

Research Project

ESBL-MS: Early diagnosis of ESBL Enterobacteriaceae in patient samples

Third-party funded project

Project title ESBL-MS: Early diagnosis of ESBL Enterobacteriaceae in patient samples

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Organisation / Research unit

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Status Completed

Enterobacteriaceae are a major cause of life-threatening infections such as sepsis. Treatment of Enterobacteriaceae infections relies mostly on β -lactams and β -lactam- β -lactamase inhibitor combinations, but the efficacy of these drugs is endangered by the accelerating spread of extended spectrum β -lactamases (ESBL). ESBLs can be detected using biochemical test, isothermal amplification, PCR and microarrays, but these data cannot predictive quantitative susceptibility as needed for targeted treatment decisions. In this project, we use ultrasensitive mass spectrometry to detect ESBLs and other resistance proteins directly in patient samples. In parallel, we determine how these proteins affect capabilities of clinical strains to rapidly evolve increased resistance in vitro, e.g. by upregulating ESBL expression. We also engineer mutants of clinical strains with precisely altered expression of ESBL and other genes, to quantify their role in resistance. Based on all these data, we will build a classifier algorithm for accurate prediction of resistance within 5 h after patient sample acquisition. Finally, we translate sensitive detection methods for relevant proteins to widely available MALDI-TOF mass instruments for simple and rapid implementation. If successful, the results of our project will enable rapid diagnostics for early targeted treatment of serious infections, while avoiding unnecessary usage of last-resort antibiotics. This strategy has large potential to enhance antibiotic stewardship in face of rising resistance.

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