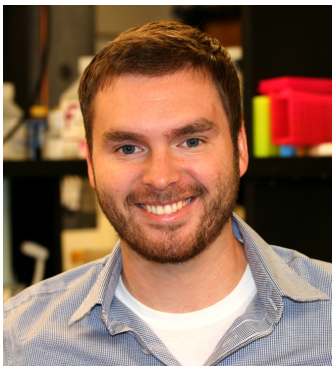
BRIGHAM AND WOMEN'S HOSPITAL
HARVARD MEDICAL SCHOOL

181 Longwood Avenue
Boston, Massachusetts 02115-5804

Department of Medicine
Channing Division of Network Medicine

Channing Microbiome Seminar

Dec 2 (Friday), 2016, 11am @ 5th floor conference room



Philip Strandwitz, Ph.D.
Antimicrobial Discovery Center
Northeastern University

The Gut-Brain-Axis: Discovering GABA-modulating bacteria

The gut microbiome affects many different diseases, and has been recently linked to human mental health1,2. The microbiome community is diverse, but much of its diversity remains uncultured3. We previously reported that uncultured bacteria from the marine environment require growth factors from neighboring species, and by using co-culture, we could cultivate novel diversity4. In the present study, we used a similar co-culture approach to grow bacteria from humans stool samples. KLE1738, a "Most-Wanted" member of the human gut microbiome only known by its 16S rDNA signature, was found to require the presence of Bacteroides fragilis KLE1758 for growth. Using bio-assay driven purification of B. fragilis KLE1758 supernatant, γ-aminobutyric acid (GABA), the major inhibitory neurotransmitter of the central nervous system, was identified as the growth factor for KLE1738. We found no other tested compound but GABA supported the growth of KLE1738, and genomic analysis suggests an unusual metabolism focused on consuming GABA. Due to this unique growth requirement, we provisionally name KLE1738 Evtepia gabavorous. In silico analysis of available genomes from human gut isolates lead to the identification of hundreds of species capable of producing or consuming GABA. In a complementary approach, using growth of E. gabalyticus as an indicator, we then cultivated novel GABA producing bacteria from the gut microbiome. Altered levels of GABA are associated with IBS and depression, and we found fewer GABA producers in a human cohort of these diseases. By modulating the level of GABA, microbial producers and consumers of this neurotransmitter may be influencing host physiology.

References

1. Cho, I. & Blaser, M. J. The human microbiome: at the interface of health and disease. Nat Rev Genet 13, 260-270, (2012).
2. Smith, P. A. Brain, Meet Gut. Nature 526, (2015).
3. Lagier, J. C. et al. The Rebirth of Culture in Microbiology through the Example of Culturomics To Study Human Gut Microbiota. Clin. Microbiol. Rev. 28, 237-264, (2015).
4. D'Onofrio, A. et al. Siderophores from neighboring organisms promote the growth of uncultured bacteria. Chem Biol 17, 254-264, (2010).
5. Brambilla, P., Perez, J., Barale, F., Schettini, G. & Soares, J. C. GABAergic dysfunction in mood disorders. Mol Psychiatry 8, 721-737, 715, (2003).

Bio: Dr. Philip Strandwitz is a specialist in the link between the microbiome and health and disease,

with a focus on the gut brain axis. In his PhD specialized in bacterial cultivation, and discovered the first bacterium that required the neurotransmitter γ-Aminobutyric acid (GABA) for growth, isolated from human stool samples. Taking advantage of this unique lifestyle, he was able to utilize this discovery to rapidly identify GABA-producing bacteria from the human gut microbiota, dramatically expanding existing knowledge of the GABA-modulating bacteria living in the human intestines. He has since established a large network of collaborators, including clinicians, leaders in the field of the microbiome, and psychologists to determine whether these GABA modulating bacteria were associated with diseases of the central and peripheral nervous systems. Philip has presented at numerous conferences, including those held by the New York Academy of Science, Keystone Symposia, and the American Society of Microbiology. Philip received his PhD in Biology under the guidance of Kim Lewis at Northeastern University and here remains a postdoctoral scholar, leading the microbiome team.

Hosted by Yang-Yu Liu