論文の内容の要旨

Controlling *P. aeruginosa* quorum sensing and its interaction with the host cells by synthetic autoinducer analogs

(合成オートインデューサー類似体による緑膿菌クオラムセンシングと宿主細胞との相互作用の制御)

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Antibacterial agents currently in use face two challenges. On one hand, they are designed to target the vital processes of the bacteria, thus leading to the bacteria developing resistance against them, and, on the other hand, they are designed against planktonic bacteria. It has been known for a while now that most bacteria live in organized communities called Biofilms. Current antibacterial agents are unable to get inside these biofilms and are ineffective against them. There is therefore a dire need for antibacterial agents that are effective against biofilms. Small molecules that inhibit Quorum sensing- a signaling mechanism utilized by bacteria, for their community behavior might fulfil that requirement.

Quorum sensing (QS) is a signaling mechanism used by over 55 different species of proteo-bacteria to organize into matrix embedded sessile communities called biofilms and their signaling molecules are called autoinducers. *Pseudomonas aeruginosa* is a sterling example of QS utilizing bacteria. It is a Gram-negative opportunistic pathogen that causes infections in immuno-compromised patients. It also forms a slimy coat on in-dwelling medical implants/devices. Like most Gram-negative bacteria, *Pseudomonas aeruginosa* has an acyl homoserine lactone (AHL) based QS, with 3-oxo-C_{12}-HSL being its main QS mediator. *Pseudomonas aeruginosa* uses 3-oxo-C_{12}-HSL for production of some of its important virulence factors, formation of biofilms and also for mediating inflammatory reactions in the mammalian host. It is therefore hoped that analogs of 3-oxo-C_{12}-HSL will attenuate the virulence of *Pseudomonas aeruginosa*, prevent the formation of its biofilms and inhibit or modulate the inflammatory reactions in the disease process.

This thesis focuses on the identification of two such analog molecules and their effect on the functions of the 3-oxo-C_{12}-HSL within *Pseudomonas aeruginosa*, its ability to form biofilms and its ability to affect the mammalian host.