



**SIGNATOPE™**

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:  
Robin Kretz  
kretz@signatope.com  
P: + 49 7121 74408 - 65

### UNLOCKING PRECISION IN DRUG-INDUCED KIDNEY 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. Biomarkers of kidney tubular injury have been extensively studied and qualified for nonclinical safety assessment as well as at a cohort level in healthy volunteers in phase 1 clinical trials. FDA recommends to analyze Kidney Injury Molecule 1, Albumin, beta-2 Microglobulin, Clusterin, N-Acetyl-beta-D-Glucosaminidase, Neutrophil Gelatinase-Associated Lipocalin and Osteopontin if there is an a priori suspicion of nephrotoxicity. In contrast, assays for urinary biomarkers of drug-induced glomerular injury are lacking. Focusing on the glomerular biomarker candidates accepted at the FDA's Biomarker Qualification Program<sup>1</sup>– Nephricin (NPHS1), Podocin (NPHS2), and Podocalyxin (PODXL) – we developed two panels addressing tubular and glomerular injury.

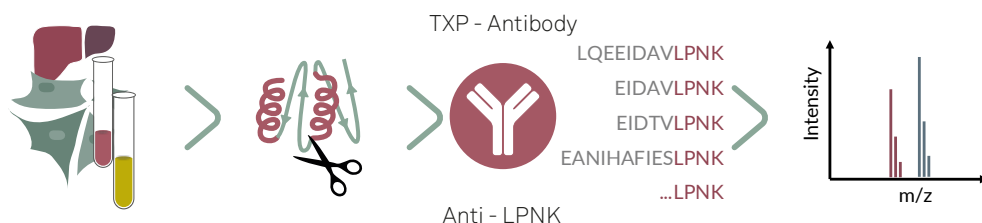
### KEY FEATURES

- Unique assay panel allows for simultaneous quantification of tubular and glomerular protein biomarkers in a single analytical run.
- Assays for tubular markers applicable for analyses of preclinical studies – non-human primates<sup>2</sup>, dogs<sup>3</sup>, rats and cats.
- 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!






































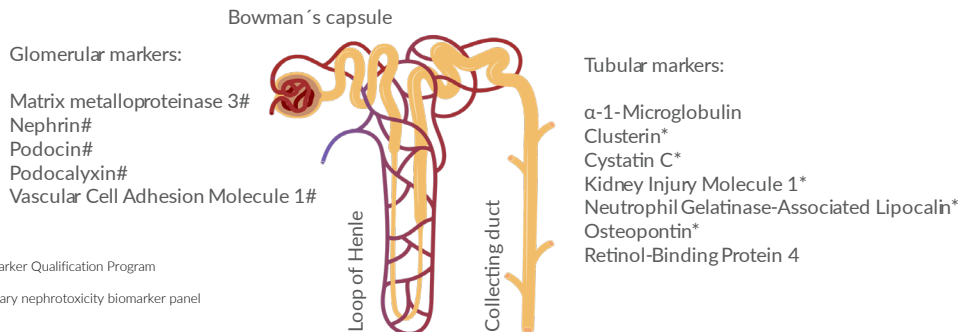
### TECHNOLOGY

SIGNATOPE has a proprietary technology that combines motif-specific antibodies to capture proteins of interest with mass spectrometric readout<sup>4</sup>. 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 biological samples: plasma, urine, tissues, cell pellets or lysates.<sup>3,5,6</sup> The final readout by mass spectrometry ensures definitive identification and quantification.

### 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 matrices. Moreover, due to epitopes of the applied antibodies the assays can be applied to preclinical and clinical samples.

DRUG-INDUCED KIDNEY INJURY (tubular)	Function	SPECIES
α-1-Microglobulin (AMPB)	Readsorption	    
Clusterin (CLU)*	Damage & Inflammation	    
Cystatin 3 (CST3)*	Readsorption	    
Kidney Injury Molecule 1 (KIM1)*	Induced protein	    
Neutrophil Gelatinase Associated Lipocalin (NGAL)*	Inflammation	 
Osteopontin (OPN)*	Damage & Inflammation	    
Retinol Binding Protein 4 (RBP4)	Readsorption	    
DRUG-INDUCED KIDNEY INJURY (glomerular)	Function	SPECIES
Nephrin (NPHS1)#	Podocyte foot processes, damage	
Podocin (NPHS2)#	Nephretic slit, damage	
Podocalyxin (PODXL)#	Nephretic slit, damage	



### 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.

### SAMPLE REQUIREMENTS

Analytes	Analytes	Sample type	Minimum amount	Storage [°C]	Shipping
MPh26	AMPB, CST3, OPN, RBP4	Urine, non spun	250 µL	-80 °C	on dry ice
MPh27	KIM1, NPHS1, NPHS2, NGAL, PODXL, CLU	Urine, non spun	50 µL	-80 °C	on dry ice
MPh33	VCAM1, MMP3, HMGB1	Urine, non spun	200 µL	-80 °C	on dry ice
Full DIKI panel		Urine, non spun	500 µL	-80 °C	on dry ice

### LITERATURE

- TransBioLine FDA Letter of Intent downloadable at: <https://force-dsc.my.site.com/ddt/s/ddt-project?ddtprojectid=126>
- Gautier JC, Zhou X, Yang Y, et al. (2016) Evaluation of novel biomarkers of nephrotoxicity in Cynomolgus monkeys treated with gentamicin. *Toxicol Appl Pharmacol* 303
- Naboulsi, W., Planatscher, H., Schmidt, F. F., Steinhilber, A., Joos, T. O., Adedeji, A. O., Pötz, O. (2024). Immunoaffinity proteomics for kidney injury biomarkers in male beagle dogs. *EXCLI Journal*, 23, 180–197.
- Hoeppe S, Schreiber TD, Planatscher H, et al. (2011) Targeting peptide termini, a novel immunoaffinity approach to reduce complexity in mass spectrometric protein identification. *Mol Cell Proteomics* 10(2):M110 002857
- 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).
- 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).

