

Investigating the metabolome of resistant bacteria by high resolution mass spectrometry imaging with desorption electrospray ionization

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Abstract

Pathogenic bacteria remains a primary target of a study due to its prevalence in the environment, specifically the healthcare setting. The use of antibiotics and antimicrobials are essential to treat the symptoms of harmful strains of bacteria. However, although medicinal alternatives exist to kill harmful microorganisms, bacteria have the capability to evolve. Because of this, resistant properties have become a growing problem in the healthcare setting, thus creating various scientific interests of study. High resolution mass spectrometry and imaging analyzes specific ions within a sample thus providing further identification of potential metabolites in *Staphylococcus aureus*. Therefore, metabolites produced by both resistant and non-resistant strains of bacteria were compared and evaluated. Profiling the metabolic production between the two strains provides a further understanding on how these resistant characteristics were formed, their biological gene function, and how they can potentially be treated.

Key words: Mass Spectrometry Imaging, *Staphylococcus Aureus*, Metabolomics.

Introduction

Nosocomial infections, which are prone to hospital settings, are secondary infections that are caused by transferred bacteria. Occasionally these pathogenic microorganisms contain multi-drug resistant properties leading to resistance against commonly used antibiotics. Resistant properties can be formed over time or through alterations of the cellular structure such as the membrane. *Staphylococcus aureus* is a critical strain of bacteria due to its high presence as a hospital acquired infection, and also for its capability to asymptotically colonize healthy individuals. There are alterations that occur in gram-positive bacteria creating enzymes that produce antibiotic resistance such as in Methicillin-resistant *Staphylococcus aureus* (MRSA). This specific resistance is acquired through horizontal gene transfer between cells. Ultimately this kind of modification poses a huge threat to clinicians when providing treatment options and diagnoses. Since this is prevalent within the healthcare setting, it has become a primary study of interest in the research field. Desorption electrospray ionization (DESI) is a high resolution mass spectrometry imaging (IMS) tool that can develop a detailed 2 dimensional image of the molecular distribution of particular compounds. Because of its capability to analyze samples in environmental conditions, compounds are able to be detected on sample surfaces. IMS has particularly become popular due to ability to locate a compound of interest by m/z investigation.

Results and Discussion

Staphylococcus aureus's metabolites were analyzed and profiled by DESI-IMS. Specific compounds and potential metabolites were compared between both the resistant and wild strains of *Staphylococcus aureus*.

Comparing the wild type to the resistant strains provides information that will aid in locating the origin of production of these resistant properties potentially providing a lead for future treatment options.

It has been observed (**Image 1**) that substances have a greater abundance in the wild colony compared to the

resistant one, such as those with m/z 156, and m/z 189. On the other hand, there are compounds present only in the resistant type, such as m/z 708 and m/z 665. The structures of the metabolites corresponding to these molecular masses are under investigation.

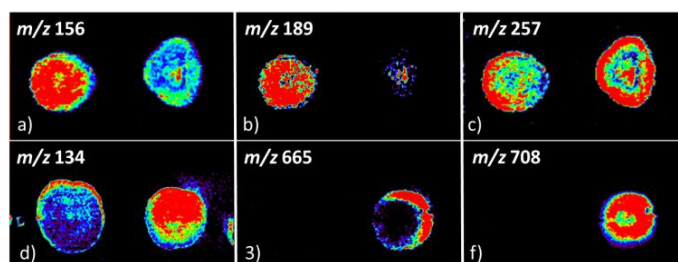


Image 1. MSI of wild-type strains of resistant bacteria in positive DESI: a), b) and c) and negative DESI mode: d), e) and f). Methanol and acetonitrile:dimethyl sulfoxide (1:1) were used for positive and negative DESI modes, respectively.

Conclusions

Higher-molecular mass metabolites were more abundant in resistant strains, while lower-molecular mass metabolites were more concentrated in wild-type strains. Different solvents can be employed for analysis, directly affecting the classes of ionized molecules.

Ambient mass spectrometry opens a new field in studies on the identification of bacteria, since wild-type and resistant bacteria strains could be differentiated.

Acknowledgement

National Institute of Science and Technology in Bioanalytics, CAPES, CNPq, FAPESP, IRES.

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