CRACK IT

Challenge 23: Retinal 3D Surgery Q&As.

Q. How will you assess the required "maturity" of the cells in the model?

A. There should be expression of a range of biomarkers that are found in the mature retina.

Q. Do you expect the photoreceptors expressed to be responsive to light?

A. We would consider this to be of significant benefit but understand that this may not be possible in all the relevant cells of the model.

Q. Do you require the microglia to demonstrate activity?

A. Evidence of an activation marker of, for example, phagocytic activity is important.

Q. What scale of throughput are you expecting?

A. The platform will primarily be used for drug discovery, toxicological assessment and mechanistic studies on a low throughput scale. A 24 well plate set up that would, for example, permit dose responses to be included in an experiment would be acceptable.

Q. How important is the recapitulation of the exact architecture and cell orientation of the human retina?

A. The Sponsors appreciate that the exact 3D architecture will be difficult to achieve and are primarily focused on achieving the functional activity as demonstrated, for example, through detection of known toxicity endpoints. However, replication of the layering seen in the retina may well be important to achieve this.

Q. What are the read outs that you require from the Retinal Pigment Epithelium cells?

A. Readouts include, but are not limited to, the presence of melanin, phagocytosis, tight junctions and morphology. Assessment of these could be, for example, through use of high content imaging.

Q. How long do you require the system to be stable for? What is the duration of the studies you perform?

A. There is increasing interest in doing repeat dose, longer term studies. Therefore, the Sponsors are interested in a system that is amenable to both acute (three days) and chronic (more than two weeks) if possible.

Q. Is the use of explants acceptable?

A. Yes the focus of the Challenge is on more developing a fit for purpose, human predictive model of the retina that delivers 3Rs benefits over the current *in vivo* approaches. If there is strong evidence that explants can deliver this, this approach will be considered.

Q. Are the Sponsors requiring a fee for service model or the ability to take the technology in-house?

A. Sponsors would ideally like access to both options, but have a stronger preference for having the ability to run the system in-house.

Q. Is there a requirement or preference for inclusion of the fovea centralis?

A. Sponsors are happy for this to be included, but it is not a formal requirement.

Q. Are the Sponsors amenable to biomaterials that may be translucent?

A. Yes, the Sponsors are happy to consider this approach as long as the functional readouts can still be obtained and the material would not absorb any dosed compounds.

Q. What is your view on the inclusion of disease modelling capabilities?

A. This is not a required Challenge deliverable. The Sponsors would consider this an added scientific benefit and are particularly interested in inherited diseases and models of wet and dry Age-related Macular Degeneration.

Q. I have expertise in certain areas, but not in all areas that are required to solve the Challenge. How can I find other expertise?

A. Speak to the NC3Rs office (crackitenquiries@nc3rs.org.uk) and we will do our best to help connect you with the expertise you are seeking. You can also make use of the Challenge-specific LinkedIn pages that have been established.

Q. Who should we email with questions?

A. General questions can be sent to the NC3Rs. Questions regarding a specific Challenge can be sent to the Sponsors, but enquiries should be sent to ALL Sponsor parties for a particular Challenge. If preferred, please email the NC3Rs to introduce you to the Sponsors at CRACKITenquiries@nc3rs.org.uk.