CRACK IT Solutions

Using human embryonic bodies from stem cells for teratogenicity testing

Assessing the potential developmental and reproductive toxicity (DART) of drugs and chemicals currently relies on animal experiments. These studies use large numbers of animals and their predictive value for human toxicity has been challenged. Human stem cell based approaches may offer an alternative to current animal models for assessing DART.

What could your solution be used for?

We have developed three dimensional (3D) aggregates to promote differentiation of embryonic stem (ES) cells *in vitro*, called embryonic bodies which give rise to three primary germ layers: ectoderm, mesoderm, and endoderm which recapitulate early embryonic development. Using this model, our aim is to develop and optimize a high-throughput, 3D human assay to screen for embryonic toxicity without animals. We propose to use a high content analysis assay to test drugs/chemicals for embryonic toxicity in these embryonic bodies. This will have the following advantages:

- Using a human cell model may overcome the significant species diff erences in signalling pathways during embryonic development which have a huge impact on the predictivity of DART studies in animals, and so aid in compound selection.
- More cost efficient and reduced animal use: *In vivo* DART studies are expensive and use large numbers of animals. Removing teratogenic compounds from development as early as possible may reduce these costs and subsequent animal testing.
- High-throughput: Our embryonic body assay has been tested and validated on 384 well plates which can be used for high-throughput teratogenicity screening of several drug libraries.

Need for collaboration

We are looking to collaborate with pharmaceutical/chemical industry partners to validate this assay as a standard model of DART screening. We would like access to a compound library with known teratogenicity and to high-content analysis machinery. In return, we will screen the compounds for teratogenicity in our optimised human embryonic body assay. The advice and guidance provided by an industry partner on using the assay in an industrial setting will be crucial to the successful application of this model. This collaboration would benefit companies and research laboratories investigating the teratogenic effects of drugs/chemicals.

3Rs impact assessment

A standard two-generation DART study typically uses around 2,500 test animals – our proposed human embryonic body assay has the potential to substantially reduce this number and improve the validity of preclinical DART screens. It will also enable better selection of drugs/chemicals for development so that the cascade of regulatory studies in animals, which are required before human clinical trials, are not conducted for drugs destined to fail in the clinic due to teratogenicity.

To find out more or to connect with the technology developer contact crackitenquiries@nc3rs.org.uk

NC 3Rs

MANCHESTER 1824
The University of Manchester

www.CRACKIT.org.uk
@CRACK_IT
crackitenquiries@nc3rs.org.uk
020 7611 2233