



# Validated Biomarker Assays Specific for Epithelial Cell Death

## 上皮细胞死亡的特异性生物标记物检测试剂盒

体内实验中，定量检测上皮细胞凋亡或者坏死的ELISA试剂盒  
可运用于肿瘤，肝脏疾病，毒理学，败血症，移植和抗宿主疾病（GVHD）等方面的研究

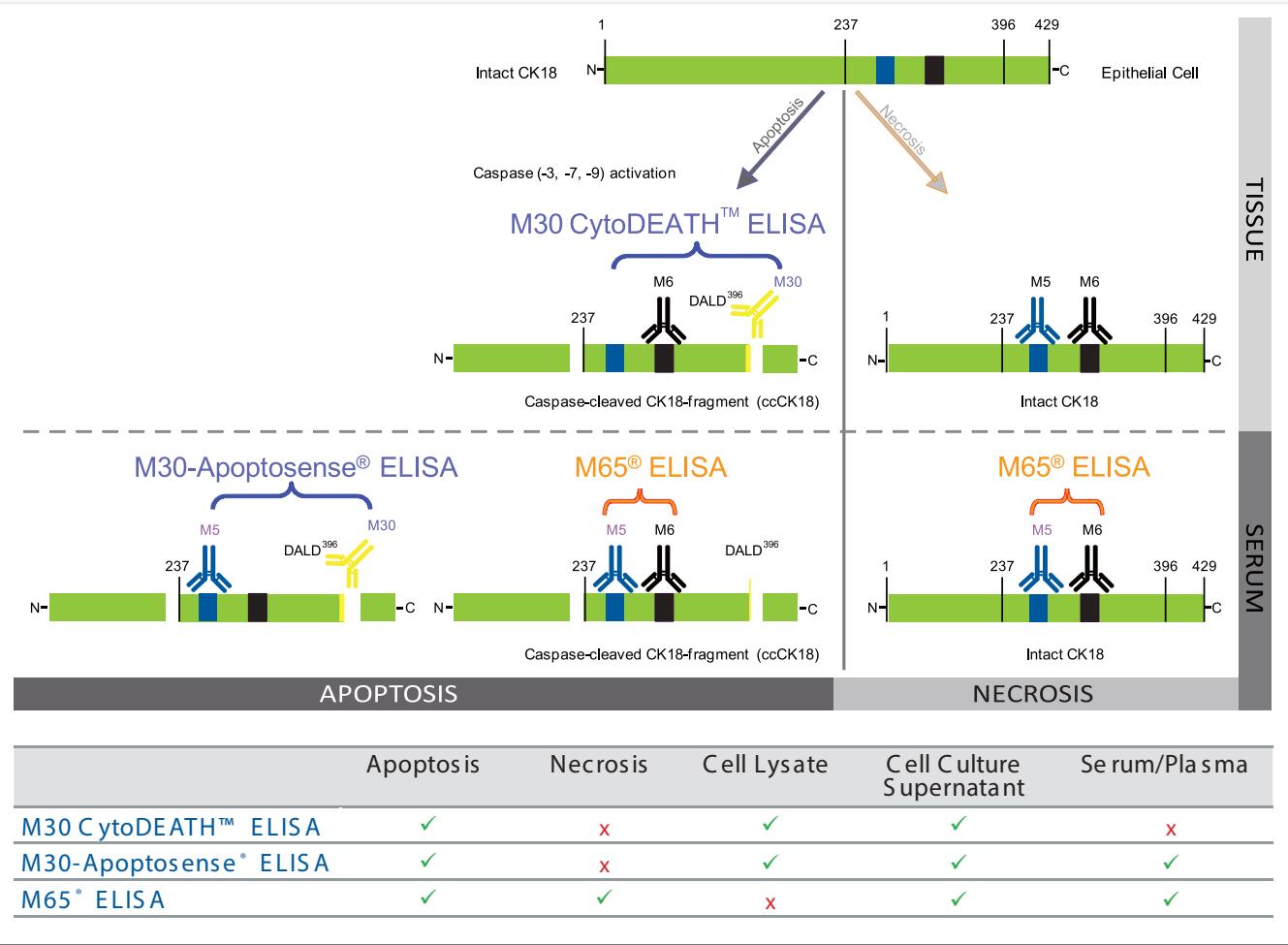
细胞角蛋白18 (Cytokeratin 18, 简写CK18或者K18) 是上皮细胞特异性表达的一类蛋白。当上皮细胞早期发生凋亡时，具有活性的caspase (比如caspase-3,-7,-9) 会酶解CK18形成三个片段，其中1个片段在aa387-396含有neoepitope (NE)，这一片段称为caspase-cleaved Cytokeratin 18 (ccCK18/ CK18F/ CK18Asp396-NE/M30)。形成凋亡小体时，这些片段释放到细胞外。当上皮细胞发生坏死时，完整的CK18 (没有被caspase酶解) 会释放到细胞外。

