Binding modes of teixobactin to lipid II: Molecular dynamics study

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Teixobactin (TXB) is a newly discovered antibiotic, targeting the bacterial cell wall precursor Lipid II (LII). In the present work, four binding modes of TXB on LII were identified by a contact-map based clustering method. The highly flexible binary complex ensemble was generated by parallel tempering metadynamics simulation in a well-tempered manner (PTMetaD-WTE). In agreement with experimental findings, the pyrophosphate group and the attached first sugar subunit of LII are found to be the minimal motif for stable TXB binding. Three of the four binding modes involve the ring structure of TXB and have relatively higher binding affinities, indicating the importance of the ring motif of TXB in LII recognition. TXB-LII complexes with a ratio of 2:1 are also predicted with configurations such that the ring motif of two TXB molecules bound to the pyrophosphate-MurNAc moiety and the glutamic acid residue of one LII, respectively. Our findings disclose that the ring motif of TXB is critical to LII binding and novel antibiotics can be designed based on its mimetics.
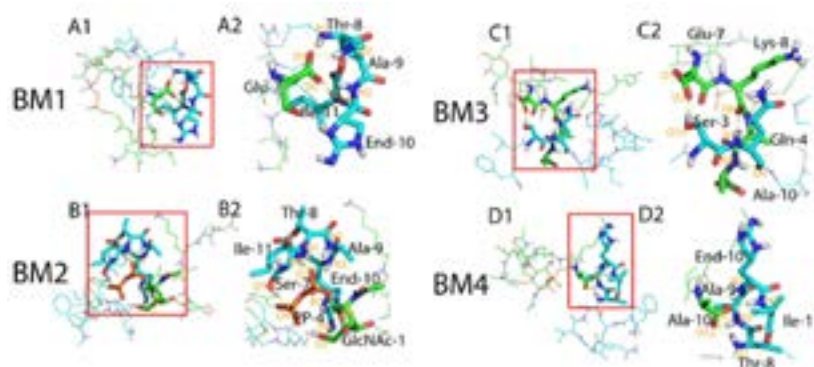
Figure 1: Four binding modes between TXB

Recent Publications

1. Jing-rong Fan, Hong-xing Zhang, Yuguang Mu and Qing-chuan Zheng (2018) Studying the recognition mechanism of TcaR and ssDNA using molecular dynamic simulations. Journal of Molecular Graphics and Modelling 80:67–75.

2. Yang Liu, Yaxin Liu, Mary B, Chan-Park and Yuguang Mu (2017) Binding modes of teixobactin to lipid ii: molecular dynamics study. Scientific Report 7:17197.

3. Nafsa M Hassan, Amr A Alhossary, Yuguang Mu and Chee-Keong Kwoh (2017) Protein-ligand blind docking using QuickVina-W With inter-process patio-temporal integration. Scientific Reports 7:15451.

4. Sheetal Sinha, Liangzhen Zheng, Yuguang Mu, Wun Jern Ng and Surajit Bhattacharjya (2017) Structure and interactions of a host defense antimicrobial peptide thanatin. Scientific Reports 7:17795.

5. Y Miao, X Han, L Zheng, Y Xie, Yuguang Mu, et al. (2016) Fimbrin phosphorylation by metaphase Cdk1 regulates actin cable dynamics in budding yeast. Nature Communication 7:11265.

Biography

Yuguang Mu has more than 20 years of experience in the area of Computational Biophysics. His main researches focuses on research fields, MD simulation method and data analysis method development, DNA dynamics, DNA protein, DNA-counterions interaction study, peptide, protein folding, unfolding study, especially aimed at folding, misfolding mechanism which could lead to amyloid fibril, RNA dynamics and folding study.

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