عنوان مقاله:

Design of peptides interfering with iron-dependent regulator (IdeR) and evaluation of Mycobacterium tuberculosis growth inhibition

محل انتشار:

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خلاصه مقاله:

Objective(s): Tuberculosis (TB), a disease caused by Mycobacterium tuberculosis (Mtb), stayed a global health thread with high mortality rate. Since TB has a long-term treatment, it leads high risk of drug resistant development, and there is an urgent to find new drugs. The aim of this study was designing new inhibitors for a new drug target, iron dependent regulator, IdeR. Materials and Methods: Based on the interaction most populated amino acids of IdeR to the related gene operators, ۵۰ short peptides were modeled. Bonding affinity of short peptides toward DNA were studied by docking. Top ۱۰ best predicted bonding affinity were selected. DNA binding assay, microplate alamar blue assay, colony counting, quantitative real time- PCR (qRT-PCR) of IdeR corresponding genes, cell wall-associated mycobactin and whole-cell iron estimation were done to prove the predicted mechanism of in silico potent constructs. Results: Amongst the ۱۰ synthesized short peptide candidates, glycine-valine-proline-glycine (GVPG) and arginine-proline-arginine (RPR) inhibited Mtb in vitro at ۲۰۰ µM concentration. qRT-PCR showed mbtB ۵۸-fold over expression that resulted in Mtb growth inhibition. Cell wall-associated mycobactin and whole-cell iron estimation confirmed the results of qRT-PCR. Conclusion: We introduced two new lead compounds to inhibit Mtb that are promising for the development of more potent anti-tubercular therapies.

کلمات کلیدی:

IdeR, Inhibitor, Modeling, Mycobacterium tuberculosis, RT-PCR