New research could significantly reduce the need for clinical animal testing

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University of Southampton researchers are investigating innovative methods of testing drugs that will reduce the need for involving animals.

Drugs based on biological proteins can cause adverse immune reactions in humans.

Scientists from the University of Southampton will start a new study in June to develop a laboratory-based system, known as assays, which will accurately predict immune responses to these drugs. These assays would be used to pre-screen candidate drugs and reduce the need for testing on animals.

It is hoped that the assays will help avoid incidents such as the TGN1412 trials in London six years ago, which saw six healthy volunteers experience severe adverse reactions to a clinical drug that had been tested on animals with no effects.

Martin Glennie, Professor of Immunochemistry and Head of Cancer Sciences at the University, says: “Animal testing remains the industry standard for predicting patient toxicity but it can underestimate or even miss the levels of toxicity observed in the first-in-human trials, as we saw with the TGN1412 trials in 2006. Predicting toxicity using in vitro human assays would reduce the risk of incidents like this and also refine pre-clinical animal testing.”

The study is funded by the National Centre for the Replacement,

Refinement and Reduction of Animals in Research (NC3Rs) under its CRACK IT scheme, a ground-breaking open innovation programme to fund projects that accelerate the application of the 3Rs.

Professor Glennie, together with Dr Tony Williams, Reader in Clinical Immunology and Allergy at the University of Southampton will work with a team of researchers, which includes Dr Mark Coles of the Centre for Immunology and Infection at the University of York, to test a range of drugs called monoclonal antibodies to see if they can find a way of predicting their toxicity in patients.

It is known that most of the toxicity seen when using monoclonal antibodies comes from blood cells called lymphocytes. When these cells become activated patients feel ill, with symptoms ranging from a mild cold, to life-threatening swelling of vital organs. These activated lymphocytes make important 'messenger' molecules called cytokines and it is these messengers which cause the toxicity during a so-called 'cytokine storm'.

Drug testing in animals does not always predict how a monoclonal antibody will behave in patients. Southampton scientists will develop laboratory-based tests that will reliably predict cytokine release when a monoclonal antibody is given to patients.

"Worldwide more than 30 monoclonal antibodies, such as Herceptin and Remicade, have now been approved for human use, and they are rapidly changing the way we control and treat diseases ranging from cancer to rheumatoid arthritis," adds Professor Glennie. "The success of this class of drugs is such that hundreds more are under development. We have a long and distinguished history of making and using monoclonal antibodies in Southampton and so we feel ideally placed to undertake this important research and hopefully reduce the need for pre-clinical testing in animals."

Provided by University of Southampton