

S5-1.4

Interaction of Quercetin with LasR of *Pseudomonas Aeruginosa*: Mechanistic Insights of the Inhibition of Virulence Through Quorum Sensing

H.V. Grabski and S.G. Tiratsuyan

Department of Medical Biology and Biotechnology, Institute of Biomedicine and Pharmacy, Russian-Armenian University, Yerevan, Armenia

Pseudomonas aeruginosa is one of the most dangerous superbugs for which new antibiotics are urgently needed. This bacterium forms biofilms that increase resistance to antibiotics and host immune responses. Current therapies are not effective because of biofilms. Biofilm formation is regulated through a system called quorum sensing, which includes transcriptional regulators LasR and RhIR. These transcriptional regulators detect their own natural autoinductors. It is known that quercetin inhibits *Pseudomonas aeruginosa* biofilm formation, but the mechanism of action is unknown. In the present study, we tried to analyse the mode of interactions of LasR with quercetin. We show that quercetin has two binding modes. One binding mode is the interaction with ligand binding domain. This interaction is not competitive and it has been shown experimentally. The second binding mode is the interaction with the “bridge”, that involves amino acids from ligand binding domain, short linker region and DNA binding domain. This part has not been shown experimentally, because LasR protein is not soluble. In our model the hydroxyl group of ring A interacts with multiple leucines during the second binding mode. This study may offer insights on how quercetin inhibits quorum sensing circuitry by interacting with transcriptional regulator LasR.