Beyond genomics, proteomics as the key to unlocking antibiotic resistance

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Pseudomonas aeruginosa, known for its adaptability and antibiotic resistance, poses a major clinical challenge, especially due to its resistance to colistin. A preliminary study examined the minimum inhibitory concentrations (MICs) of various antibiotics in 11 strains. The isolates displayed intrinsic resistance to certain antibiotics, particularly polymyxins like colistin, with no plasmid-mediated resistance observed. Colistin resistance was linked to genetic mutations and specific endogenous proteins. The objective of this study was to analyze the protein expression levels of three of *these P. aeruginosa* isolates with different MICs in response to colistin treatment at three concentrations (0, 2, and 4 mg/L). The proteomic study focused on two subsets of proteins: the intracellular proteome and the cell wall/debris proteome. The separate extraction and analysis of these sub-proteomes aimed to provide a more comprehensive view of the expressed proteins, to better understand the mechanisms of colistin resistance, whether common to the three isolates or specific. Protein samples were digested with trypsin, and the resulting peptides were analyzed by nano-liquid chromatography coupled with tandem mass spectrometry (nano-LC-MS/MS). Proteomic analysis revealed unique protein expression patterns under colistin stress, with strain-specific responses. Clustering analysis showed differential expression of proteins related to metabolism, stress response, and antibiotic resistance. Protein interactions suggested complex adaptive strategies, highlighting the multifaceted nature of bacterial resistance. These findings underscore the importance of understanding strain-specific resistance mechanisms in combating antimicrobial resistance and developing effective treatment strategies against multidrug-resistant pathogens like *P. aeruginosa*.

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