

# Keratin 18 in Drug-Induced Liver Injury

## Research of liver damage with the biomarker total keratin 18

### The Safer and Faster Evidence-based Translation (SAFE-T) Consortium

The SAFE-T Consortium is a unique partnership between the European Union and the pharmaceutical industry, initiated under the IMI. The consortium aims at addressing hurdles in the development of new pharmaceuticals, such as withdrawal of drug candidates in a late stage of development or from the market. An overall goal for the consortium is to find and clinically qualify new biomarkers with high sensitivity and specificity that detect Drug-induced liver, kidney and vascular injury in an earlier state than what is possible today.

### Hepatotoxicity and Drug-Induced Liver Injury

The early detection of potential hepatotoxicity is crucial during drug safety testing and during the development of new drugs in order to reduce the risk of withdrawal of drug candidates in a late stage of development or even withdrawal from the market after the drug has been launched.

Today, Drug-Induced Liver Injury (DILI) is a leading cause of patient mortality and morbidity and the cause of more than 50 % of all acute liver failure cases in the clinics. Standard hepatic injury biomarkers show inadequate sensitivity and specificity with limited predictive values. Around 40 % of patients with DILI are not detected in safety studies during drug development, and therefore new biomarkers are much needed.

### Biomarkers for Drug-Induced Liver Injury

Sensitive and specific biomarkers for the prediction, monitoring and diagnosis of drug-induced liver injuries are lacking. The Drug-Induced Liver Injury (DILI) Work Package 3 (WP3) of the SAFE-T Consortium was undertaken to address these issues by assessing a large number of available biomarkers.

- **Total keratin 18** (also known as cytokeratin 18) is one of four biomarkers recommended by the SAFE-T.
- **Total keratin 18** and **caspase-cleaved keratin 18**, in addition to four other biomarkers, are also the biomarkers with high potential to **provide additional information beyond current biomarkers** in clinical research.
- Both **Total keratin 18** and **caspase-cleaved keratin 18** were also recommended, together with three other biomarkers as biomarkers with high potential in early stage clinical research to **asses liver injury before standard biomarkers are elevated**.



Total Keratin 18 can be measured with M65 EpiDeath ELISA

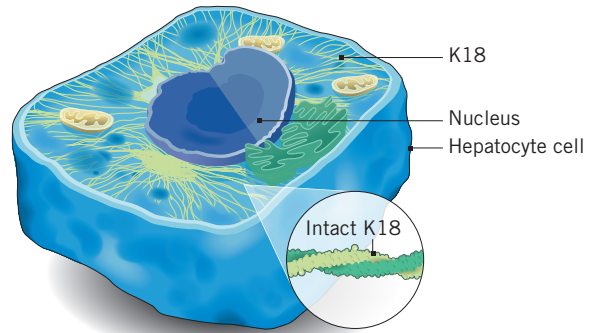
### M65 EpiDeath® ELISA (Prod. No P10040)

The M65 EpiDeath® ELISA measures the concentration of soluble keratin 18 in human plasma, serum and cell culture supernatants. The keratin 18 levels reflect the amount of total cell death, due to apoptosis or necrosis.

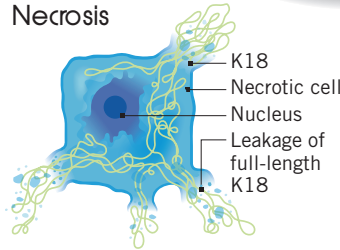
The M65 EpiDeath® ELISA represents the next generation of keratin 18 positive biomarker assays. All reagents are provided in a convenient ready-to-use format.

For research use only in the US & Canada

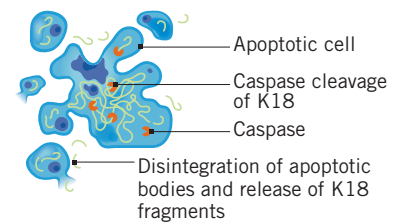
### Hepatocyte cell death



### Necrosis



### Apoptosis



Only intact K18	Caspase-cleaved K18
	Asp396-Neopeptide 
<b>M65 EpiDeath® ELISA</b>  Measurement of intact and cleaved K18 <b>The M65 ELISAs measures total cell death (necrosis and apoptosis)</b>	 Measurement of cleaved K18 only <b>The M30 ELISAs measure only apoptosis</b>

### PEVIVA Product Line

ELISA Products	Prod. No
M65 EpiDeath® ELISA	P10040
M65® ELISA	P10020
M30 Apoptosense® ELISA	P10011
M30 CytoDeath™ ELISA	P10900

Please visit our DILI page at [diapharma.com/dili](http://diapharma.com/dili)

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