Title: The human gut metabolome shows antibiotic activity against *Staphylococcus aureus*

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Abstract:

In recent years, we have seen a significant rise of infections caused by antibiotic-resistant pathogens, and this represents a major public health issue. Pathogens that are resistant to every kind of available antibiotic can already be found. Thus, there is a critical need to identify new leads for the design of therapeutics to combat antibiotic-resistant infections. A rich resource for discovering new therapeutic leads are microbes themselves, because bacteria have optimized strategies for competition with other microbes. It is well established that bacteria communicate actively through the production of small molecules in a phenomenon called quorum sensing. Our group has demonstrated that the human microbiome is a rich source of chemical diversity, some of which have strong biological activity. For example, molecules produced by the intestinal microbiota have antivirulence activity against *Salmonella enterica*. These and other observations brought about the hypothesis that small molecules represent a crucial tool during pathogen-host interactions, and that studying these interactions may lead to the discovery of new bioactive molecules. Thus, we reasoned that the human gut metabolome could contain molecules with antibiotic activity. In order to test this hypothesis, we tested the effect of fecal extracts on the growth of methicillin resistant *Staphylococcus aureus* (MRSA) and found that members of the human microbiota produce molecules with antibiotic activity against this pathogen. Our goal with the present study was to deepen this preliminary observation, and further investigate if the human microbiome may in fact be a source of molecules with antibiotic activity. Our long-term goal is to use compounds produced by bacteria to develop completely new approaches to combat antibiotic-resistant infections. Our results have demonstrated that human intestinal microbiome-derived small molecules have strong antimicrobial activity against MRSA. In addition, we performed a preliminary characterization of the bioactive molecule present in the fecal extract using molecular weight filters and C_{18} cartridges. These experiments showed that the active compound is smaller than 3 KDa and hydrophobic. Determining the role of small molecules in the interactions between microbiota and pathogens during host homeostasis may reveal new compounds with potential therapeutic applications in infectious diseases.

Keywords: antibiotic-resistant pathogens; microbial communities; human gut; bioactive molecules.

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Excluído: for nutrients and space in the complex microbial communities where they usually reside

Excluído: One such community is that occurring in the human gut, which is home to trillions of microbes that have evolved intricate interactions over millions of years.