Bacterial protein transport machinery: An emerging therapeutic target for small molecule inhibitors

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Abstract:

Small molecule based drug development methods are potent therapeutic strategies to combat various diseases related to human health. Among these diseases, bacterial infections are becoming very challenging to treat due to increasing antibacterial resistance against many known antibiotics.[1] The development of resistance in bacteria is a natural evolutionary process which cannot be stopped but can be slowed down using appropriate targeting strategies. One of the strategies is to target the protein transport machinery like Signal Recognition Particle (SRP) which is known to be responsible for transportation of about 30 percent of the membrane proteins in bacteria.[2] The functional SRP cycle is a GTP dependent process where two GTPases (Ffh and FtsY) interact with each other. Interaction of the GTPs with Ffh and FtsY are very crucial to maintain SRP cycle active.[3] Hence, we propose to exploit this unique cellular machinery (SRP) by designing modified forms of GTP which upon interaction will possibly form a non-dissociable complex of Ffh and FtsY. This will compromise protein transport via the essential SRP pathway and might lead to bacterial cell death. Our current efforts in this direction will be discussed in more detail during the presentation.

References and Notes:

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3. Zhang X.; Schaffitzel C.; Ban N.; Shan S. O. *Proc. Natl. Acad. Sci. USA*. **2009**, 106, 1754-1759