**Caspase酶解Cytokeratin 18 (ccCK18/CK18F/CK18Asp396-NE/M30)  
作为上皮细胞凋亡的生物标记物的优势：**

- 上皮细胞和组织特异性标记物 (比如：乳腺癌，肺癌，前列腺癌，结肠癌等上皮细胞来源的肿瘤细胞，肝脏细胞)
- 释放到血液循环中，在血清或者血浆的样品中稳定存在。
- 可检测多种caspase介导的细胞凋亡 (比如caspase-3,-7,-9)
- 可通过常规的实验方法进行检测：流式细胞仪，ELISA，免疫组化，免疫细胞组化和免疫印迹。
- 特异性检测细胞凋亡 (检测caspase激活；在增殖/分化/感染时没有假阳性信号)
- 可用于早期细胞凋亡的研究，比常规的Annexin V检测的灵敏度更高。

**Caspase酶解Cytokeratin 18 (ccCK18/CK18F/CK18Asp396-NE/M30)  
运用：**

- 作为血清细胞凋亡标记物，在乳腺癌，肺癌，前列腺癌，结肠癌的临床前和临床治疗研究中使用，监测肿瘤细胞凋亡情况;可用于促肿瘤细胞凋亡药物的药效研究。
- 肝脏细胞 (来源于上皮细胞) 凋亡可引起肝纤维化。作为细胞凋亡标记物，可用于肝纤维化的研究。
- 肝脏损伤中存在肝脏细胞发生凋亡的现象，ccCK18可作为评价肝脏损伤的标准。
- 可用于乙肝，丙肝等肝脏疾病引起的肝脏损伤的研究。
- 可用于监测药品的不良反应 (通过检测肝脏细胞的状态)



在体内实验时，M30- Apoptosense® ELISA试剂盒可以定量检测caspase酶解的CK18片段（ccCK18 /CK18F /CK18Asp396-NE/M30）；而M65® ELISA试剂盒可以定量检测总的CK18的含量（包括酶解和完整的CK18）。这两种试剂盒配套使用，可以用来确定细胞死亡的形式。

## M30 CytoDeath™ ELISA kit

Prod. No. #10900

1 Kit

在体外实验中定量检测上皮细胞的凋亡情况；用3D-细胞培养上清，人类器官（比如肝脏）匀浆液、多细胞球样体（比如肿瘤干细胞）或培养的组织（比如活体组织）进行毒理学研究；可用于高通量筛选和鉴定促凋亡药物。

特异性	人, 猴子, 牛
样品类型	表达CK18的凋亡细胞上清液和表达凋亡组织的细胞裂解液
灵敏度	60 U/l, Standard Z (0 U/l) + 3 S.D.
范围	250 – 3,000 U/l
检测目标物	可溶性caspase酶解的CK18(ccCK18/CK18F/CK18Asp396-NE/M30)
特点	<ul style="list-style-type: none"> <li>● 检测范围广</li> <li>● 样品制备容易</li> <li>● 冷冻的细胞裂解液也可以进行检测</li> <li>● 可用于自动化操作</li> </ul>

