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Microfluidic droplet platform for ultrahigh-throughput single-cell screening of biodiversity

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Abstract

 Ultrahigh-throughput screening (uHTS) techniques can identify unique functionality from millions of variants. To mimic the natural selection mechanisms that occur by compartmentalization in vivo, we developed a technique based on single-cell encapsulation in droplets of a monodisperse microfluidic double water-in-oil-in-water emulsion (MDE). Biocompatible MDE enables in-droplet cultivation of different living species. The combination of droplet-generating machinery with FACS followed by next-generation sequencing and liquid chromatography-mass spectrometry analysis of the secretomes of encapsulated organisms yielded detailed genotype/phenotype descriptions. This platform was probed with uHTS for biocatalysts anchored to yeast with enrichment close to the theoretically calculated limit and cell-to-cell interactions. MDE-FACS allowed the identification of human butyrylcholinesterase mutants that undergo self-reactivation after inhibition by the organophosphorus agent paraoxon. The versatility of the platform allowed the identification of bacteria, including slow-growing oral microbiota species that s uppress the growth of a common pathogen, Staphylococcus aureus, and predicted which genera were associated with inhibitory activity.

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Keywords

Butyrylcholinesterase, Cell-cell interactions, Microfluidic encapsulation, Staphylococcus aureus, Ultrahigh-throughput screening

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