SIGNATOX™

Drug-induced liver injury

SIGNATOPE™

UNLOCKING PRECISION IN DRUG-INDUCED LIVER INJURY DETECTION

At SIGNATOPE, we present a cutting-edge assay family designed to quantify clinically relevant biomarkers, addressing the crucial need for accurate biomarker quantification. Focusing on the biomarker candidates accepted at the FDA´s Biomarker Qualification Program[1]- Macrophage colony-stimulating factor 1 receptor (MCSF1R), osteopontin (OPN), high mobility group protein B1 (HMGB1), and glutamate dehydrogenase (GLDH), complemented with caspase-cleaved keratin 18 (ccK18) and keratin 18 (K18) - our panel raises the standard for DILI safety.

March 2024

SIGNATOPE GmbH
Markwiesenstr. 55 •
D-72770 Reutlingen
P: + 49 7121 744 08 - 61

info@signatope.com
www.signatope.com

General management:
Dr. Oliver Poetz
Dr. Hannes Planatscher

Product specialist:
Tobias Meisinger
meisinger@signatope.com
P: + 49 7121 74408 - 67

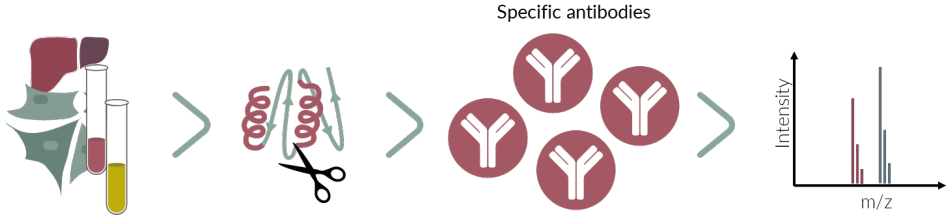
KEY FEATURES

- Complements established markers such as albumin, total bilirubin, transaminases, and prothrombin.
- Multiplexed assay allows for simultaneous quantification of MCSF1R, OPN, HMGB1 and GLDH in a single analytical run.
- Employing advanced immunoprecipitation and mass spectrometry techniques for high accuracy, sensitivity and specificity.
- Compared to ELISA methods no matrix effects for OPN and MCSF1R.[2]
- Validated assays according to FDA and EMA guidelines.

WHY SIGNATOPE?

- Experience in biomarker quantification since 2016.
- Workflows require minute amounts of sample and allow analysis of hundreds of samples within a week, compared to standard targeted proteomics approaches.
- Batch processing concept includes calibration curves and biological quality control samples, making results reliable, and reproducible.
- Report as supportive data ready for submission.

Enhance your clinical study with accurate protein data of the validated SIGNATOX panels!



TECHNOLOGY

SIGNATOPE has a proprietary technology that combines antibodies to capture proteins of interest with mass spectrometric readout. These antibodies are designed to recognize and bind to the target biomarker with high affinity, ensuring accurate quantification. The technology provides high sensitivity, enabling detection of low abundant biomarkers in complex biological samples – plasma, urine, tissues, cell pellets or lysates.[2, 3, 4, 5] The final readout by mass spectrometry ensures definitive identification and quantification.

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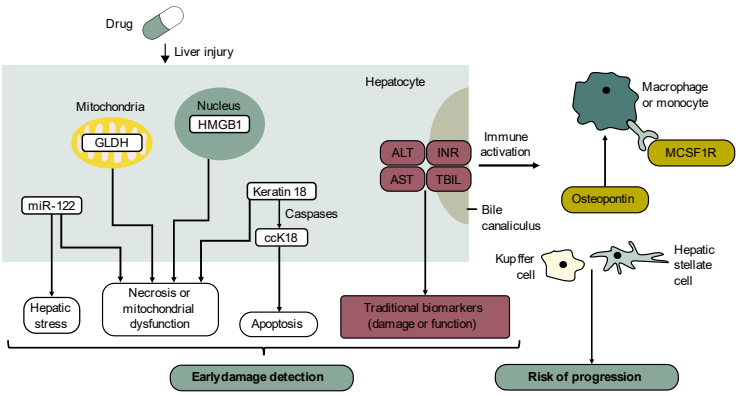
VALIDATED & RELIABLE RESULTS

We have extensively validated our assays to ensure reliable and reproducible results. The technology has been tested in various sample types, including EDTA-plasma, tissues, and cells, to ensure its applicability across different experimental setups.

