

New Technologies - Bioengineering II

Establishing respiratory organoids for modeling viral infections

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Conventionally, *in vitro* studies of human biology and pathology, including virus-host interaction, have hinged on the immortalized and cancer-derived cell lines that comprise homogenous clonal cells. These cell lines can barely model native human epithelia composed of multiple cell populations. Thus, a biologically relevant and readily available *in vitro* model system is desperately needed. We derive organoids from primary lung tissues and nasal cells highly efficiently, which provide a stable and self-renewable source for long-term expansion. We then induce differentiation in the long-term expandable organoids and generate mature nasal, airway and alveolar organoids that morphologically and functionally phenocopy the human respiratory epithelium (PNAS 2018, Cell Discovery 2022, mBio 2022). Namely, we have established the first adult stem cell-derived respiratory organoid culture system that enables scientists to rebuild and expand the entire human respiratory epithelium in culture plates with super efficiency and stability. These biologically-active respiratory organoids are robust and universal *in vitro* models for basic science, translational research and clinical medicine.