How organ-on-a-chip technology can get safer medicines to market sooner

At a Glance

- Human-specific technologies have the power to transform the slow and costly drug development process, where urgently needed new drugs are overwhelmingly failing safety and efficacy tests before they can reach patients.
- Damage to the human liver – a leading cause of this failure rate – can be predicted in humans more accurately by using liver-on-a-chip technology to test drugs than using animals.
- Globally, countries are taking action to support human-specific technologies in medical research, and it is time the UK joined them at the forefront of scientific innovation.

How can you help?

- Join the **All Party Parliamentary Group on Human Relevant Science** which supports the uptake of human-specific technologies in the UK.
- Contact us for more information using our details at the end of this document.

The Status Quo

Bringing new drugs to market is challenging, slow and expensive. Since 1950, the cost of developing a new drug has doubled every nine years.[i] Around 75% of research and development costs are thought to be due to drug failure, driving up the price of medicines. Problems in translating the results of pre-clinical tests to human patients play a major role in this high failure rate, and tests on animals are a central element of this. Over 92% of drugs that show promise in animal tests currently fail to reach the clinic and benefit patients, mostly for reasons of poor efficacy and safety that were not predicted by animal testing.[ii]

The risk of damage to patients' livers is one of the most common reasons why new drugs fail or are withdrawn from the market, resulting in a considerable waste of time and resources. Despite animal tests having a poor ability to predict the risk of human liver damage, it remains the case that safety testing for new drugs is typically conducted on both a rodent and non-rodent species of animal, including monkeys and dogs.

What is Drug-Induced Liver Injury (DILI)?

Drug-Induced Liver Injury (DILI) refers to damage to the liver caused by prescription drugs and can result in liver transplants and even deaths. For instance, Benoxaprofen was launched in 1980 to treat rheumatoid arthritis but was later withdrawn from the market after causing 139 DILI-related patient fatalities. Similarly, the osteoarthritis drug lumiracoxib (Prexige) was withdrawn from the UK market in 2007, following 159 reports of suspected adverse liver reactions worldwide. Around 50% of post-approval market withdrawals of drugs are due to toxicity.[iii]

DILI remains a leading patient safety concern in the pharmaceutical industry. The problem persists because safety studies undertaken in animals have poor predictive value for human DILI. There is growing recognition that improved, human-specific models are needed to better protect patients.

The Solution: Liver-on-a-chip Technology

Human-specific technologies such as organ-on-a-chip more accurately replicate human biology than animal models. About the size of an AA battery, the organ-on-a-chip is a small device on which human cells are grown that can mimic organs of the human body.

A recent study published in Nature's Communications Medicine journal found that liver-on-a-chip technology developed by leading US biotech **Emulate** was able to correctly identify 87% of drugs that carried a risk of liver

toxicity in humans, despite those drugs having passed through animal safety tests. The liver-on-a-chip technology also correctly identified 100% of the tested drugs that were known not to be toxic to the human liver. As well as providing clinical benefit, the paper estimated that this technology could generate over $3 billion annually for the pharmaceutical industry through increased research and development productivity.[iv] In recognition of the value of this technology, the US Food and Drug Administration (FDA) has partnered with Emulate through a co-operative research agreement spanning different divisions including the **Centre for Drug Evaluation and Research (CDER),** allowing them to use Emulate's organ-chips to study the safety, efficacy and mechanisms of action of drugs.

This technology must move from these very promising evaluation data to routine adoption in drug safety evaluation. To facilitate this, improved support is needed for the development and qualification of new models, and training must be provided for end users in the pharmaceutical industry and the next generation of research scientists. In addition, legislative and regulatory changes must be made.

Global Developments

Countries around the world are taking action to seize the opportunities presented by human-specific technologies.

- In December 2022, **US** Congress passed the **FDA Modernization Act 2.0,** removing the requirement for the submission of animal data to support new drug applications. Through small amendments to the wording of the Federal Food, Drug and Cosmetics Act, the FDA has made it explicitly clear that data from human-specific sources can be used in place of animal tests.
- In December 2020, the PAAM Act was introduced to the **South Korean** National Assembly supporting prioritization of human-biology based methods and cross-ministry collaboration.
- In September 2021, the **European Parliament** voted overwhelmingly in favour of a resolution to phase out animal use for research, testing, and education by adopting an action plan.
- Recent developments have also seen **India** and **Canada** act to replace the use of animals in research. India's *New Drugs and Clinical Trial Rules (2023)* authorises researchers to use human-specific methods such as organ-chips to test the safety and efficacy of new drugs, while Canada has passed a bill to phase-out animal-based toxicity testing which includes a mandate for Ministers to publish a plan to promote alternatives to animal use and commits to law the need for the Canadian Government to promote and implement non-animal methods.

The UK risks falling behind if it does not similarly embrace and encourage human-specific technologies in its research and pharmaceutical industries. These methods are crucial to the future success and productivity of these sectors, as well as for the improved health of the UK population. The **Alliance for Human Relevant Science** is calling on the UK Government to adopt a *Human-Specific Technologies Act*, which would facilitate the long-term transition to use of the technologies with timebound action plans. Read more **here.**

Contact us

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[ii] https://www.bio.org/clinical-development-success-rates-and-contributing-factors-2011-2020
[iii] Siramshetty et al., 2016 Nucleic Acids Research, 44 (D1), D1080-D1086
[iv] https://www.nature.com/articles/s43856-022-00209-1