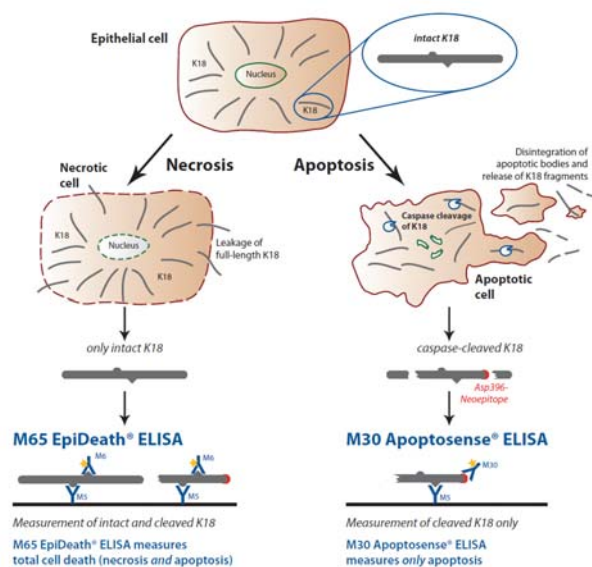


Chronic Liver Disease

M30 Apoptosense® and M65 EpiDeath® ELISA

Serum Apoptosis Markers

- Reliable and non invasive biomarkers for liver fibrosis (cleaved CK18 is detect on serum/plasma samples)
- Real Time monitoring of therapy response
- Convenient and Time Saving (Results from up to 39 serum/plasma samples in duplicate in just 4 hours)



Chronic Liver Disease

Liver fibrosis results from chronic damage to the liver. The main causes of liver fibrosis include chronic hepatitis B and C virus (HBC, HCV) infection, alcoholic (ASH) and non-alcoholic steatohepatitis (NASH). It is becoming increasingly clear that hepatocyte apoptosis contributes to liver fibrogenesis. Recent studies of chronic HBV and HCV infection as well as non-alcoholic fatty liver disease (NAFLD) show that hepatocyte apoptosis correlates with disease severity and stage of fibrosis. A number of investigators have used the M30 Apoptosense® ELISA to show that the serum/ plasma levels of caspase-cleaved keratin 18 (K18) are elevated in patients with NASH and chronic hepatitis C infection. A major advantage of this approach is that the analyte measured by the M30 Apoptosense® ELISA is an end product of the apoptotic process, reflecting the extent of active disease (ongoing apoptosis). Moreover, patients with normal ALT values may have active HCV disease as assessed by histopathology. Patients with normal ALT and active HCV-related liver diseases were reported to have elevated levels of caspase-cleaved keratin 18 products in their serum (Bantel et al., 2004). Available evidence suggests caspase-cleaved keratin 18 to be a more sensitive marker than liver transaminases for the detection of early liver injury.

Monitoring Disease Progression and therapy response

The dramatic increase of obesity and metabolic syndrome in many parts of the world has caused a striking increase in fatty liver disease. NASH (non-alcoholic steatohepatitis) is the most serious form of fatty liver disease and there is an increasing medical need for non-invasive markers for this condition. A number of scientific reports from well reputed institutions have established that the M30 Apoptosense® ELISA is a useful test for monitoring disease progression in patients with NASH. About 50 % of all HCV patients do not respond to treatment. The serum levels of caspase-cleaved K18 were found to be higher in patients responding to anti-viral therapy compared to non-responders (Volkman et al., 2006).

Liver Toxicity induced by adverse drug reactions or by potent liver toxic chemical used in the industry.

Adverse drug reactions (ADR) are of major concern in drug development. A common form of ADR is liver toxicity, caused by the metabolism of drugs in hepatocytes. Drugs (or their metabolites) may trigger apoptosis or necrosis of hepatocytes. Different toxic stimuli are expected to be associated with different cell death modes. Vinyl chloride (VC) is a potent liver toxic chemical widely used in the industry. VC workers exposed to VC on a regular basis may develop liver steatosis and fibrosis. Liver injuries in VC workers, verified by liver biopsies, were reported to correlate with K18 blood concentrations, despite normal ALT values (Cave et al., 2010). An influence of obesity or alcohol abuse could be ruled out, leaving the toxic effect of VC as the only reasonable cause for the liver diseases. Keratin 18 (K18) biomarkers can be used to determine cell death modes in plasma samples. Caspase-cleaved K18 reflects apoptotic cell death, whereas total K18 is a measure of total cell death (necrosis and apoptosis). Apoptosis can be measured using the M30 Apoptosense® ELISA and the M65 EpiDeath® ELISA quantifies total cell death.

M30 Apoptosense® ELISA ALX-850-270-KI01	Serum/plasma biomarker for in vivo studies of human cancer, liver disease (hepatitis C and NASH), response to anticancer agents, tumor cell apoptosis in xenograft models.
M65® ELISA ALX-850-310-KI01	Measures soluble keratin 18 (K18) released from dying cells and can be used to assess overall cell death (due to apoptosis and necrosis)
M65 EpiDeath® ELISA PEV-10040	Shows improved characteristics with regard to linearity/dilution and spiking recovery compared to the M65® ELISA.
M30 CytoDeath™ ELISA ALX-850-336-KI01	Similar to the M30-Apoptosense, optimized to suit in vitro applications (not suitable for serum/plasma samples).
M5 Keratin™ 18 mAb ALX-804-640-T200	Staining of epithelial cells by IHC and WB.
M6 Keratin™ 18 mAb ALX-804-641-T200	Staining of epithelial cells by IHC and WB.
30 CytoDEATH™ mAb ALX-804-590-T200	Epithelial cell apoptosis by IHC in formalin-fixed paraffin-embedded tissue, flow cytometry and western blotting. Biotin: ALX-804-590B-T200 ; FITC: ALX-804-590F-T200 ; Orange: ALX-804-590OR-T200 ; Red: ALX-804-590RD-T200

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