UNIVERSITY OF Southampton

Advancing Drug Discovery through the Development of 3D Mini-Organs

Improving how new drugs are tested will speed up the development of ground-breaking treatments for the world's most challenging diseases.

Research by biological scientists at the University of Southampton has led to the development of an innovative method of testing new drugs without using animals.

Tissue from human volunteers is used in the laboratory to develop a variant of versatile stem cells. These can be induced to group together to form human 'mini-organs' such as the pancreas, liver or heart, a few millimetres in size. Researchers can use these human 'mini-organs' to test and analyse the results of targeting diseases with new drugs accurately, quickly and safely.

Discovering and developing new drugs is a lengthy and expensive business. Many potential breakthroughs turn out to be ineffective or have damaging side effects. For every drug that makes it to market and transforms the lives of patients, many hundreds fail.

Testing on animals, although useful in many ways, cannot predict the effect of drugs on humans with 100 per cent accuracy but human trials at an early stage are too dangerous to contemplate. Pharmaceutical companies need accurate, fast and safe ways to screen new drugs, they want to know as soon as possible if they are toxic, useless or worthy of more development work – the 'fail fast' concept.

Scientific advances in the 1990s improved our understanding of individual biological molecules that could hold the key to tackling disease. However, the process of investigating their potential value in drug treatment was inefficient because research relied on either isolated cell cultures or whole animals.

Professor John Chad and colleagues discovered that a sample of brain tissue from a rat, cultured in the laboratory and viewed using high-resolution optical imaging could act as a 'mini-brain' with neuronal networks, synaptic connections and functions similar to living brain tissue. This provided a relevant and useful model for investigating neurological conditions such as ischemic damage and traumatic injuries.

This research led to the successful University spin-out company Capsant Neurotechnologies Ltd, founded by Professor Chad, Professor Lars Sundstrom and Dr Ashley Pringle in 2002 which received more than £2.3m in investment and grew to become an autonomous company with its own laboratories.

For the last ten years, investigations have continued into tissue-level models within both the University and Capsant laboratories. These have attracted major grants from UK research councils and partnerships with many international pharmaceutical companies. The team believed there was potential for further developments: If biological material from animals could be used for this kind of research, the researchers reasoned, it could be possible to use human cells instead. Happily, this proved to be the case, stem cells being

shown to be capable of forming 3-D mini-organs of brain, heart, pancreas, and liver. This research success has led to filing of patents, and branding of the system as OrganDOT™. The rights to use the OrganDOT intellectual property have now been out-licensed commercially. Collaborations with US stem cell technology developer VistaGen, and Asterand, a global specialist in human tissue research, have resulted in practical applications for this research. VistaGen has demonstrated the use of OrganDOTs for studies of drug candidate cardiac toxicity; Asterand has licensed the technology and is using it for diabetes, fibrosis and oncology studies.

This pioneering research at the University of Southampton and its spin-out company Capsant has led to the development of important new methods to test potential new drugs quickly and safely for effectiveness and toxicity on human cells. Pharmaceutical companies across the world are interested in this breakthrough and are increasingly using it in their research. The importance of bringing human cell studies forward in studies of potential drugs is underscored by the US National Institute for Health programme to encourage further research into ‘human chips’, and the realisation that the genetic make-up of individual human beings determines the efficacy and side-effects of drugs. OrganDOTs open the prospect of human pharmacogenomic studies to allow the development of treatments tailored to tackle particular conditions in people with specific genotypes, hopefully leading to better and safer treatments.