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Short Communication

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Alanine Enhances Aminoglycosides-Induced ROS Production by Metabolic Regulation

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Abstract:

Metabolite-enabled killing of antibiotic-resistant pathogens by antibiotics is an attractive strategy to manage antibiotic resistance. Our previous study demonstrated that alanine or/and glucose increased the killing efficacy of kanamycin on antibiotic-resistant bacteria, whose action is through up-regulating TCA cycle, increasing proton motive force and enhancing antibiotic uptake. Despite the fact that alanine altered several metabolic pathways, other mechanisms could be potentially involved in alanine-mediated kanamycin killing of bacteria which remains to be explored. In the present study, we adopted proteomic approach to analyze the proteome changes induced by exogenous alanine. Our results revealed that the expression of three outer membrane proteins was altered and the deletion of nagE and fadL decreased the intracellular kanamycin concentration, implying their possible roles in mediating kanamycin transport. More importantly, the integrated analysis of proteomic and metabolomic data pointed out that alanine metabolism could connect to riboflavin metabolism that provides the source for reactive oxygen species (ROS) production. Functional studies confirmed that alanine treatment together with kanamycin could promote ROS production that in turn potentiates the killing of antibiotic-resistant bacteria. Further investigation showed that alanine repressed the transcription of antioxidant-encoding genes, and alanine metabolism to riboflavin metabolism connected with riboflavin metabolism through TCA cycle, glucogenesis pathway and pentose phosphate pathway. Our results suggest a novel mechanism by which alanine facilitates kanamycin killing of antibiotic-resistant bacteria via promoting ROS production.

Biography:

Ye Jinzhou is passionate about metabolic regulation of bacterial resistance. During his Ph.D. and postdoctoral periods, he devoted himself to studying the Metabolic regulation mechanism in the process from tolerant to resistant.