Structural insight into the transferrin-iron import system from pathogenic Neisseria

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N. gonorrhoeae and N. meningitidis are obligate human pathogens that cause gonorrhea and meningitis, respectively. Vaccines are available against N. meningitidis; however, they are not universally effective and there is currently no vaccine against N. gonorrhoeae. And the rapid emergence of drug resistance in these pathogens has elevated their threat to public health, underpinning an immediate need to find better countermeasures. Essential surface machineries are promising therapeutic targets against Neisseria, one of which is called the Tbp system consisting of a transporter called TbpA and a co-receptor TbpB. Together, these proteins mediate iron scavenging from human transferrin (hTF). Based upon previous studies it's known that the Tbp system is crucial for Neisseria virulence and second, in mouse models, it shows a very nice immune response against the pathogen. So, this system has the potential to offer a broad protection against the bug. Despite knowing the structures of both receptor proteins for more than a decade, exactly how they coordinate with one another and the mechanism for how iron is extracted/imported remain unknown. In our recent studies, we have determined the cryo-EM structures of the double complex between TbpA+holo-hTf and the triple complex between TbpA+TbpB+holo-hTF. Our structural studies have provided new insight into their interactions with each other provides the framework for deciphering the mechanism for iron piracy.