186 Timely and effectively profile bacteria in cystic fibrosis lungs

Sousa, A.M.[1], Lourenço, A.[1,2], Fdez-Riverola, F.[2], Diniz, J.[3], Capelo, J. L.[3], Pereira, M.O.[1]

[1]IBB – Institute for Biotechnology and Bioengineering, Centre of Biological Engineering, University of Minho, Campus de Gualtar, 4710–057 Braga, Portugal. [2]Department of Computer Science, School of Engineering, University of Vigo, Ourense, Spain. [3]Grupo BIOSCOPE, Departamento de Quimica Fisica, Faculdade de Ciências, Campus de Ourense, Universidad de Vigo, 32004, Spain.

Bacterial lung infections are typical of cystic fibrosis (CF) disease due to accumulation of airway mucus. Despite the use of aggressive antibiotic therapy, the mortality rate of CF patients is still high. Unsuccessful bacterial eradication is often due to several evolutional strategies adopted by bacteria to achieve anaerobic or microaerophilic adaptation and antibiotic resistance, such as biofilm formation and phenotypic switching. By triggering these strategies, bacteria have the potential to better survive to airway stressful conditions, without the fitness costs of irreversible mutations. Indeed, phenotypic switching provides a source of microbial diversity through interchange between phenotypic states, analogue to a mechanism ON/OFF. This interchange of states, often visible in terms of colony morphology, can have serious impact on bacterial virulence, antimicrobial resistance and persistence[1]. However, the specific correlation between some colony traits and the biological impact is unknown. This study was designed to inspect *P. aeruginosa* and *S. aureus* colony phenotypic alterations, particularly morphology changes, by visual inspection, and protein profiles by MALDI MS, and correlate them with some virulence determinants expression and antibiotic susceptibility profiles. The visual identification of colony morphologies was supported by a novel, in-house developed identification system, ColMIS[2]. MALDI MS profiling grouped colony morphotypes differently from conventional morphological

classification and antibiotic susceptibility. However, MALDI MS colony differentiation seems to match with changes in some virulence factors expressed by the different bacterial morphotypes, such as the increase of flagella, swarmer cell differentiation, ability to form biofilm and toxin production. Despite exhibiting distinct colony morphologies, the variants grouped by MALDI shared a common morphological feature, the heterogeneity of colony surface (more than one type of texture). Therefore, these data seems to indicate that MALDI MS clustered colony variants according their virulence, that can be inspected by just the heterogeneous surface of the colonies, than the whole morphology. However, this association have to be deeper studied, since other colonies with heterogeneous surfaces were differentially clustered by MALDI MS and, despite decreased virulence, exhibited high resistance to in-use antibiotics. These results highlighted the potential and the need of using a combination of proteomic high-throughput screening of pathogenic bacteria with culturing and physiologic methods to reach a comprehensive understanding of the virulence and antibiotic resistance. Efforts are already underway to develop a new tool based on combinatorial methodologies to help clinical diagnosis and medical decision support, as well the design of new therapeutic strategies.

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