Challenge 16: Virtual Infectious Disease Research

Q. How will CRACK IT work with NC3Rs being sponsor, in terms of in-kind contributions etc?

A. The NC3Rs has a wide variety of contacts and can provide a good support network. We will also facilitate dialogue between potential participants. For Phase 2 we will investigate the possibility of an industry co-sponsor.

Q. Research of some infection systems uses a lot more animals than others. Should we focus on those with the most potential impact in terms of animal numbers?

A. The system chosen by the applicant needs to balance the likelihood of success, potential uptake of the system, scientific impact and 3Rs impact. The largest impact on animal numbers may come from a system that works well in a focussed area rather than one that is not predictive but tackles a more broad area where significant numbers of animals are used.

Q. Confidence in models is important. What level of confidence do we need to demonstrate in Phase 1?

A. The model is eventually only going to be accepted if it can be taken through to an end product that works and is predictive. The Phase 1 study should provide enough confidence to the Review Panel that this can be achieved during Phase 2. At the moment, there are no appropriate models and we do not expect to get a model which reflects the systems 100% accurately. Therefore even if the model has limited capabilities it will still be useful to help to focus research and identify targets.

Q. How will networks be facilitated through NC3Rs to solve the Challenge?

A. We have a CRACK IT LinkedIn group set up for this Challenge (http://linkd.in/1gsHm9w). We can also send the contact details of people that were at the surgery, if you were not at the event and would like this information please contact Cathy.Vickers@nc3rs.org.uk. The NC3Rs also has a network of mathematicians who we can introduce potential applicants to. Attendees of the workshop also mentioned the Turing Gateway to Mathematics initiative which was launched in March 2013 and works with mathematicians to incorporate mathematics into other research areas. We will be advertising the Challenge to this group.

Q. The brief does not specify a specific area of focus. Is this intentional?

A. Definitely. The aim was to leave the Challenge open to avoid stifling the most innovative approaches. We have identified a market need and want to leave it up to the applicants to determine which area will have most impact. This might be a broad area or a very narrow one.

Q. Would it make more sense to start with a limited model looking at one host (human) and one pathogen (or closely related group of pathogens)?

A. Possibly, if it makes the deliverables in Phase 1 more achievable. It would be better to have a model that only answers one issue but does it well and if the approach we find solves a very small subset of questions in a small area then it is still useful. It also gives the potential to expand based on the knowledge gained from developing that system.

Q. What is the specific question we are trying to address? Different modelling approaches will be needed depending on the question.

A. The decision on which question to focus on is left to the applicants. We are trying to develop a specific tool that can be used to improve basic research and/or the drug development process so a question that addresses any element of this would be within scope.

Q. Has a survey been done within pharma to ask what particular challenges are out there currently? Is it worth doing this?

A. No, but this could be done. The NC3Rs would be happy to facilitate interactions with the pharmaceutical industry and also to ask appropriate industry contacts specific questions that relate to your application. Please contact Cathy.Vickers@nc3rs.org.uk who will facilitate this.

Q. How would regulatory bodies view the system?

A. It is unlikely and not the intention that this system be presented to regulators. If it used to input into decisions about which targets to take forward during screening it will decrease late-stage attrition.

Q. How would we approach the validation of the system as some animal models are not representative of the natural disease state?

A. Any virtual model will have to be representative of the natural disease state and not an overloaded state that may sometimes be seen in animal models. Ideally, the model would represent the human system; however it is acknowledged that it may be difficult to validate a human system against potentially poor *in vitro* data. It may be that virtual models have to have some validation with appropriate animal models in the short term with the long term objective of reducing these. A route to validation (something that is 'fit for purpose') will be dependent on the system and should be included in the application.

Q. How would this system reduce animal use?

A. The model could be used for screening which would result in improved candidate selection and reduce the *in vivo* efficacy and safety studies that would be carried out with drugs that fail later in development. Additionally, virtual animals could be used alongside *in vivo* studies providing data and knowledge, resulting in fewer animals being used in a study.

For further information, please email Cathy Vickers Cathy.Vickers@nc3rs.org.uk