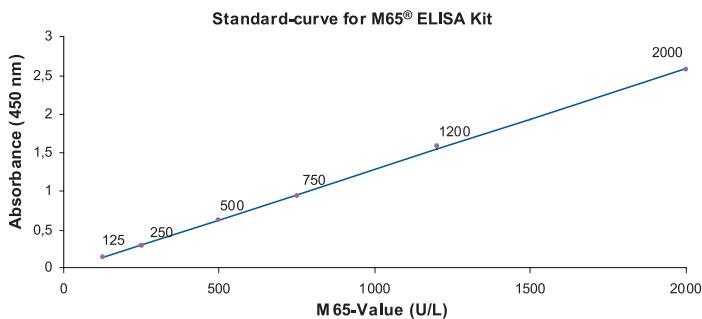
Li T: Identification of a Novel Topoisomerase Inhibitor Effective in Cells Overexpressing Drug Efflux Transporters: W. Fayad, et al.; PLoS ONE 4, e7238 (2009) ■ Conditional drug screening shows that mitotic inhibitors induce AKT/PKB- insensitive apoptosis: M. Berndtsson, et al.; J. Chem. Biol. 2, 81 (2009) ■ For a comprehensive bibliography please visit our website.

## M65® ELISA kit (CE-Mark)

Prod. No. #10020

1 Kit

体内, 体外实验中, 定量检测总的细胞死亡 (凋亡和坏死)。



特异性	人
样品类型	含有从死亡细胞中释放的CK18的血清或者血浆 (EDTA, citrate, heparin plasma)
灵敏度	11 U/l, Standard A (0 U/l) + 2 S.D.
范围	125 – 2 000 U/l
检测目标物	完整的CK18和可溶性 caspase 酶解的CK18 (ccCK18/CK18F/CK18Asp396-NE/M30)

## M30- Apoptosense® ELISA kit (CE-Mark)

Prod. No. #10010

1 Kit

在体内外实验中定量检测上皮细胞的凋亡。使用血浆样品, 可以特异性定量检测小鼠模型中人的异种移植植物的凋亡情况。

特异性	人
样品类型	含有从凋亡上皮细胞中释放的CK18的血清或者血浆 (EDTA, citrate, heparin plasma); 含有CK18阳性的凋亡细胞或者组织的细胞裂解液或者上清
灵敏度	25 U/l, Standard A (0 U/l) + 2 S.D.
范围	75 – 1 000 U/l
检测目标物	可溶性 caspase 酶解的CK18

### Literature References M<sup>30</sup>-Apoptosense® ELISA /M65® ELISA :

#### Cancer Research

Differentiation between cell death modes using measurements of different soluble forms of extracellular cytokeratin 18: G. Kramer, et al.; Cancer Res. 64, 1751 (2004) ▪ Determining tumor apoptosis and necrosis in patient serum using cytokeratin 18 as a biomarker: S. Linder, et al.; Cancer Lett. 214, 1 (2004) ▪ Apoptosis pathway-targeted drugs--from the bench to the clinic: J. Cummings, et al.; Biochim. Biophys. Acta 1705, 53 (2004) ▪ Induction of lysosomal membrane permeabilization by compounds that activate p53-independent apoptosis: H. Erdal, et al.; PNAS 102, 192 (2005) ▪ Validation of pharmacodynamic assays to evaluate the clinical efficacy of an antisense compound (AEG 35156) targeted to the X-linked inhibitor of apoptosis protein XIAP: J. Cummings, et al.; Br. J. Cancer 92, 532 (2005) ▪ Apoptosis in a tissue like culture model of human colorectal adenoma cells: K. Leuhuber, et al.; Tissue Cell 238, 203 (2006) ▪ Sense and sensitivity: the use of cell death biomarker assays in high throughput anticancer drug screening and monitoring treatment responses: M. Shoshan, et al.; Expert Opin. Drug Discov. 1, 585 (2006) ▪ Screening for Compounds that Induce Apoptosis of Cancer Cells Grown as Multicellular Spheroids: R. Herrmann, et al.; J. Biomol. Screen. 13, 1 (2007) ▪ Specific demonstration of drug-induced tumour cell apoptosis in human xenograft models using a plasma biomarker: M.H. Olofsson, et al.; Cancer Biomark. 5, 117 (2009) ▪ Docetaxel induces apoptosis in hormone refractory prostate carcinomas during multiple treatment cycles: G. Kramer, et al.; Br. J. Cancer 94, 1592 (2006) ▪ Cytokeratin 18 is a useful serum biomarker for early determination of response of breast carcinomas to chemotherapy: M.H. Olofsson, et al.; Clin. Cancer Res. 13, 3198 (2007) ▪ Evaluation of circulating tumor cells and serological cell death biomarkers in small cell lung cancer patients undergoing chemotherapy: J.M. Hou, et al.; Am. J. Pathol. 175, 808 (2009)

