Human liver cell lines HepaRG and HepaRG-CAR for modelling human liver
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Need for human liver cells

- Prediction safety of medicinal products and other compounds
- Development therapeutics against human liver infections (e.g. hepatitis virus, Plasmodium)
- Basic liver research
- Regenerative medicine (liver tissue engineering, Bio-artificial liver)
Current options for human liver cells

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<thead>
<tr>
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<th>Detoxification</th>
<th>Other liver functions</th>
<th>Stability</th>
<th>Viability</th>
<th>Availability/Costs</th>
<th>Reproducibility</th>
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</thead>
<tbody>
<tr>
<td>Primary liver cells</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
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<tr>
<td>Liver cell lines</td>
<td>-</td>
<td>+/-</td>
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<td>Stem cells</td>
<td>-</td>
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<tr>
<td>Liver cell line HepaRG (+DMSO)</td>
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<tr>
<td>Liver cell line HepaRG (-DMSO)</td>
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HepaRG cell line

- HepaRG: liver progenitor cell line from hepatocellular carcinoma
  (INSERM, Gripon et al, PNAS 2002) commercialized by Biopredic International
Transcriptome of HepaRG resembles that of primary human hepatocytes most closely

- Hepatotoxicity related genes
- Liver metabolism, transporter and nuclear receptor related genes

→ Still room for improvement

New cell line HepaRG-CAR

- CAR: constitutive androstane receptor
- Transcription regulator of detoxification & energy metabolism in liver
- Overexpression by lentiviral transduction (Van der Mark et al., DMD 2017)
Increased detoxification

*: P<0.05 vs HepaRG-CAR no DMSO, all groups n>3
Improved albumin production & mitochondrial energy metabolism

*: P<0.05 vs HepaRG-CAR no DMSO, all groups n≥3
HepaRG-CAR cells

Key benefits:
- A stable, proliferative hepatocyte cell line
- Unparalleled hepatic functionality over other proliferative sources of human hepatocytes
- No requirement of DMSO: high viability
- Improved energy metabolism
  - highly suitable as source for human hepatocytes

Stage of Development:
- Further validation of the cell line is ongoing
- Create a fully characterized HepaRG-CAR line with the CAR gene inserted at a defined position
- Open for cooperations for further validation
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