PEVIVA

Keratin 18 in Drug-Induced Liver Injury

Detection and quantification 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.[1]

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.[2] 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.[3]

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.

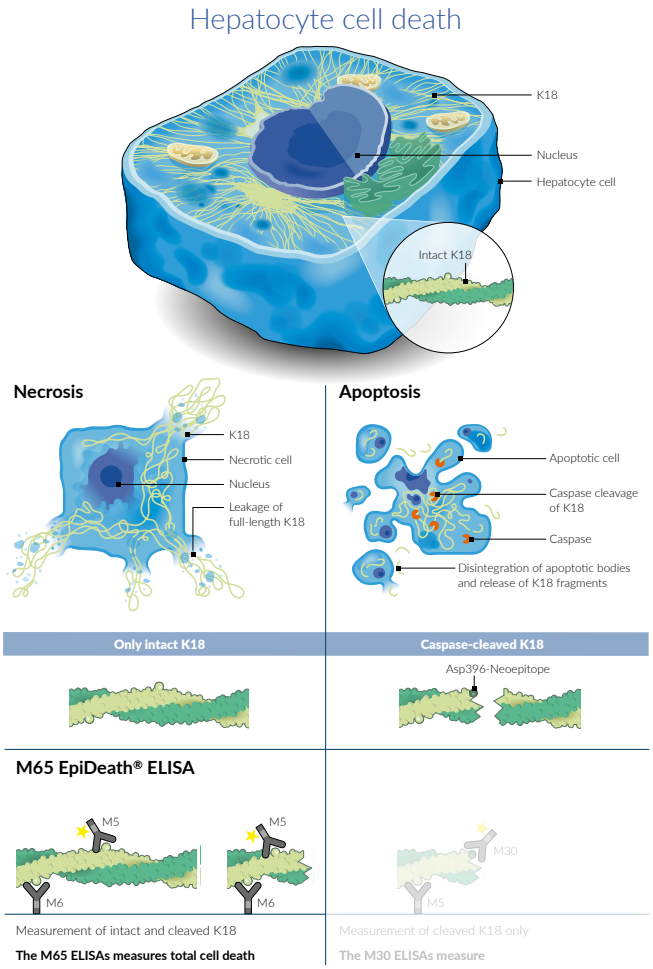
- **Total keratin 18** (also known as cytokeratin 18) is one of four biomarkers recommended by the SAFE-T as the biomarkers, among the evaluated, holding the highest potential in **assessing and anticipating the risk of progression in severe DILI patients** in clinical trials.
- **Total keratin 18** and **caspase-cleaved keratin 18**, in addition to four other biomarkers, are also the biomarkers with the highest potential in order to **provide additional information beyond the diagnostic value of current biomarkers** in clinical trials.
- 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 trials to **asses liver injury before standard biomarkers are elevated**.[4]

M65 EpiDeath® ELISA

(Prod. No 10040)

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. The assay is CE marked as a medical device for *in vitro* diagnostic use. All reagents are provided in a convenient ready-to-use format.



PEVIVA Product Line	
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M30 Apoptosense® ELISA	10011
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