		MCSF1R	OPN	HMGB1	GLDH	K18	ccK18
Parameter	Acceptance criteria	Max (%)	Max (%)	Max (%)	Max (%)	Max (%)	Max (%)
Intra assay precision (% CV)	≤ 20%, ≤ 25% at LLOQ/ULOQ	5	7	15	9	5	10
Intra assay accuracy (% accuracy)	± 20%	12	12	11	18	6	13
Intra assay total error (% TE)	≤ 40%	23	18	37	28	11	23
Inter assay precision (% CV)	≤ 20%, ≤ 25% at LLOQ/ULOQ	14	17	16	18	11	18
Inter assay accuracy (% accuracy)	± 20%	9	4	6	5	1	15
Inter assay total error (% TE)	≤ 40%	20	17	16	20	12	20

SCIENTIFIC BACKGROUND

The international Translational Safety Biomarker Pipeline (TransBioLine) project is currently investigating several mechanistic protein biomarkers for the characterization of DILI.[1] Information on these biomarker candidates will complement established markers such as albumin, total bilirubin, transaminases and prothrombin to improve the diagnosis and prediction of prognosis of DILI. MCSF1R, OPN, HMGB1, GLDH, K18, and ccK18 reflect apoptotic, necrotic and immunological processes that contribute to the pathogenesis of DILI.



EXPERT SUPPORT & GUIDANCE

We provide expert support and guidance throughout the quantification process. Our team of scientists can assist you in experimental design, sample preparation, and data analysis, ensuring that you obtain meaningful and interpretable results.

Assay name	Assay type	Batch size	Analytes
MPh11	IA-LC-MS/MS	36	MCSF1R, OPN, HMGB1, GLDH
ELISA007	ELISA	36	K18
ELISA002	ELISA	36	ccK18

SAMPLE REQUIREMENTS

Analytes	Sample type	Minimum amount for single analysis	Storage temperature	Shipping
Multiplex: MCSF1R, OPN, HMGB1, GLDH	EDTA-plasma	60 µL	-80 °C	on dry ice
K18	EDTA-plasma	70 µL	-80 °C	on dry ice
ccK18	EDTA-plasma	70 µL	-80 °C	on dry ice
Full DILI panel	EDTA-plasma	200 µL	-80 °C	on dry ice

LITERATURE

1. TransBioLine FDA Letter of Intent downloadable at: https://www.fda.gov/media/151077/download
2. Anselm, V. et al. Matrix and sampling effects on quantification of protein biomarkers of drug-induced liver injury. J Proteome Res, 20:4985-94, 2020.
3. Anselm, V. et al. Immunoaffinity-Based Liquid Chromatography Mass Spectrometric Assay to Accurately Quantify the Protein Concentration of HMGB1 in EDTA Plasma. Methods Mol Biol, 2261:277-89 (2021).
4. Wegler, C. et al. Variability in Mass Spectrometry-based Quantification of Clinically Relevant Drug Transporters and Drug Metabolizing Enzymes. Mol Pharm 14, 3142-3151 (2017).
5. Hammer, H., Schmidt, F., Marx-Stoelting, P., Potz, O. & Braeuning, A. Cross-species analysis of hepatic cytochrome P450 and transport protein expression. Arch Toxicol 95, 117-133 (2021).
6. Image modified after: Andrade RJ et al, Drug-induced liver injury. Nat Rev Dis Primers. 2019 Aug 22;5(1):58. doi: 10.1038/s41572-019-0105-0. PMID: 31439850