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Extended Abstract

In Silico Design of Bacterial *N*-acetylglucosaminidase Inhibitors with Potential Antibacterial Activity †

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† Presented at the 2nd Molecules Medicinal Chemistry Symposium (MMCS): Facing Novel Challenges in Drug Discovery, Barcelona, Spain, 15–17 May 2019.

Published: 14 November 2019

Staphylococcus aureus is a widespread gram-positive pathogen in humans and animals. Autolysin E (AtlE) is an enzyme from *S. aureus* which belongs to the glycoside hydrolase 73 family. It catalyzes the hydrolysis of the β-1,4-glycosidic bond between the *N*-acetylglucosamine and *N*-acetylmuramic acid units of bacterial peptidoglycan [1]. Autolysins play an important role in biofilm formation, cell growth, and reproduction of bacteria, and they are involved in the separation of the daughter and mother cells during vegetative growth and cell division [1,2]. Cells without *N*-acetylglucosaminidases have morphological abnormalities as a result of their reduced ability to increase size following cell division and to expand into the mature morphology [3,4]. We have applied *in silico* methods for the discovery of novel AtlE inhibitors. According to the crystal structures of the AtlE–ligand complexes (PDB ID: 4PI7, 4PI9) [1], structure-based virtual screening was employed for hit identification. Based on the results of virtual screening with Gold and Discovery Studio software, we chose the ligands for the quantitative analysis of their binding interactions to AtlE. The experimental tests with surface plasmon resonance technique (SPR) are currently in progress. Identified hit compounds that interact with AtlE will represent valuable starting points for further development of autolysin inhibitors acting via a novel mechanism leading toward novel antibacterials.

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