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Addressing the Billion-Dollar Problem of Drug-Induced Liver Injury

Ultra-sensitive hepatotoxicity assays for the development of safer drugs

Drug-induced liver injury (DILI) is frequently detected in post-marketing resulting in drug withdrawals and box warnings that shrink the market and cost drug developers billions.

40%
Of drugs fail due to toxicity

#1
DILI is the #1 cause of toxicity

23%
Of drug withdrawals are caused by DILI

60%
Of drugs carry DILI box warnings

Lena Biosciences' hepatotoxicity assays predict DILI with high sensitivity using a single drug treatment

	Drug	Approval status	DILI status	DILI type	1 dose 1 day study IC50/Cmax	Predicted
Structurally similar drugs	Troglitazone	Withdrawn	Positive	Idiosyncratic	0.09	Yes
	Pioglitazone	✓	Negative/low DILI	Intrinsic	> 34	Yes
	Tolcapone	Withdrawn	Positive	Intrinsic	0.06	Yes
	Entacapone	✓	Positive/lower DILI	Intrinsic	9.48	Yes
	Sitax(s)entan	Withdrawn	Positive	Intrinsic	4.15	Yes
	Ambrisentan	✓	Negative	Intrinsic	> 1025	Yes
	Clozapine	✓	Positive	Intrinsic	11.4	Yes
	Olanzapine	✓	Negative	Intrinsic	> 625	Yes
	Trovafloxacin	Withdrawn	Positive	Idiosyncratic	1.48	Yes
	Levofloxacin	✓	Negative/low DILI	Intrinsic	> 32	Yes
	Nefazodone	Withdrawn	Positive	Intrinsic	1.84	Yes
	Trazodone	✓	Negative/low DILI	Intrinsic	32.93	Yes
	Buspirone	✓	Negative	Intrinsic	26010	Yes
	Diclofenac	✓	Positive	Intrinsic	8.49	Yes
	Zileuton	✓	Positive	Intrinsic	14.91	Yes
	Isoniazid	Box Warning	Positive	Idiosyncratic	21.28	Yes

DILI positive: IC50/Cmax < 25

De-Risking Drug Development

with Perfused Organ Panel and proprietary assay services

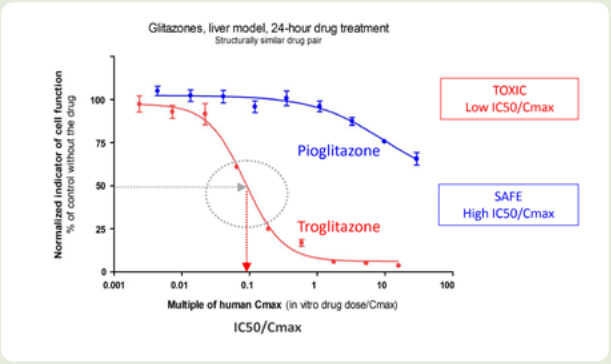
Lena Biosciences' hepatotoxicity assays isolate early toxicity signals and provide actionable insights for drug developers

- **Detect DILI early**
- **Understand what causes the toxicity**
- **Find active mechanisms for a given dose**
- **Identify safe doses**
- **Exclude at-risk patient groups**

Cutting-edge services to predict and mitigate DILI using the Perfused Organ Panel microphysiological system which combines 3D cell cultures with in-well perfusion using synthetic hemoglobin, Blood Substitute.

Case Studies Involving Structurally Similar Drugs

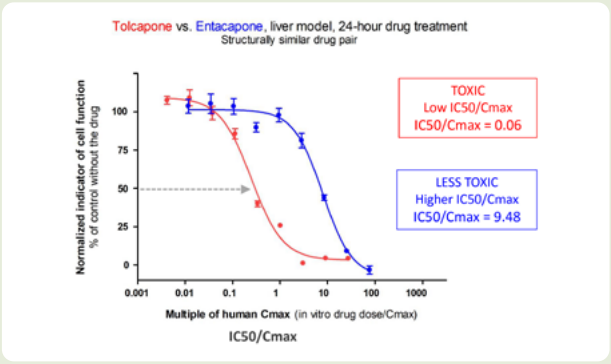
Detecting toxicity at low dose for a withdrawn Type II diabetes drug



Troglitazone was withdrawn
- $1.3 B annual sales loss
- 63 patients died from DILI

Pioglitazone is approved

Differentiating severity of DILI symptoms for Parkinson's disease drugs



Tolcapone was withdrawn
- Later approved with careful monitoring

Entacapone is approved
- Prescribing information lists hepatitis in post-marketing

Contact us for additional case studies including Isoniazid, Phenformin, Metformin, and Diclofenac in liver and brain models, and mitochondrial complex-specific toxicity for Nefazodone, Trazodone and Buspirone.

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Partner with Lena Biosciences for your DILI Testing

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