IN SILICO STUDY OF SULFORAPHANE INTERACTION WITH LasR OF P. AERUGINOSA

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One of the most important public health challenges of the 21st century is the search of new preventive or therapeutic anti-infective strategies, based on a combination of the plant-derived quorum-sensing inhibitors (QSI) with anti-inflammatory agents, and immunomodulators without pressure on the selection factors and the effect of dysbiosis [1]. Among the family Brassicaceae crucial secondary metabolites are isothiocyanates, such as sulforaphane (SFN), erucine etc. which have anticancer, anti-atherogenic, hepatoprotective, antimutagenic, antioxidant, antifungal, antibacterial, and bioherbicidal activities [2, 3].

The aim of this work was *in silico* study of the direct interaction of SFN with transcription regulator LasR of signaling network of opportunistic pathogen *P. aeruginosa* and the comparison with N-3-oxo-dodecanoyl homoserine lactone (3OC12-HSL)-LasR complex. The interactions of SFN and 3OC12-HSL with LasR were computationally investigated by methods of molecular dynamic and docking [4], RCSB Protein DataBank etc.

Molecular docking of 3OC12-HSL, one of autoinducers in signaling network of *P.aeruginosa*, was conducted with a monomer LasR receptor, which showed the interaction energy of -7.1 ± 0.6 kcal / mol. The interaction energy of SFN with a LBD LasR monomer was equal to 5.0 ± 0.24kcal / mol. Thus, SFN does not compete with 3OC12-HSL binding site for LasR. Analyze of docking SFN in LasR, after prior binding to a LBD LasR two molecules of 3OC12-HSL, demonstrates that SFN interacts with the interface dimerization of two monomers LasR, activated by its 3-O-C12-HSL, with a high bonding energy (-4.08 ± 0.12 kcal/mol), changing LasR conformation. But SFN asymmetrically interacts with two identical monomers LasR (E and G). A hydrogen bond (3.03 A °) forms between the SFN and the residue Asp 43 of E chain, which is also well established with 9 hydrophobic interactions, involving Leu 125, His 119, Glu 124, Gly 123, Gly 120 (chain E) and Ala 121, Gly 123, Gly 120, His 119 (chain G). SFN increasingly interacts with the chain E, thus impacting on the architecture and breaking the symmetry of the active dimer LasR. This in turn can lead to the shielding of DBD of LasR in the ternary complex and cause the dissociation of DNA from LasR with completion of transcription [5]. Thus, for the first time by docking and binding energies methods are shown, that SFN acts as an QSI, interacting with the dimer LasR, and uncompetitive with autoinducer 3-O-C12-HSL for binding to the LBD and changing the conformation LasR. It demonstrates the benefit of allosteric signal transmission mechanism action of SFN in the regulation of DNA binding and expression of virulence regulating gene. This can be very promising in terms of new management of anti-infective therapy.

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