Why do we need stem cells to help us make safer medicines?

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Drug-Induced Liver Injury is a significant problem for society.

- Dose-dependent
- Species-selective
- Selective individuals
- Idiosyncratic
- Immunological
Drug-Induced Liver Injury

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Multiple and variable forms of disease
Multi-cellular and multifunctional organ

• Acute fatty liver with lactic acidosis
• Acute hepatic necrosis
• Acute liver failure
• Acute viral hepatitis-like liver injury
• Autoimmune-like hepatitis
• Bland cholestasis
• Cholestatic hepatitis
• Cirrhosis
• Immuno-allergic hepatitis
• Nodular regeneration
• Nonalcoholic fatty liver
• Sinusoidal obstruction syndrome
• Vanishing bile duct syndrome
Predictive Models of Drug-Induced Liver Injury

Is the TEST system fit for purpose?
What purpose is the TEST system fit for?
Laboratory Models of DILI

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Relevance to European Pharmaceutical Industry

Major reason for:

- regulatory actions against marketing approval
- restriction of prescribing indications
- removal from the market post-licensing
- and can lead to attrition of potentially good medicines...therefore also a patient problem....

Challenge of DILI increases from non-clinical - to post-marketing

Stats: APBI 2008; Stevens and Baker 2008
Drug-Induced Liver Injury
a significant problem for patients

- Genetic associations:
  - Can help to develop stem cell models for specific drug-induced liver injury
  - not predictive but potentially mechanistic
- Other stem cell models using integrated reporter may be predictive
Thank you

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