Elucidating the structure and function of the zinc uptake regulator (Zur) protein

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Neisseria gonorrhoeae cause the sexually transmitted disease gonorrhea. Gonorrhea is a debilitating disease that affects mucous membranes in the body, and if left untreated can lead to infertility, ectopic pregnancy, and even increases the chances of acquiring human immunodeficiency virus (HIV) and other life-threating diseases. Currently, there are no vaccines against *N. gonorrhoeae.* Due to rapidly emerging resistant strains of *N. gonorrhoeae*, ceftriaxone remains the only antibiotic for treatment against gonorrhea. According to the 2019 Antibiotic Resistance Threats Report, every year this obligate human pathogen causes an estimated 550,000 new drug-resistant infections in United States alone. There is a desperate need for novel antibiotics and therapeutics against *N. gonorrhoeae*.

Transition metals, such as zinc, are essential for an organism's survival. Our body sequesters zinc using calprotectin and psoriasin so that the invading bacteria are unable to acquire them. The Gram-negative *N. gonorrhoeae* overcomes this nutritional immunity by expressing transport proteins such as TdfH and TdfJ on its surface to mediate piracy of zinc from calprotectin and psoriasin. Once zinc is imported into the cell, it binds to the zinc uptake regulator (Zur) protein which promotes its dimerization and subsequent binding to the Zur binding consensus motif (Zur box) on the bacterial chromosome. This results in suppression of zinc-responsive genes in *N. gonorrhoeae*. The goal of this project is to characterize the structure of Zur in complex with is DNA recognition sequence, which would bring us closer to developing therapeutics against this obstinate pathogen.