Graduate Students Seminar

Department of Chemistry

Sunday, May 12, 2019
Time 16:00
Bldg. 37 Room 202

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Designing a new class of covalent QS inhibitors to target
P. aeruginosa virulence

Bacteria have the ability to communicate with each other and sense their population densities through secretion of small signaling molecules called autoinducers, in a process that is known as ‘quorum sensing’ (QS). These days, the increasing prevalence of antibiotic resistance constitutes a worldwide problem and targeting bacteria through QS inhibition may provide a sophisticated new strategy to engage this issue. P. aeruginosa is an opportunistic pathogen which regulates its pathogenicity through QS. Its main autoinducer, 3-oxo-C12-homoserine lactone (C12), binds to the LasR transcriptional regulator protein and activates a cascade of events that regulates biofilm formation and secretion of virulence factors. By targeting covalently the Cys79 residue inside the LasR binding pocket, irreversible inhibition of the QS in P. aeruginosa can be achieved. In this project, a covalent inhibitors containing Michael acceptors with different chain lengths were designed and their bio-activity was examined. Two of the designed probes were found to bind covalently to LasR but surprisingly none of them were able to reduce pyocyanin production, a hallmark of Pseudomonas virulence. On the other hand, even though some of these probes were partial agonists, they still were able to reduce the bacterial virulence and damage its ability to form biofilms.
References:

