Next-Generation Trachea-Esophageal Organoids for Scalable Disease Modeling

A scalable, reproducible, and human-specific platform for modeling trachea-esophageal development and congenital malformations such as Esophageal Atresia (EA)/ Tracheoesophageal Fistula (TEF).

Technology

Researchers at NYU have developed a novel micropattern-assisted differentiation system that enables scalable *in vitro* reconstitution of human trachea-esophageal (TE) organs using human pluripotent stem cells (hPSCs). Specifically, this platform generates mini-organs (mini-tracheas and mini-esophagi) on glass-supported microchips with defined spatial geometry, allowing for controlled morphogenesis that recapitulates human fetal development. The system integrates AI-driven phenotypic profiling to predict and quantify developmental outcomes, enabling high-throughput analysis of genetic and environmental perturbations relevant to Esophageal Atresia (EA) and Tracheoesophageal Fistula (TEF). This first-in-class approach offers an unprecedented opportunity to uncover new therapeutically targetable mechanisms of human TE development and congenital malformations.

Background

Malformations of the trachea-esophageal tract, including EA and TEF, affect approximately 1 in 3,000 live births in the U.S., with no available disease-modifying therapies. Existing models, such as animal models, traditional 2D monolayers, and 3D organoids, fail to capture the spatial-temporal precision and reproducibility needed for developmental modeling and drug screening. This technology addresses this gap by combining micropattern technology with high-content imaging and AI-based phenotypic classification to generate robust, quantitative models of TE development. This enables the study of key signaling pathways such as BMP and FGF, as well as the effects of genetic mutations (e.g., Noggin loss) that drive EA/TEF. This system sets a new benchmark in disease modeling and screening, vastly outperforming current methods in scalability, predictive accuracy, and ability to study human developmental disorders previously beyond reach.

Development Stage

The platform has been validated for generating human-like tracheal and esophageal mini-organs on microchips. AI-based classifiers have been trained and tested on image databanks, demonstrating predictive accuracy for fate specification and morphogenesis. Disease modeling has been demonstrated using Noggin-knockout lines, which successfully recapitulates key features of EA/TEF observed in patients. Additional studies are underway to expand screening capabilities and gene perturbation mapping.

Applications

Technology ID

ROS09-02

Category

Life Sciences/Platform Technology
Life Sciences/Research tools/Tissue Engineering
Life Sciences/Research tools/Drug Development
Life Sciences/Rare Diseases
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- **High-throughput screening:** To identify drug candidates able to treat or prevent TE developmental defects and/or TE congenital malformations
- **Basic research:** To understand the drivers and mechanisms underlying TE developmental defects and/or TE congenital malformations

Advantages

- **High-throughput compatibility:** Supports generation and analysis of thousands of micropatterned human mini-organs in a multi-well plate format.
- **Reproducible tissue development:** Yields consistent tracheal and esophageal structures with spatial and temporal fidelity.
- **Human-specific relevance:** Overcomes limitations of animal models by recapitulating human TE development.
- **High resolution imaging analysis**: Compatible with high-content confocal microscopy, enabling parallelized, high-resolution analysis of tissue architecture and differentiation.
- **AI-driven phenotyping:** Enables unbiased, automated classification of tissue identity and developmental defects.
- **Versatile modeling capacity:** Accommodates genetic and environmental perturbations relevant to rare congenital diseases, as well as exogenous agents (drug screens).

Intellectual Property

NYU has filed a U.S. provisional patent application covering the compositions and methods for generating tracheal and esophageal tissues on microchips and the method for AI-based predictive phenotypic profiling of mini-organs.