[P8] Investigation of the structure of LecA and multivalent ligands with crystallography and MD simulation

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The increasing number of infections with antibiotic resistant bacteria in hospitals is a serious problem for current medicines. The ability to form biofilms is of the mechanisms bacteria use to acquire resistance against many treatments. Among the many different bacteria is also the pathogen *Pseudomonas aeruginosa(1),* this bacteria also form biofilms. It is an opportunistic pathogen which can be fatal for people with weak immune system. This problem leads to the initiative to discover new targets and new drugs against *Pseudomonas aeruginosa.*

LecA(2) is a homo-tetrameric protein which is known to be crucial for the formation of biofilm and to explain the pathogenicity of *Pseudomonas aeruginosa*. There are some high affinity multivalent (3,4) ligands already published. These compounds are galactosides with different sorts of linkers to connect the galactosyl groups and to make additional contacts. Here we wanted to understand how LecA and the ligands interact and how this explains the different strength of bindings. Some of these multivalent ligands were investigated by us with crystallography and later we studied with MD simulation the system to gain a deep insight in the binding mode and behavior of this ligands. This study helps to explain why this type of ligands shows such a strong binding to the LecA protein. Finally, this allows it to see how these drugs could be optimized in the sense of structure based drug design.

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