592 of FhuA. Amino acid asparagine, polar and uncharged at 166 of TonB was changed to phenylalanine, a large polar uncharged residue. The backbone of TonB was colored lightpink, with the mutated amino acid colored red, and the Ton Box region involved in binding colored in light green. The rest of FhuA is colored light gray.



Model 2: Anti-TonB2, residues 225-235 of TonB were manipulated with mutations N227L and K231A. Amino acids Asp227 and Lys231 were changed to Leu227 and Ala231. Changing the previously charged and polar amino acids to nonpolar amino acids would hypothetically help Anti-TonB stronger to Ton Box. The backbone of Ton Box region that binds to TonB is colored light green, with the mutated residues colored in red. The backbone of TonB is colored light gray, with the original TonB backbone colored in light pink. Additional References

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