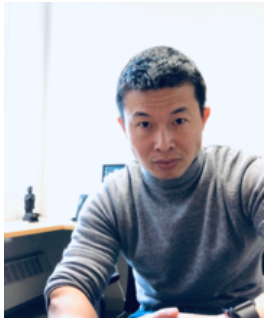
Channing Network Science Seminar

Date: **May 3 (Friday)**, 2019, **11am @ 5th-floor conference room**



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Human oral nanobacteria: walking the fine line between parasitism and mutualism

A significant recent event in microbiology was the discovery of the candidate phyla radiation (CPR) group, which comprises more than 26% of bacterial diversity and potentially contains over 70 new phyla. Several of these CPR phyla, including TM7, SR1 and GN02 are commensal members of human microbiome. However, their potential role in host's heath and disease are largely unknown due to their recalcitrance to the cultivation. Among host associated CPR, TM7 phyla is of particularly interest. TM7 are ubiquitous members of human microbiome from Neanderthal to modern human and have consistently been found associated with mucosal infection, particularly increasing in abundance with gingivitis severity and in subjects with periodontal diseases. However, their physiology and lifestyle remained elusive until we recently isolated the first cultivated representative, strain TM7x from human oral cavity. Strain TM7x is very unique among all bacteria, it has an ultra-small size (200-300 nm) and lives on the surface of a host bacterium, a relationship that had never been reported in the human microbiome or in the Bacteria domain. With a highly-reduced genome of only 705 genes, TM7x cannot synthesize any of its own amino acids, vitamins or cell wall precursors and must parasitize other oral bacteria which impacts their growth. When cultivated under laboratory condition, TM7x reduces the growth of its bacterial host, and even induces host lysis when experiencing starvation, indicating a parasitic lifestyle. Intriguingly, TM7x association enhances bacterial host's biofilm formation capability, a crucial trait that promotes bacterial persistence within human oral cavity. Meanwhile, TM7x can protect bacterial host against oral phage infection, enhancing its survival within oral microbiome. Furthermore, although equipped with a reduced genome and lacking numerous biosynthetic pathways, TM7x encodes a complete arginine deiminase (ADI) pathway which is missing in its host XH001's enzymatic portfolio. In addition to being a major means of energy production, ADI pathway produces ammonium which plays an important role in protecting bacteria from the harmful effects of acidic environments, such as oral cavity where microbial biofilm experience drastic pH drop during carbohydrate intake. Our data indicate that, while metabolically heavily relying on its host and exerting growth burden on its host, TM7x could offer certain benefits to increase host fitness. Strikingly, across the CPR, all genomes obtained from metagenomics study revealed a lack of numerous biosynthetic pathways. Like TM7x, many are predicted to be unable to produce membrane lipids or de novo nucleotides and have minimal amino acid and cofactor biosynthetic capacity. Thus, most CPR members are predicted to have symbiotic lifestyles. As the impetus for the study of ultra-small bacteria increases, a more detailed comprehension of the relationship between TM7x, the only cultivated representative TM7 and the CPR thus far, and its bacterial host will provide a valuable prototype for understanding the unique lifestyle of the CPR group.

Bio: Dr. He received his DDS from Peking University Health Science Center in 1997 and obtained his PhD in Microbiology from Indiana University in 2006. He joined School of Dentistry at UCLA in 2007 as a Postdoctoral Research Associate, held position as Assistant Professor in 2010 and Associate Professor in 2016, and has become a faculty at Forsyth Institute since 2018. Dr. He has a broad background in Microbiology, particularly oral microbiology with comprehensive knowledge of microbial genetics, cell-cell communication and microbial ecology and microbial-host interaction. Some of his research interests include: 1) Understanding the interaction between the newly discovered human oral epiparasitic nanobacteria and their bacterial host; 2) Using novel culturing methods to isolate and study the physiology and pathogenesis of thus far "uncultivated" oral bacteria, including Candidate Phyla Radiation group within oral cavity; 3) Understanding the ecological and social aspects of host-associated microbiome, 4) Investigating the role of host-tRNA derived small RNA (tsRNA) in modulating host-oral microbial interaction. Dr. He is the contact PI of multiple active R01 grants from NIH. The national and international impact of Dr. He's research can be proved by his over 60 well-cited publications in peer-reviewed leading scientific journals including PNAS, PLOS Pathogens, ISME J, Journal of Endodontics, Journal of Dental Research, Trends in Microbiology.

Hosted by Yang-Yu Liu