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Channing Microbiome Seminar

September 22 (Friday), 2023, 9AM (ET)

Zoom: https://us02web.zoom.us/j/81070959105?pwd=RFJNd3dSZmR6dXJZNjJiYVVzQ3NEQT09
Meeting ID: 810 7095 9105
Passcode: 984617

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Reduced-Representation Metagenome Expands the Boundary and Accuracy of Microbiome Research

The microbiome plays a pivotal role in numerous research fields today, yet decoding the microbiome still presents significant challenges. Whole Metagenomic Sequencing (WMS) faces issues such as high host contamination, low microbial biomass, severe DNA degradation, and false-positive identifications. We propose the Reduced-Representation Metagenome approach to address these challenges. The Type IIB restriction-modification (RM) system, unlike other RM systems, cleaves DNA on both sides of its recognition sites, producing short iso-length DNA fragments (termed '2b tags'). We have demonstrated that 2b tags are widely and abundantly distributed across all microbial genomes. Furthermore, single-copy species-specific 2b tags greatly outnumber universal single-copy markers and exhibit minimal overlap with host DNA. Capitalizing on these unique properties, we developed 2bRAD-M sequencing, which can process microbiome samples with as little as 1pg of total DNA, 50bp of highly degraded DNA, and up to 99.9% host contamination. In conjunction with this new sequencing technique, we also introduced a computational pipeline named MAP2B, which effectively reduces false-positive identifications. It's worth noting that MAP2B is compatible with WMS data since the 2b tags are inherently present within it. Moreover, MAP2B has the largest number of identifiable species to date.

Bio: Dr. Sun is an Instructor in Medicine at Harvard Medical School. His research goal is to develop innovative methodologies to bridge the gap between the human microbiome and human diseases. His interests in the microbiome include advancing methods for decoding the taxonomic structure, engineering novel microbial features associated with host status, and investigating the mechanisms underlying dysbiosis diseases. His research has been published in top-tier microbiology journals, e.g., *Nature Methods*, *Nature Communications*, *Genome Biology*, *Microbiome*, *eBioMedicine*, *Gut Microbes*, and *mSystems*. In recognition of his contributions to the field, he has been awarded the Charles A. King Trust Postdoctoral Research Fellowship and the NIH Pathway to Independence Award (K99).

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