CRACK IT

Challenge 35: *In vitro* TDAR

Q. Do you have a preference on the source of cells used in the assay system?

A. The cells used in the system should demonstrate the relevant functionality that is required in this assay. It is unlikely that cell lines will be able to capture the full range of functionalities required, and primary cells may be more suitable for this reason. Human induced pluripotent stem cell (hiPSC)-derived cells would also be acceptable as long as they reach the correct differentiation stage and are not in a pre-mature state.

Q. Are you looking for a complex *in vitro* model approach (e.g. organ-on-a-chip/microphysiological system (MPS))?

A. An MPS-based model may be more likely to recapitulate the full functionality required, due to the physical cues in place, but the Sponsors are open to the approach taken as long as it fulfils the Challenge brief. A desirable deliverable for Phase 2 is the potential to be able to link the model developed through the Challenge to other MPS organ systems, which could be used, for example, for oncology applications and to interrogate other immune-tissue interactions, including the relationship to toxicity mechanism.

Q. Is primary or memory antibody response the focus, or both?

A. The Sponsors are initially interested in the primary response. Evaluating the secondary immune response would be of interest and is a desirable Phase 1 deliverable.

Q. Is there interest in more streamlined, precise and accurate detection to complement the assay i.e. continuous readout or flow in an organ-on-a-chip system?

A. The Sponsors are open to suggestions and would be happy to discuss potential approaches with applicants.

Q. Does it matter if the assay is in 2D or 3D?

A. No, as long as the assay demonstrates the relevant functionality required. However, considering the complex nature of the immune response that needs be modelled (i.e. involves the interaction of several key cell types and mediations in the morphologically coordinated architecture of lymphoid organs), it is less likely that a 2D model can achieve this.

Q. Could the Sponsors provide model antigens or vaccines?

A. Several potential model antigens are commercially available; the Sponsors can advise on the appropriate one to choose. The Sponsors can provide benchmarking compounds as part of their in-kind contributions (but input on these would be appreciated as well).

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.

NC 3Rs

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 Challenge. If preferred, please email the NC3Rs to introduce you to the Sponsors at crackitenquiries@nc3rs.org.uk