DOI 10.18699/BGRSSB-2018-078

SRM-based approach for β-lactamases profiling

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Key words: β-lactamase, antibiotics, mass-spectrometry, proteomics

Motivation: In recent years, multidrug resistant strains are actively spreading, which are resistant to several or even all antibiotics. Resistance to antibiotics is a big botnet in the selection of personalized therapy. In this regard, there is a problem of identifying bacteria resistable to β-lactam antibiotics. The main mechanism of this type of resistance is the production of beta-lactamase enzymes. They are extremely different in structure and substrate specificity. In this work several approaches have been developed for the MS profiling of beta-lactamases to determine the family and type, depending on which antibiotic therapy is selected.
Materials and methods: From the UniProt and literary sources amino acid sequences belonging to mutant forms of beta-lactamases (1) of different types (2) were loaded. Using Skyline virtual trypsinolysis was performed and using BLAST-search proteotypic peptides (specific for each form) were determined for subsequent mass spectrometric analysis.
Results: Proteorypic peptides for several TEM, SHV, CTX-M families were chosen. Methods for their detection using SRM mass-spectromical technology were developed. It was shown that this peptides can be used for mass-spectrometric identification basing on more than 50 experiments in PRIDE. At the same time, it was not possible to select specific peptides that distinguish mutant forms TEM-1 from TEM-84.
Conclusions: Bioinformatic analysis of mutant forms of beta-lactamases allowed to determine specific peptides, taking into account the changes in the nucleotide sequence for the subsequent creation of a set of peptides and their mass spectrometric identification in the samples. An experimental verification of the proposed approach presupposes a directional mass spectrometric analysis of beta-lactamases in the periplasmic fraction of producer strains to identify types and key, clinically relevant mutations.
Acknowledgements: Ek.I. acknowledge the Leading Scientific School of Prof. Andrey Lisitsa (No. NSh6313.2018.4).