Docket #: S21-364

A 3D Human Immune Organoid System for High Throughput Screening

Stanford researchers in the Mark Davis Lab have developed a human cell culture system to grow 3D immune organoids within hydrogel structures using limited cellular input that can be adapted to large screening assays for flexible downstream immunological readouts. The system is technologically simpler, more scalable, more reproducible, more accurate, and more flexible than current screening methods. The method embeds human immune cell suspensions within 3-dimensional hydrogel structures as functionalized immune organoids, dramatically improving reproducibility, immunobiology response accuracy, assay flexibility, and throughput capacity. Antigen compounds, vaccine candidates or adjuvants can be co-embedded along with the cells within the 3-dimensinal structures to construct a miniaturized 3-dimensional artificial lymph node. The resulting solidified suspensions are then distributed in tissue culture plates with a defined supplemented media. For high throughput use, multiplex plates can be configured for surveying culture media for antibody responses, and organoids can be harvested by removal from the plate for flexible readouts such as high dimensional imaging, flow cytometry and DNA/RNA sequencing. The structures manifest many in vivo immune responses, and can therefore be used to model the complex human immune system.

Stage of Development

Research *in vitro*: Researchers are using tonsil immune organoid arrays to identify immunosuppressive drug effects on vaccine responses. They continue to tune the larger scale format assay operating characteristics, to test the assay's detection limits and real world applications for compound screening and high dimensional imaging, to optimize growth conditions and define cell parameters for larger scale use, to define detection limits, to explore characteristics for high throughput screening, and to deploy multiple flexible readouts.

Applications

- **Vaccine and adjuvant candidate screening**, especially for seasonal viral illness like flu and COVID19.
- **Immunomodulatory / Immunotoxicity screening of existing**, clinically available drugs for adverse vaccine responses.
- **Drug development** screening of compound libraries for focused development of new immunomodulatory drugs.

Advantages

- Technological **simplicity – no need for complex bioreactor preparation**.
- **Accurate - more closely recapitulates in vivo vaccine responses** compared with peripheral B cells.
- **Flexible, adaptable** - more flexible in input/output. Can be adapted for high throughput imaging, flow cytometry, and many downstream immunological sequencing readouts with minimal modulation.
- **Scalable with reduced variability**

Patents

- Published Application: WO2023244669

Innovators

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