TITLE: MICROBIOME OF CHRONIC WOUNDS AND THE IMPACT OF MICROBIAL BIOACTIVE SMALL MOLECULES ON WOUND PATHOGENS

AUTHORS: TEIXEIRA, F.L.[1]; VALENTE, G.L.C.[1]; OLIVEIRA, B.C.[2]; PAUER, H.[3]; TEIXEIRA, L.A.[1]; OLIVEIRA, B.G.R.B.[2]; PAULA, G.R.[1]

INSTITUTION: [1] UNIVERSIDADE FEDERAL FLUMINENSE - FACULDADE DE FARMÁCIA, NITERÓI, RJ (RUA DR. MARIO VIANNA, 523, CEP: 24241-002, NITERÓI - RJ, BRASIL); [2] UNIVERSIDADE FEDERAL FLUMINENSE - ESCOLA DE ENFERMAGEM AURORA DE AFONSO COSTA, NITERÓI, RJ; [3] FUNDAÇÃO OSWALDO CRUZ, RIO DE JANEIRO, RJ.

ABSTRACT

Chronic wounds present a major burden on both individual patients and the broader health system. Disruption of the normal healing cascade is a key factor on these chronic, non-healing wounds. These wounds are often colonized by different species of bacteria, and this process, most of the time, delay healing of the wound. Establishment and development of microbial communities in the skin are highly dependent on the chemical composition of the niche they are colonizing/infecting. Small molecules produced by both host and its associated microbiota as a byproduct of their metabolism may inhibit establishment of potential pathogens and contribute to mitigation of inflammation and reversion of wound chronicity. Thus, our main goal is to evaluate the bioactive potential of small molecules produced by wound microbiota, with analysis of impact on virulence of bacteria associated with skin infection. Four patients with chronic wounds admitted at the Wound Repair Clinic of the *Ambulatório de Reparo de Feridas* in *Hospital Universitário Antônio Pedro* (*Universidade Federal Fluminense*) were selected for initial triage. Swab samples of the wounds were collected and used to inoculate aerobic and anaerobic cultures. After 48 hours of incubation at 37 ºC, 7 of the 8 cultures (4 in aerobiosis and 3 in anaerobiosis) presented growth and were submitted to extraction of small molecules by ethyl acetate. The dried extracts obtained after evaporation of ethyl acetate were suspended on hexane and methanol (1:4) and used to analyze interference of small molecules produced by the wound microbiota on growth and virulence of *Staphylococcus aureus* ATCC 29213 and *Pseudomonas aeruginosa* ATCC 27853. Growth analysis showed inhibition of *S. aureus* by one of the seven extracts, but no difference on growth was seen in *P. aeruginosa*. We also observed an alteration in motility and pigment production by *P. aeruginosa* when exposed to two of the seven extracts. Our findings are in accordance to other studies that have shown that small molecules produced by the microbiota modulates virulence of pathogens, such as *Salmonella enterica.* We are currently expanding the analysis to clinical isolates of these species, to check if the phenotype changes are species- or strain-specific. We believe that this study will provide new insights on host-microbe interactions in chronic wounds and will allow the development of new strategies to help reversing this clinical condition.

Keywords: Microbiome; Bioactive small molecules; Chronic wounds; *Pseudomonas aeruginosa*; *Staphylococcus aureus*.

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