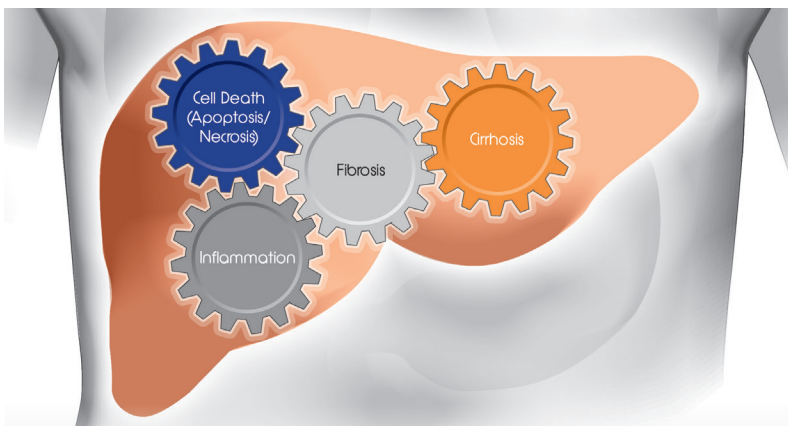




# Biomarker Assays for NASH Clinical Trials

Cytokeratin 18 (CK18 and ccK18): Non-invasive biomarkers for assessing hepatocyte apoptosis and necrosis



Biomarker	Utility in NASH Clinical Trials	Available Assays	Catalog #
Caspase-cleaved CK18 (ccK18/M30®)	Biomarker for hepatocyte apoptosis	M30® Apoptosense® ELISA	P10011
Total CK18 (M65®)	Biomarker for hepatocyte cell death (apoptosis and necrosis)	M65® ELISA	P10020
		M65® EpiDeath® ELISA	P10040

- CK18 and ccK18 have been used as secondary endpoints in over 60 NAFLD/NASH clinical trials to **assess efficacy of new therapeutics**
- **Mechanistic biomarkers:** Hepatocyte apoptosis and necrosis are underlying mechanisms involved in the pathogenesis of NAFLD. Changes in CK18 and ccK18 may reflect changes in disease activity in study subjects in response to drug therapy

- More **specific for liver** than ALT & AST
- **Sensitive:** Depending on mechanism of action of the drug, changes can be observed within weeks, or even hours
- **Non-invasive:** Changes in serum CK18 and ccK18 have been shown to correlate with changes in liver histology (ballooning, inflammation, and fibrosis)

\*Research use only in the U.S. and Canada. Not for diagnostic procedures.



## Additional NASH Biomarker ELISAs Available from Diapharma:

Biomarker	Utility in NASH Research	Available Assays	Catalog #
Collagen	Quantification of total collagen in liver tissues.	QuickZyme Sensitive Collagen Assay Kit (Also available in 5x 96-assays bulk pack (QZBtisco15))	QZBtisco1
FABP4	Plays a crucial role in insulin resistance and type 2 diabetes; circulating levels correlate with liver inflammation and fibrosis.	ImmunoDiagnostics Fatty-Acid Binding Protein 4	31030
FGF-19	Regulator of hepatic bile acid synthesis & glucose homeostasis.	ImmunoDiagnostics FGF-19	31200
FGF-21	Regulator of hepatic glucose and lipid metabolism.	ImmunoDiagnostics FGF-21	31180
Fibronectin	Component of the ECM; biomarker for hepatic fibrosis.	Technozym® Fibronectin	TC12030
GDF-15	Cytokine induced by mitochondrial stress; possible role in regulating inflammation.	ImmunoDiagnostics Human GDF-15 ELISA Kit	31980
Hyaluronic Acid (HA)	Component of the ECM; biomarker for hepatic fibrosis.	TECO® Hyaluronic Acid (HA) PLUS	TE1018-2
Intact Proinsulin	Sensitive and specific marker of pancreatic $\beta$ -cell function, potential pro-atherogenic action through increasing PAI-1 synthesis	TECO® Intact Proinsulin	TE1011
L-FABP	Regulated by PPARs, responsive/upregulated with lipid toxicity, and leaks out of cell as early indicator of cellular stress.	Diapharma L-FABP (FABP1)	DPGLFABP
Lipocalin-2/NGAL	Biomarker for hepatic inflammation.	NGAL	DPG-NGAL
		NGAL	DPG-2NGAL
		ImmunoDiagnostics Lipocalin-2	31050
Mac-2 BP	Biomarker for hepatic fibrosis.	Mac-2 Binding Protein	DPG27362
Matrix Metalloprotease 7 (MMP7)	Biomarker of fibrosis; Inhibited by TIMP-1. Active OR Total protease readout with one kit.	QuickZyme human MMP-7 Activity	QZMmp7H
Matrix Metalloprotease 9 (MMP9)	Proteinase involved in ECM remodeling; Inhibited by TIMP-1.	QuickZyme human MMP-9 Activity	QZBmmp9H
Noggin	TGF- $\beta$ family antagonist; levels have been shown to be decreased in subjects with NAFLD.	FluoBolt™ Noggin	FIA-1701
Osteopontin	Involved in activation of hepatic stellate cells; biomarker for hepatic fibrosis.	Osteopontin	DPG27158
		Osteopontin N-half	DPG27258
PAI-1	Promotes hepatic fibrogenesis by inhibiting metabolism of extracellular matrix proteins; potential link between NAFLD and cardiovascular disease.	Technozym® PAI-1 Antigen	TC12075
		Technozym® PAI-1 Actibind®	TC16075
		ImmunoDiagnostics PAI-1 (Antigen)	31070
sCD163	Macrophage activation marker.	IQ Macro163™	IQP-383
Thrombospondin-2 (TSP-2)	Matricellular protein involved in collagen and fibrin formation. Up-regulated in NASH.	ImmunoDiagnostics Human Thrombospondin-2 (TSP-2) ELISA Kit	31101

**Questions about any product in our lineup?**

We're just a click or phone call away.

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