Electronic Supplementary Material (ESI) for Toxicology Research.

Table S1. Comparison of Various Assays Measuring Key Mechanisms of Toxicity Endpoints Associated with DILI (Adapted from Reference 15).

Criteria	Sensitivity	Specificity	% Correct (Positive Predictive Value, PPV)	% DILI Missing (False Negative Rate, FNR)	% Accuracy (ACC) (True Positive + True Negative)/106
GSH	47.9%	85.5%	71.9%	52.1%	69.1%
TDI	18.8%	95.2%	75.0%	81.3%	61.8%
Cytotoxicity (3T3 cells)	29.2%	75.8%	48.3%	70.8%	55.5%
Mitotox	20.8%	93.5%	71.4%	79.2%	61.8%
BSEP	37.5%	87.1%	69.2%	62.5%	65.5%
All assays	85.4%	64.5%	65.1%	14.6%	73.6%
BDDCS Class 1	25.0%	61.3%	33.3%	75.0%	45.5%
BDDCS Class 2	64.6%	72.6%	64.6%	35.4%	69.1%
GSH and BDDCS Class 2	35.4%	96.8%	89.5%	64.6%	70.0%
BSEP and BDDCS Class 2	29.2%	96.8%	87.5%	70.8%	67.3%
BSEP Inhibitior and Mitotox Positive	4.2%	96.8%	50.0%	95.8%	56.4%
BSEP Inhibitor and Negative Cytotox or Mitotox	18.8%	95.2%	75.0%	81.3%	61.8%
BSEP Inhibitor or Positive Cytotox or Mitotox	68.8%	64.5%	60.0%	31.3%	66.4%

Table S2. Comparison of Toxicity Endpoints Associated with DILI for 3D Spherical Human Liver Microtissues (hLiMT), 2D Primary Human Hepatocytes (PHH) for the 110 Compound Data Set[52]

Measurement	Sensitivity	Specificity	% Correct (Positive Predictive Value, PPV)	% DILI Missing (False Negative Rate, FNR)	% Accuracy (ACC) (True Positive + True Negative)/110
3D hLiMT IC_{50} cutoff 10µM	18.8%	92.7%	81.3%	81.2%	46.4%
3D hLiMT IC_{50} cutoff 25µM	37.7%	87.8%	83.9%	62.3%	56.4%
3D hLiMT IC_{50} cutoff 50µM	52.2%	85.4%	85.7%	47.8%	64.5%
3D hLiMT IC_{50} cutoff 100µM	60.9%	85.4%	87.5%	39.1%	70.0%
3D hLiMT Margin of Safety (IC_{50}/C_{max}) 10µM	36.2%	97.6%	96.2%	63.8%	59.1%
3D hLiMT Margin of Safety (IC_{50}/C_{max}) 25µM	47.8%	92.7%	91.7%	52.2%	64.5%
3D hLiMT Margin of Safety (IC_{50}/C_{max}) 50µM	52.2%	85.4%	85.7%	47.8%	64.5%
3D hLiMT Margin of Safety (IC_{50}/C_{max}) 100µM	59.4%	80.5%	83.7%	40.6%	67.3%
2D PHH IC_{50} cutoff 10µM	4.3%	97.6%	75.0%	95.7%	39.1%
2D PHH IC_{50} cutoff 25µM	17.4%	92.7%	80.0%	82.6%	45.5%
2D PHH IC_{50} cutoff 50µM	29.0%	90.2%	83.3%	71.0%	51.8%
2D PHH IC_{50} cutoff 100µM	33.3%	85.4%	79.3%	66.7%	52.7%
2D PHH Margin of Safety (IC_{50}/C_{max}) 10µM	20.3%	97.6%	93.3%	79.7%	49.1%
2D PHH Margin of Safety (IC_{50}/C_{max}) 25µM	27.5%	95.1%	90.5%	72.5%	52.7%
2D PHH Margin of Safety (IC_{50}/C_{max}) 50µM	33.3%	85.4%	79.3%	66.7%	52.7%
2D PHH Margin of Safety (IC_{50}/C_{max}) 100µM	40.6%	85.4%	82.4%	59.4%	57.3%

Table S3. Comparison of Toxicity Endpoints Associated with DILI for 3D Spherical Human Liver Microtissues (hLiMT), 2D Primary Human Hepatocytes (PHH) [52] and Other Measures for the 100 Compounds where BDDCS Classification was Known

Measurement	Sensitivity	Specificity	% Correct (Positive Predictive Value, PPV)	% DILI Missing (False Negative Rate, FNR)	% Accuracy (ACC) (True Positive + True Negative)/100
3D hLiMT IC_{50} cutoff 10μM	17.7%	94.7%	84.6%	82.3%	47.0%
3D hLiMT IC_{50} cutoff 25μM	38.7%	89.5%	85.7%	61.3%	58.0%
3D hLiMT IC_{50} cutoff 50μM	53.2%	86.8%	86.8%	46.8%	66.0%
3D hLiMT IC_{50} cutoff 100μM	62.9%	86.8%	88.6%	37.1%	72.0%
3D hLiMT Margin of Safety (IC_{50}/C_{max}) 10μM	33.9%	97.4%	95.5%	66.1%	58.0%
3D hLiMT Margin of Safety (IC_{50}/C_{max}) 25μM	46.8%	92.1%	90.6%	53.2%	64.0%
3D hLiMT Margin of Safety (IC_{50}/C_{max}) 50μM	50.0%	84.2%	83.8%	50.0%	63.0%
3D hLiMT Margin of Safety (IC_{50}/C_{max}) 100μM	58.1%	78.9%	81.8%	41.9%	66.0%
2D PHH IC_{50} cutoff 10μM	4.8%	97.4%	75.0%	95.2%	40.0%
2D PHH IC_{50} cutoff 25μM	16.1%	94.7%	83.3%	83.9%	46.0%
2D PHH IC_{50} cutoff 50μM	29.0%	92.1%	85.7%	71.0%	53.0%
2D PHH IC_{50} cutoff 100μM	32.3%	86.8%	80.0%	67.7%	53.0%
2D PHH Margin of Safety (IC_{50}/C_{max}) 10μM	21.0%	97.4%	92.9%	79.0%	50.0%
2D PHH Margin of Safety (IC_{50}/C_{max}) 25μM	27.4%	94.7%	89.5%	72.6%	53.0%
2D PHH Margin of Safety (IC_{50}/C_{max}) 50μM	32.3%	84.2%	76.9%	67.7%	52.0%
2D PHH Margin of Safety (IC_{50}/C_{max}) 100μM	40.3%	84.2%	80.6%	59.7%	57.0%
BDDCS Class 2	41.9%	76.3%	74.3%	58.1%	55.0%
C_{max} > 1.3 uM	71.0%	76.3%	83.0%	29.0%	73.0%