An *in ovo* model for safety and efficacy testing

The biotechnology company Inovotion partnered with AstraZeneca, to test the utility of a chick egg embryo model to potentially replace some mouse xenograft studies in drug development.

Solution provider:
Dr Jean Viallet

Organisation:
Inovotion

Award type:
CRACK IT Solution

Start date: 2016
Duration: 6 months

Amount:
£30k

Project partners:
AstraZeneca

Background

- The model comprises human tumour cells grafted on the chorioallantoid membrane (CAM) of embryonated chicken eggs. The CAM is a highly vascularised extra-embryonic membrane that is readily visualised and experimentally manipulated.
- The model is well established in academic research for studying tumour growth, invasion and metastasis but its use in industry has been relatively under-explored. Inovotion had previously tested 12 different human tumour cell lines and a small number of commercial drugs in the *in ovo* assay but needed a pharmaceutical partner to build confidence in the model.

3Rs and scientific benefits

- Working with AstraZeneca scientists, Inovotion conducted proof-of-concept studies to assess the efficacy and toxicity of therapeutic antibody-drug conjugates (ADCs) using the CAM model.
- Using a cytotoxic pyrrolobenzodiazepine (PBD) warhead bound to a HER2-targeting antibody, a comparison with clinical data showed that very low doses of the ADC could significantly reduce tumour weight in the CAM model, and that total tumour regression was possible at concentrations equivalent to clinically-relevant doses of trastuzumab, the current gold standard treatment.
- The efficacy of four ADCs using the same antibody, but with different cytotoxic PBDs, was assessed and ranked by comparing tumour weights and metastatic invasion. The ranking from the most to the least efficacious was the same in the CAM as that observed in the mouse model, demonstrating strong correlation.
- There are around 60 companies involved in developing ADCs and the market is set to grow at 19% a year over the next four years. With further work, the CAM model has the potential to replace some mouse xenograft studies for ADCs.

Wider impacts

- Inovotion and AstraZeneca continue to collaborate on assessing whether the CAM model can reliably predict the toxicity and pharmacokinetic measurements of ADCs.

Collaborator in-kind contributions:

- AstraZeneca provided a range of in-kind contributions. This included cell lines, ADCs, conjugate molecules and control compounds; processing and statistical analysis of new data; and historic *in vivo* data for validation studies.