

Rational Design of *Quorum sensing* Inhibitors Using Docking Strategies

[Alfredo Fuentes-Gutiérrez, Alberto Martínez, José Correa-Basurto, Alicia Reyes-Arellano*]

Abstract— The *quorum sensing* communication system is based on small molecules called autoinducers, which trigger pathogenic effects like biofilm formation. [1] This small molecule signaling construct provides the target for a pharmaceutical chemistry intervention. With the design and synthesis of anti-*quorum sensing* small molecules, the bacteria communication can be blocked. [2] As a result, the pathogenic development is dismantled and additionally the access of antibiotics is promoted. In our group we were able to design and synthesis a pilot series of the heterocyclic compounds as *quorum sensing* inhibitors.

In addition docking strategies were used to explore the binding free energies and binding pose of the heterocyclic compounds on CviR, LasR y MvfR, the receptor proteins in *Chromobacterium violaceum*, and LasR and MvfR in *Pseudomonas aeruginosa* respectively.

To this docking study a set of heterocycles: imidazoline, thiazoline, quinoxalin-2-(1H)-onas, pyridines, benzimidazoles and thiazoles derivatives were used. (Figure 1).

Docking studies allow us to infer the hot-spot for ligand binding on CviR, LasR y MvfR depicting the non-bond interaction of protein-ligand complexes. (Figure 2).

The docking results were compared with other reported ligands showing that our compounds have better affinity properties on the mentioned proteins suggesting as promisory *quorum sensing* inhibitors.[3, 4] (Figure 3)

Currently the above mentioned compounds are being tested in *Chromobacterium violaceum* and in *Pseudomonas aeruginosa*.

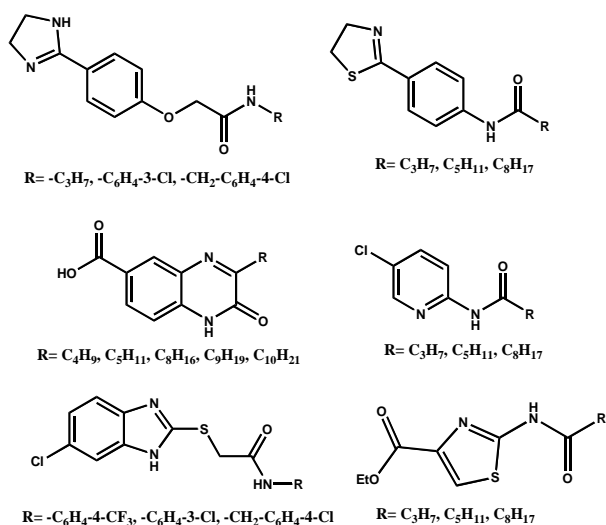


Figure 1. Chemical structure of the heterocycle compounds analyzed by docking.

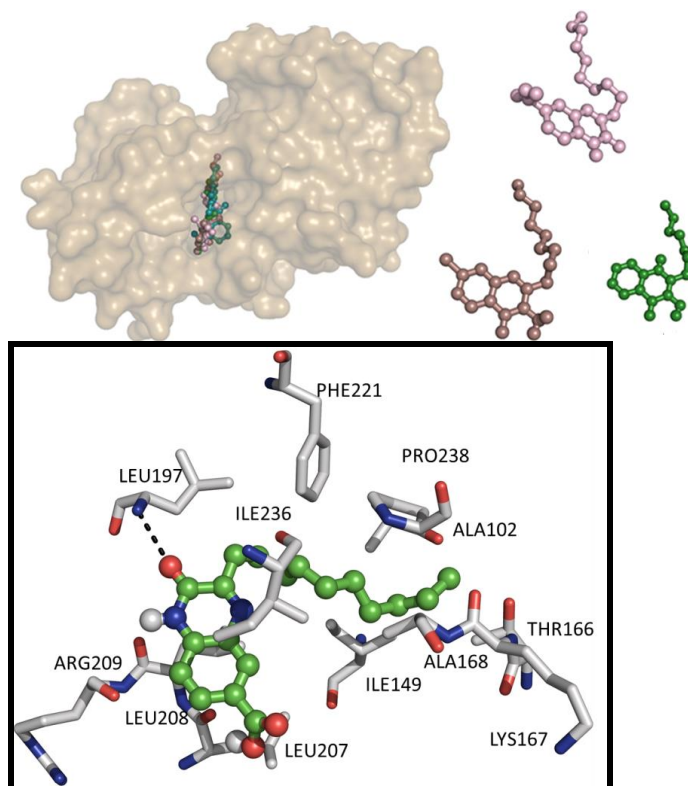


Figure 2. a) Protein Surface representation couple to ligands on MvfR endogen (green), reported ligand QZZ (orange), quinoxalin-2(1H)-one (pink),). b) non bond interactions of protein-ligand complexes for quinoxalin-2(1H)-one.

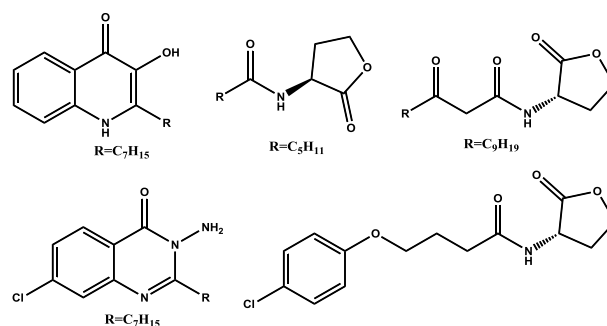


Figure 3. Endogen ligands of MvfR, CviR y LasR (up); know inhibitors of MvfR and CviR(below).

References

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~~Alfredo Fuentes-Gutiérrez~~

Escuela Nacional de Ciencias Biológicas. Instituto Politécnico Nacional
Ciudad de México, México

Alberto Martínez.

Escuela Superior de Medicina. Instituto Politécnico Nacional
Ciudad de México, México

José Correa-Basurto

Escuela Superior de Medicina. Instituto Politécnico Nacional
Ciudad de México, México

Alicia Reyes-Arellano

Escuela Nacional de Ciencias Biológicas. Instituto Politécnico Nacional
Ciudad de México, México