O-20 - S. EPIDERMIDIS LIFECYCLE: HOW BACTERIA TRICK THE HOST AND THE CLINICIAN?

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Background
In the clinical setting, biofilms were thought to be an alternative phenotype to planktonic pure cultures but scientific evidence from the last decade has revealed that bacteria, similar to more evolved species, undergo a specific lifecycle containing: (i) biofilm formation (ii) dispersion and (iii) planktonic growth phases. This results in constant alterations in bacterial physiology, with significant consequences to the outcome of biofilm-related infections. *S. epidermidis*, a common commensal of the human skin and mucosae, is the leading causative agent of medical device-associated infections due to its tenacious ability to form biofilms. Here, we performed a multi-factorial analysis to understand how the physiological alterations associated with *S. epidermidis* biofilm lifecycle enable this bacterium to (i) evade the host immune response, (ii) tolerate higher concentrations of antibiotics, and (iii) avoid detection by standard diagnostic methods.

Methods
We developed *in vitro* models to obtain biofilms with distinct proportions of dormant bacteria (1), as well as to collect biofilm dispersed cells (2). The host immune response was assessed using an *in vivo* murine model and characterized by analyzing the transcriptome of splenocytes, cytokine levels in the serum and bacterial colonization in the host. Antibiotic tolerance to vancomycin, rifampicin and tetracycline was assessed by CFU counting and flow cytometry. Confocal laser scanning microscopy was used to assess structural differences in biofilms exposed to antibiotics.

Results & conclusions
Mouse organs colonization and splenocytes transcriptome demonstrated that bacteria in the different stages of the biofilm lifecycle presented distinct and unique adaptations to the host immune response. Biofilm cells induced a lower production of pro-inflammatory cytokines. Conversely, the cells' tolerance to antibiotics was higher. Presumably, this will allow a more efficient evasion from the host immune response and antimicrobial therapy. Furthermore, we observed that cells dispersed from biofilms, retained their high tolerance to antibiotics, confirming that tolerance is a phenomenon not only related to the tridimensional structure of biofilms. Finally, we observed that after antimicrobial treatment, significant discrepancies between CFU counts and the total load of viable but not cultivable bacteria, could explain the high rates of diagnose failure and recurrence rates.

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