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Perspective

Better Understanding of Bacterial Antibiotic Resistant Strategies through Proteomics

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INTRODUCTION

Bacterial pathogens continue to threaten human health and animal husbandry industry by affecting millions of lives worldwide and causing significant economic loss [1]. Antibiotics are the primary means of treating or preventing bacterial infections. It provides enormous benefits to human health and animal husbandry. However, over use and/or misuse of antibiotics increase the incidence of drug-resistant bacteria which are insensitive to most current antibiotic weapons. Existing antibiotics are more prevalent in clinics and settings than before. New antibiotics can be developed to target multi-drug resistant bacteria, but developing new antibiotics takes a very long time. More importantly, it is not a viable approach to address the spread of multi-drug resistant drugs, drought induced infections in the antimicrobial development pipeline, therefore, there is an urgent need to investigate antibiotic resistance mechanisms in developing new strategies to combat and treat antibiotic-resistant pathogens infection caused by it. Since its discovery, research into antibiotic resistance mechanisms has not been stopped [2]. Ongoing research suggests that bacteria acquisition of resistance to antibiotics including gene mutation, plasmid/episomal, antibiotic target modification or degradation, inhibition or downregulation of membrane permeability and enhancement of drug efflux. Proteomics was initially applied as a methodology to profile the proteomes or sub proteomes of antibiotic-sensitive and antibiotic-resistant bacteria, and to identify the differential abundance of proteins, which is termed as "discovery proteomics". The key players need to be identified and subjected to functional validations such as gene-deletion and overexpression and enzyme activity to confirm the proposed roles of the proteins of interest [3]. In the very early stage of proteomics, proteome profiling was always started with an immobilized pH gradient based two-dimensional gel electrophoresis (2-DE) to identify the differential abundance of proteins between samples in company with validation by qRT-PCR and/or western blot. Now, it is convenient to use LC-MS/MS quantitative proteomics to identify proteins of interest, coupled with additional OMIC approaches like genomics, transcriptomics, and metabolomics, which is a more accurate, convenient and high-throughput approach than the 2-DE method. Proteomic approach provides a more holistic molecular view of antibiotic resistance compared to non-OMICS approaches. Bacteria react differently a class of antibiotics commonly used clinically, including beta-lactams, aminoglycosides, quinolones, tetracyclines, and macrolides because they are different. Each class of antibiotics has its own mechanism of action. Combining proteomics and qRT-PCR and applying it to study levofloxacin antibiotic resistance in *V. alginolyticus*. It is established that carbon and energy metabolism are suppressed after gaining resistance. In particular, transcription level glycolysis/gluconeogenesis, TCA cycle, fatty acid biosynthesis, Na (+)-NQR [4].

DESCRIPTION

Therefore, the reduced central carbon and energy metabolisms form a characteristic feature of *V. alginolyticus* in resistance to levofloxacin as fitness costs. A recent combinatorial quantitative proteomics and other OMICs studies further confirmed the relationship between bacterial metabolism and quinolone resistance, where the whole genome sequence is used to predict fluoroquinolone susceptibility in clinical isolates, and proteomics is needed to identify protein variants that are functionally important in the whole genome sequence data. The proteomic investigation provides novel insight into bacterial aminoglycoside resistance, including the antioxidant system, lipid metabolism, as well as intermediary metabolism and respiration, indicating that the metabolic environment is key to aminoglycoside resistance, as revealed by functional proteomics. Comparative proteomics analysis of isolated sarcosine-insoluble outer membrane protein fractions between clarithromycin-susceptible and resistant *Helicobacter pylori* strains identifies iron-regulated membrane protein, ureaseB, EF-Tu, and putative outer membrane proteins that are downregulated; HopT (BabB) transmembrane protein, HofC, and Omp31 that are up-regulated in clarithromycin-resistant H. *Helicobacter pylori*. Thus proteomics study suggested changes in outer membrane proteins and profiling of those proteins may be a novel mechanism in clarithromycin resistance of *H. pylori*. Microbial

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proteomics helps identify proteins associated with microbial activity, microbial host-pathogen interactions, and antimicrobial resistance mechanisms. Microbial activity of pathogens can be confirmed using 2-D gel based and gel-free methods combined with MALDI-TOF-LC-MS/MS. For many years, researchers have tried to use antibiotics to eliminate the persistence of pathogens. However, these infectious agents are able to recover from antibiotic attack through various mechanisms such as drug resistance and antibiotic resistance, and continue to pose a global threat to human health. In-depth knowledge of the response to bacteria is needed to develop more efficient treatments for pneumonia. Commonly used antibiotics are needed. Proteomics is a convenient and powerful tool for studying molecular responses to antimicrobial compounds by antibiotics. Generating bacterial response profiles from systems-level studies has the potential to enhance the understanding of bacterial adaptation, the mechanisms behind antibiotic resistance, and resistance development. Antimicrobial Resistance (AMR) is naturally acquired by mutation or ingestion of genetic material in microorganisms such as bacteria, viruses, fungi and parasites. Today, AMR is one of the greatest threats to global health. The most pressing problem is AMR in bacteria, and over the years it has been observed that bacteria have developed resistance to all antibiotics on the market is the main problem. Bacteria can naturally mutate and develop resistance mechanisms to antibiotics. In addition, bacteria can transfer resistance genes through horizontal gene transfer between species. Resistance mechanisms can be broadly categorized into her three basic patterns.

CONCLUSION

Prevent drug accumulation, modify cellular targets, and inactivate antibiotics. There are still challenges in using proteomics as a tool to identify and quantify proteins that need to be addressed. In bacteria, identifying low level modifications can be difficult and depends on biological conditions. In parallel with the use of these advanced proteomics techniques, there is still room for development, so data processing and characterization may differ. An important factor to consider when initiating proteomic analysis is accessible mass spectrometer capabilities. Second, the scope of the project, sample volume, time available for mass spectrometry, reagent budget, availability of suitable bioinformatic analysis, etc. should be considered for bacterial antibiotic resistant.

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