Abstract

Many medicines are harmful to the liver, and drug-induced liver injury (DILI) now ranks as the leading cause of liver failure and transplantation in Western countries. However, predicting which drugs will prove toxic to the liver is extremely difficult, and often problems are not detected until a drug is already on the market. The Innovative Medicines Initiative (IMI) Mechanism Based Integrated Systems for the Prediction of Drug Induced Liver Injury (MIP-DILI) project brings together Europe’s top industrial and academic experts in the field. Together, they will develop new tests that will help researchers detect potential liver toxicity issues much earlier in development, saving many patients from the trauma of liver failure. The expected project duration is 60 months.

Mission

The goal of MIP-DILI is to dramatically improve the tools used to test for liver toxicity during drug development. The team aims to deepen the understanding of the science behind drug-induced liver injury and use that knowledge to overcome the many drawbacks of the tests currently used.
A major focus will be on a systematic and evidence-based evaluation of currently available and new laboratory test systems, including cultures of liver cells in one-dimensional and three-dimensional configurations.

The project will also develop models that take into account the natural differences between patients. This is important because factors such as certain genes, the liver’s immune response, and viral infections have all been associated with an increased risk of DILI.

The project will seek to address the current lack of human liver cells available to researchers by using induced pluripotent stem cells (iPSCs) generated from patients who are particularly sensitive to DILI.

Another strand of the project will develop computer models to unravel the complex, often interrelated mechanisms behind DILI. Finally, the team will assess how accurate the results of laboratory tests are at predicting actual outcomes in patients.

**Consortium History**

Feb. 29, 2012: The project was launched.

**Structure & Governance**

The Scientific Advisory Board is responsible for providing an external independent evaluation of the project on a regular basis by:

**Financing**

This project is funded by the Innovative Medicines Initiative, a public-private partnership between the European Union (EU) and EFPIA, resources of which are composed of financial contribution from the EU Seventh Framework Programme and EFPIA companies’ in kind contribution. Large pharmaceutical companies participating in IMI projects do not receive IMI funding. Funding has been received from IMI.
For a total cost of (€32.4 million).

**Intellectual Property**

The IMI intellectual property (IP) policy governs the IP regime of all projects funded by the IMI Joint Undertaking. To assist with specific IP queries, IMI has set up a dedicated IP Helpdesk, which can be contacted by emailing IMI-IP-Helpdesk@imi.europa.eu. The IMI IP policy can be accessed at http://www.imi.europa.eu/sites/default/files/uploads/documents/imi-ipr-policy01august2007_en.pdf

**Data Sharing**

According to IMI’s IP policy, the participants undertake to disseminate the data as soon as reasonably practicable but not later than one year after the termination or expiry of the project. The project agreement shall include a description of the material, which must be disseminated in accordance with the IP policy and referenced in the grant agreement. If the participants do not disseminate within such time periods without good reason, then the Executive Office has the right to disseminate such results in a manner consistent with the grant agreement.

**Impact/Accomplishment**

By bringing together experts from these sectors in a single, coordinated effort, MIP-DILI promises to advance understanding of drug-induced liver injury and deliver tests to detect it early on in drug development. Academic partners in the project will benefit from access to reference compounds, with known liver toxicity, that are held by pharmaceutical companies. For their part, pharmaceutical companies will gain a greater understanding of the complex science behind DILI. By helping researchers to detect DILI problems during drug research, before drugs are evaluated in clinical trials and approved for use, MIP-DILI will prevent considerable pain and suffering on the part of patients.
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