3-D Retina Organoid Challenge (3-D ROC) Submission Template

Submissions should be emailed to NEI3dROC@mail.nih.gov

National Eye Institute

Team Lead:
Submission Title:
Submission Category: Drug Screening

In order to receive full points, all questions in this document must be addressed.

1. ***Administration Requirements***

   a. Do all team members meet eligibility requirements (U.S. citizen or company residence)?

   b. Were any federal funds used for this submission? If so, are federal funds consistent with the purpose of team members grant awards?

   c. Did your team write the required 300-word maximum public abstract that clearly states the advantages and novelties of the retina organoid prototype? Submit the abstract as a separate document.

   d. Did your team create the required abstract video link? If so, include link here:

2. ***Evaluation Criterion: Impact and Innovation***

   a. State how your approach significantly advances current retina organoid generation protocols.

   b. How will this solution have a lasting impact on how retinal diseases and treatments are studied?

   c. State how the current substantial physiological barriers to the field are shown to be overcome in significant ways in your approach.

   d. How are existing technological barriers of in vitro human retina organoid development are addressed?

   e. Explain how the submitted data has been well validated in a robust manner.

3. ***Evaluation Criterion: Cell Types, Structure, and Function***

   a. State how your solution demonstrates all major retinal neuron cell types: Rod and photoreceptor (at least 2 types of cones), horizontal cells, amacrine cells (at least 5 types), bipolar cells (representatives in 3 major groups-rod bipolar; ON-Cone; Off-cone), and Retinal Ganglion Cells (identify at least three subtypes).

   b. Explain how the data shows a majority of non-neuronal cell types are present including astrocytes, Muller glia, RPE cells, pericytes, endothelial cells, and microglia.

   c. Describe the analysis that shows cell types and cell populations reflect the proportions of what is seen in the human eye using robust methods including gene expression (e.g. RNAseq), immunohistochemistry or flow cytometry, and histology.

   d. Do the retina organoids have foveae that are highly representative of human anatomy? If so, describe:

   e. Explain how the retina organoids have retinal and choroidal vasculature or is recapitulated with microfluidics or accounted for by other perfusion techniques.

   f. Summarize how the 5 layered neural retina (3 cell layers, 2 synaptic layers) has been validated in a robust manner and the RPE lamina is morphologically well-defined.

g. Are the ribbon synapses and optic nerve/retinal nerve fiber layer are definitively shown? If so, describe:

h. Is electrophysiology of light perception demonstrated? If so, explain it along with how photoreceptor signal transduction/phototransduction is robustly evidenced, functional synapses at inner and outer plexiform layer are shown, and RGC action potentials in response to light stimuli are exhibited.

i. Describe the characterization of distinct On- and Off- pathways.

4. Evaluation Criterion: Reproducibility, Quality Control, and Standardization

a. Is the demonstration of inter-laboratory consistency of the protocol and its applicability to multiple cell lines, shown with the statistical rigor of the presented data (e.g. error bars) highlighted? If so, describe the protocol with sufficient detail to ensure its reproducibility.

b. Explain and justify protocol's robustness in terms of organoid production and yield rate and the ability to decrease the differentiation time, etc. in the context of the prescribed utility of the organoid.

c. Thoroughly explain the standardization strategy describing the scalability of the protocol to a large production, as well as a streamlined assay platform for higher throughput. Ensure it is aligned with the proposed commercialized utility of the organoid.

d. Clearly describe the methods and criteria employed to ensure proper quality control (e.g. free of microbial contamination and chromosomal defects via karyotyping, STR analysis, FISH analysis).

e. Do you have a commercialization strategy including details of target users, a market analysis, and a comparative analysis with competing technologies that is well-developed? Filed patents should be listed. Discussions with FDA, third-party commercialization/entrepreneurship consultant, or enrollment in commercialization training programs should be documented. Any agreements with industry, or transferability to industry partners (MOUs, licensing, CRADA, in-kind or discounted validation) should be presented. Summarize the commercialization strategy along with the above detailed information.

5. *Evaluation Criterion: Endpoint Assay Specific Goals – DRUG SCREENING*

a. Include data that robustly shows retina organoid screening protocols are amendable to high content screening, which may include high content imaging, drug validation/toxicology, or functional genomic screening (e.g. does not include materials known to show strong compound absorption). Include information on methods to mass-produce (e.g., 100s) organoids. Show how multiple replicates of plates are compared in the same experiment to show variability is minimal.

b. Include data that shows minimal variation occurs between different stem cell lines under screening conditions. Describe how the morphological and functional features are maintained so readouts are easy to normalize.

c. Show effects of shipping or freezing/thawing on screening methods. Demonstrate how viability of cells and transferability of screening protocols to other labs or companies shown to be robust and reproducible.

d. Include data that robustly shows the retina organoids recapitulate known retina toxicities or known drug effects based on morphological and functional readouts.

Contact the NEI Office of Regenerative Medicine if you have any questions at NEIORM@nei.nih.gov or NEI3dROC@mail.nih.gov.