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Control rather than eradication of pathogenic bacteria: Quorum sensing of Vibrio vulnificus

Sang Ho Choi Seoul National University, Republic of Korea

Bacterial pathogenicity involves numerous virulence factors required for successful survival in host environments as well as invasion and destruction of host tissues. The pathogenic marine bacterium *Vibrio vulnificus* is a causative agent of foodborne diseases such as gastroenteritis and life-threatening septicemia. It has been reported that expression of V. vulnificus virulence factors is well-coordinated and regulated by sophisticated mechanisms consisting of many global regulatory proteins. Among them, SmcR, a quorum-sensing master regulator and homologue of V. harveyi LuxR, has been identified and found to play a critical role in the regulation of the V. vulnificus virulence factors. The crystal structure of SmcR reveals that SmcR belongs to the TetR family protein possessing putative ligand-binding pockets. To identify the small molecules which bind to and inhibit SmcR, chemical libraries were screened and a SmcR inhibitor exhibiting the most effective SmcR-inhibition activity was selected and named QStatin. The lack of reduction of intracellular levels of SmcR in QStatin-treated V. vulnificus suggested direct binding of the chemical to SmcR. Isothermal titration calorimetric (ITC) and crystallization analyses confirmed the chemical binding of QStatin into the pockets of SmcR. Although no big conformational changes were observed in the crystal structure, binding of QStatin reduced the DNA binding affinity of SmcR and thereby changed the expressions of SmcR regulon similar to those of SmcR mutants. Accordingly, QStatin significantly inhibits expression of V. vulnificus virulence genes, leading to the decreased mortality of a brine shrimp infected with V. vulnificus. Most interestingly, OStatin attenuates pathogenicity of V. vulnificus, but does not inhibit growth itself at all, unlike existing antibiotics. Consequently, the combined results indicate that QStatin could be a novel lead compound to control QS-mediated pathogenesis of V. vulnificus with the lowest possibility of the appearance of resistant strains.

Biography

Sang Ho Choi is the Director of National Research Laboratory (NRL) of Molecular Microbiology and Toxicology, Director of Center for Food Safety and Toxicology, Director of Foodborne Omics Research Center and has research interest in bacterial pathogenicity.

choish@snu.ac.kr

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