

MICROBIOLOGY

Culturing uncultivated bacteria

Researchers develop a genome-informed approach to isolate and grow targeted cells into pure cultures from microbial communities.

Advances in sequencing technology have rapidly expanded our vision into the microbial world. Yet, the vast majority of microorganisms remain unexplored due to the difficulties of bringing microorganisms to *in vitro* culturing. Mircea Podar, a microbiologist from Oak Ridge National Laboratory comments that, “We still need to culture microbes. Fewer and fewer people do that.”

There are many reasons why some microorganisms are challenging to culture, for example the variation of growth speeds as well as the co-dependence, competition or inhibition among microorganisms. Microbiologists have developed numerous cultivation approaches to isolate and grow individual organisms. However, current approaches are typically limited in isolating new organisms in an untargeted way. It is thus difficult to

characterize specific groups from yet-uncultured taxa.

Genomics data offer an opportunity to make the association between genotype and cell characteristics. Podar and colleagues develop a reverse genomics isolation approach that enables physical isolation of organisms based on the presence of a membrane protein.

They first identify the membrane-protein-encoding genes using available genomic data and select the exposed epitopes that can be used for antibody development. They then use the produced antibodies to sort cells into individual populations via flow cytometry. In a case study of human oral saccharibacteria (TM7), they were able to culture several species of TM7 and their interacting Actinobacteria, which suggests that TM7 directly contacts other organisms and that the interacting

Actinobacteria are not strictly specific to one species.

Using reverse genomics isolation, researchers can now grow the targeted cells and test the growing conditions for different populations, as well as identify interactions between microorganisms. Podar remarks that, “Culturing is hard, and there is no guarantee of success. But a novel microbe in culture opens the road for doing so much more biology down the road.”

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Research Paper
 Cross, K. L. et al. Targeted isolation and cultivation of uncultivated bacteria by reverse genomics. *Nat. Biotechnol.* <https://doi.org/10.1038/s41587-019-0260-6> (2019).

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