BRIGHAM AND WOMEN'S HOSPITAL
HARVARD MEDICAL SCHOOL

181 Longwood Avenue
Boston, Massachusetts 02115-5804

Department of Medicine
Channing Division of Network Medicine

Channing Microbiome Seminar

March 31 (Friday), 2023, 9AM (ET)

Zoom: https://us02web.zoom.us/j/81070959105?pwd=RFJNd3dSZmR6dXJZNjJiYVVzQ3NEQT09
Meeting ID: 810 7095 9105
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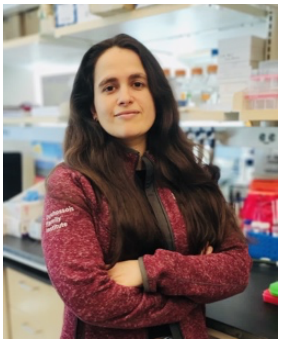

Rita Almeida Oliveira, PhD
Postdoctoral Researcher
University of Chicago

Gut microbiota modification of dietary metabolites to guide symbiotic bacterial consortium design against Klebsiella pneumoniae gut colonization

Abstract: The human gut microbiome is comprised of hundreds of species that establish complex interactions with each other. The net output of the microbiome, which includes a wide range of metabolites, impacts host fitness and provides resistance to dense colonization by Enterobacteriaceae, such as *Klebsiella pneumoniae* (Kp). When microbiota-mediated colonization resistance is compromised by antibiotics, Kp expands markedly in the gut lumen, thereby enhancing the risk of healthcare-associated infections. In the case of Kp, increasing resistance to carbapenem and broad-spectrum beta-lactam antibiotics leaves patients with very limited and at times no available antibiotic treatment options. Reconstitution of gut microbiota composition in dysbiotic settings by fecal microbiota transplantation from healthy donors can reduce gut colonization by Kp but has been associated with potentially severe complications. Assembly of defined consortia of commensal microbiota species can prevent gut colonization by some pathogens, however optimal symbiotic strain combinations to reduce Kp colonization have yet to be identified. Our goal is to identify human microbiota-derived symbiotic bacterial strains that recapitulate a healthy subjects' metabolome and provide Kp-specific colonization resistance. We used a reductionist and unbiased approach to identify bacterial strains associated with colonization resistance to Kp by leveraging the ability of human-derived microbiomes from healthy donors to resist Kp colonization. We collected feces from 3 healthy donors, serially diluted fecal samples and colonized germ-free mice with these dilutions. One thousand-fold and ten-thousand-fold dilutions of feces led to varying colonization resistance to the MH258 strain of carbapenem-resistant ST258 Kp, and were categorized as 'resistant', 'intermediate', or 'non-resistant'. Compositional and metabolic profiling of these microbiomes identified potential new players and metabolic signatures, derived from dietary components and modified by microbes, that might be involved in colonization resistance against Kp. We used a collection of >1,600 genome-sequenced and metabolically-profiled commensal bacterial strains cultured from healthy human donors, and we are currently assembling and testing bacterial consortia that reflect the genomic and metabolic profiles associated with resistance conferred by FMT of fecal dilutions. This work provides a novel combinatorial strategy for discovery and assembly of metabolically-optimized human-derived bacterial consortia that provide colonization resistance against Kp, and that can be applied to a range of optimizable bacterial functions that target other pathogens or gut disorders.

Bio: *Dr. Rita Almeida Oliveira received a BS degree in Genetics and Molecular Biology in 2009 and a Master's degree in Evolution and Developmental Biology in 2011 from the Faculty of Science at Lisbon University in Portugal, where she studied Human mesenchymal stem cell differentiation. Thereafter, she joined Dr. Karina Xavier's laboratory at the Gulbenkian Institute of Science to study quorum sensing manipulation of the gut microbiota, where she also joined the Integrative Biology and Biomedicine program in 2015 to start a PhD in Interspecies interactions in recovery from microbiota dysbiosis, which she completed in 2020. In 2021, she joined Dr. Pamer's laboratory to study the assembly of microbial consortia to prevent colonization by Klebsiella pneumoniae and its impact on gut metabolism and host immunity.*

Hosted by Shanlin Ke & Yang-Yu Liu