Characterisation of microbial dark matter by electron cryo-tomography.

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Just as the development of the first light microscopes uncovered a new microbial frontier, the use of high-throughput sequencing and metagenomics has uncovered a new frontier of unculturable microorganisms, often referred to as "microbial dark matter". The biology of these organisms, which have been found in many environmental and human microbiomes, profoundly impacts our understanding of evolution. However, many of these organisms are difficult to culture, genetically intractable, and rely on other microbes within their niche to proliferate.

CryoET is an ideal method to study genetically intractable microbial communities as it can determine high-resolution cellular details and macromolecular structures in situ without recombinant expression systems. We used electron cryo-ET to observe the intercellular interactions of microbes. We embark on microbial safari, observing the fascinating biology of ultra-small parasitic bacteria, marvel at the complex macromolecular machinery of obligate ectosymbiotic archaea and ponder the very origins of eukaryotic life with asgard archaea. Tomographic reconstructions combined with 3D segmentation cast light on the diverse plethora of microbes in microbial dark matter and reveal cellular features such as intercellular nanotubes, enormous attachment organelles, and macromolecular lances that facilitate the interactions between microbial cells.

Our work shows the vast the resources that microbial communities commit to intercellular interactions and provides mechanistic insights into the primordial nature of symbiosis, parasitism, and eukaryogenesis.

Papers

Johnson MD, Shepherd DC, Sakai HD, Mudaliyar M, Pandurangan AP, Short FL, Veith PD, Scott NE, Kurosawa N, Ghosal D. *Cell-to-cell interactions revealed by cryo-tomography of a DPANN co-culture system*. **Nat Commun**. **2024 Aug** 16;15(1):7066. doi: 10.1038/s41467-024-51159-2. PMID: 39152123

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