

# Scientists develop novel method to generate functional hepatocytes for drug testing

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Scientists have for the first time produced liver cells from adult skin cells using the induced pluripotent stem cell (iPSC) technology.

The study, led by the University of Edinburgh's MRC Centre for Regenerative Medicine, paves the way for the creation of a stem cell library that can be used for in vitro hepatic disease models.

Presently primary human hepatocytes (PHHs) are the 'gold standard' cell type used in predictive drug toxicology. These cells are derived from dead or donor tissue. The cells can only survive for three to five days and do not have the ability to multiply. PHH cells are therefore a scarce and expensive resource.

This study shows an alternative way of sourcing hepatocytes, by creating hepatic endoderm using the iPSC technology and then differentiating it into hepatocytes.

The in vitro derived hepatocytes showed similar attributes to PHH cells used for predictive drug toxicology assays, including CYP3A4 and CYP1A2 metabolism.

The method was successfully carried out with a variety of polymorphic variants, with cells derived from males and females of different ethnic origins.

Drug development is a long and cost-intensive business. Each new drug

takes many years to develop and pre-approval costs are in the region of \$1,3 billion per approved drug. Often drugs have to be withdrawn at this stage because of unwanted side-effects.

The new method has the potential to supply an unlimited and reliable source of hepatocytes. These hepatocytes are highly characterised and reproducible and should therefore enable earlier use in the screening cascade used by industry for [drug discovery](#).

Gareth Sullivan, of the University's MRC Centre for Regenerative Medicine, said: "What we have been able to do will help drug discovery because it means we are able to test drugs for adverse reactions at a much earlier stage."

Prof Sir Ian Wilmut, Director of the University's MRC Centre for [Regenerative Medicine](#), said: 'We are now looking for ways to bring this technology into routine use for drug testing. This is an exciting opportunity and it gives me great pleasure to be able to turn the first recommendation of the UK Stem Cell Initiative into a reality.'

The UK Stem Cell Initiative was an advisory board of the Government. It was set up in 2005 to formulate a ten-year vision of stem cell research in the UK. The board came up with a list of recommendations, the first one being: the UK Government should establish a public-private partnership to develop predictive toxicology tools from stem cell lines.

The research, which was carried out in collaboration with Harvard Medical School, is published by the journal *Hepatology*. As well as using liver cells created from stem cell lines to test drugs, it is hoped the cells could eventually be used in therapy for patients suffering from liver disease. They could also play a role to aid research into liver disease.

Source: University of Edinburgh

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