#### Liver Diseases (NAFLD/NASH/HCV/HBV/ALF/HCC) Research

Soluble forms of extracellular cytokeratin 18 may differentiate simple steatosis from nonalcoholic steatohepatitis: Y. Yilmaz, et al.; World J. Gastroenterol. 13, 837 (2007) ▪ Noninvasive diagnosis of nonalcoholic fatty liver disease using serum biomarkers: R.R. Mitry, et al.; Hepatology 46, 2047 (2007) ▪ A Novel Diagnostic Biomarker Panel for Obesity related Nonalcoholic Steatohepatitis (NAS H): Z.M. Younossi, et al.; Obes. Surg. 18, 1430 (2008) ▪ Cytokeratin 18, a marker of cell death, is increased in children with suspected nonalcoholic fatty liver disease: M. B. Vos, et al.; J. Pediatr. Gastroenterol. Nutr. 47, 481 (2008) ▪ The clinical utility of biomarkers and the nonalcoholic steatohepatitis CR N liver biopsy scoring system in patients with nonalcoholic fatty liver disease: R. Malik, et al.; J. Gastroenterol. Hepatol. 24, 564 (2009) ▪ Cytokeratin-18 fragment levels as noninvasive biomarker for nonalcoholic steatohepatitis: A multicenter validation study: A. Feldstein, et al.; Hepatology 50, 1072 (2009) ▪ Effects of ursodeoxycholic acid in combination with vitamin E on adipokines and apoptosis in patients with nonalcoholic steatohepatitis: M.L. Balmer, et al.; Liver Int. 29, 1184 (2009)

#### Septic Research

Elevated serum levels of epithelial cell apoptosis-specific cytokeratin 18 neopeptide M30 in critically ill patients: G.A. Roth, et al.; Shock 22, 218 (2004) ▪ Cell death serum biomarkers are early predictors for survival in severe septic patients with hepatic dysfunction: S. Hofer, et al.; Critical Care 13, R93 (2009)

For a comprehensive bibliography please visit our website .

Purified (PF) = Purified (Purified free); FC = Flow Cytometry; ICC = Immunocytochemistry; IP = Immunoprecipitation; IHC = Immunohistochemistry (FS = Frozen Sections, PS = Paraffin Sections); WB = Western blot; BP = Blocking Peptide

## M30 CytoDEATH™, antibody – 检测上皮细胞凋亡的黄金标准品

Prod. No. #10700 Unlabeled 200 tests

M30 CytoDEATH™ antibody特异性识别被Caspase酶解后的CK18片段，不能识别完整的CK18结合。  
应用：可以用于WB, IHC (PS和FS) , ICC和流式细胞检测 (FACS)

## M5 Keratin 18 antibody

Prod. No. #10600 200 tests

可以识别CK18片段和完整的CK18。  
应用：WB, ICC, IHC (FFPE和FS) , IP, 流式细胞检测 (FACS)

## M6 Keratin 18 antibody

Prod. No. #10650 200 tests

可以识别CK18片段和完整的CK18。  
应用：WB, ICC, IHC (FFPE和FS) , IP, 流式细胞检测 (FACS)

### 产品资料：

产品编号	品名	包装
10010	M30 Apoptosense® ELISA*	96 wells
10020	M65® ELISA*	96 wells
10040	M65 EpiDeath® ELISA	96 wells
10900	M30 CytoDeath™ ELISA	96 wells
10700	M30 CytoDEATH™ (unlabeled)	200 tests
10750	M30 CytoDEATH™ Biotin	200 tests
10800	M30 CytoDEATH™ Fluorescein	200 tests
10830	M30 CytoDEATH™ Orange	200 tests
10850	M30 CytoDEATH™ Red	200 tests
10600	M5 Keratin 18 antibody	200 tests
10650	M6 Keratin 18 antibody	200 tests

\*通过欧洲 CE 认证

以上试剂仅用于科学研究，请勿用于临床诊断

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广州市越秀区先烈中路69号  
东山广场30楼3002-3003室

北京 Tel: 13611333218

上海 Tel: 021 62884751

广州 Tel: 020 87326381

香港 Tel: 852 27999019

询价：

wkgz.info@fujifilm.com

官网：

labchem.fujifilm-wako.com.cn

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