

MERCK

# 肿瘤科学生物标志物 研究策略

默克MILLIPLEX®MAP多重蛋白检测平台  
——高通量，高灵敏，小体积

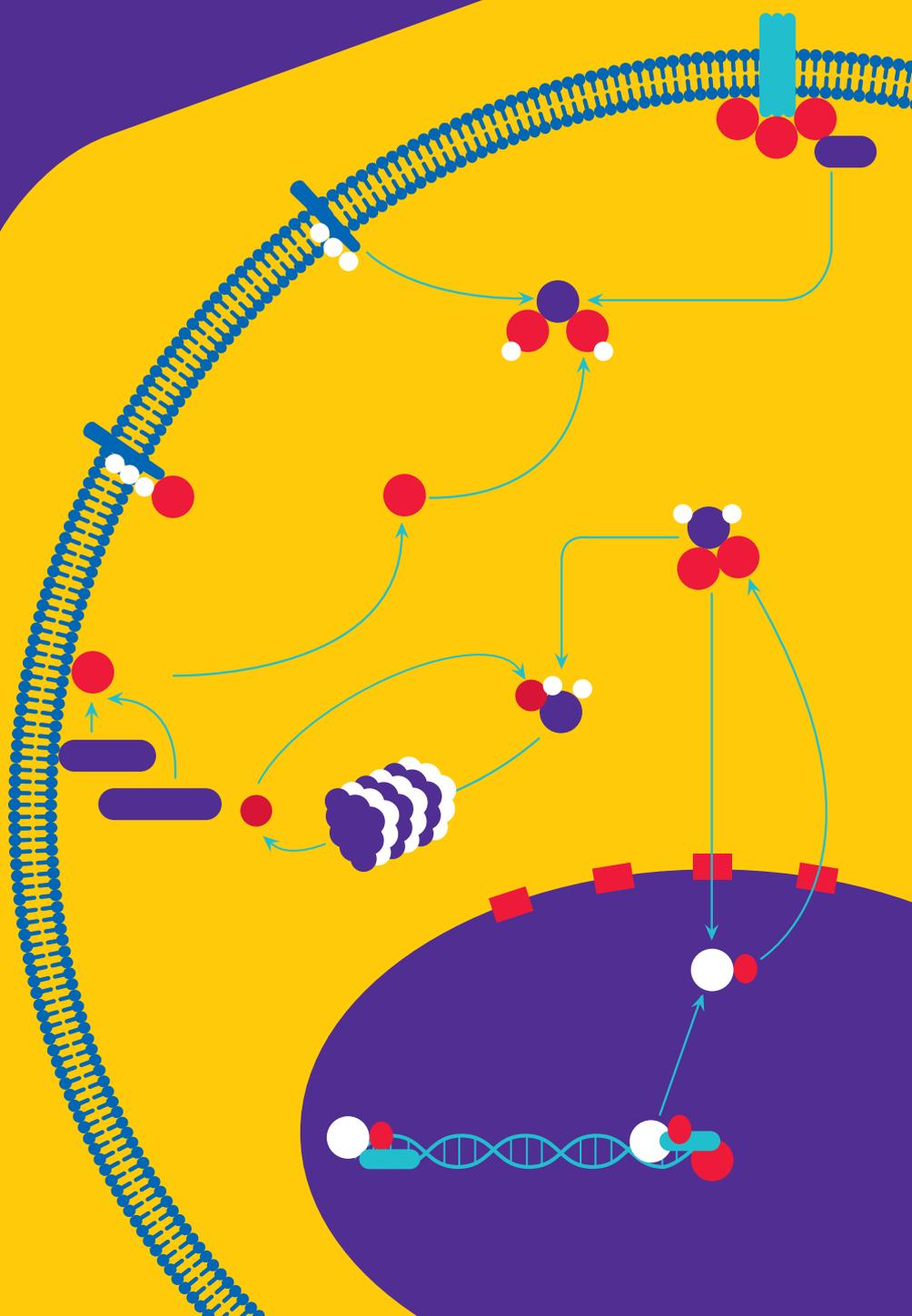


在美国和加拿大, 默克的生命科学  
业务使用MilliporeSigma的名称

# 您精准稳定实验的保证， 源自默克生命科学全方位蛋白免疫检测解决方案

肿瘤作为威胁人类健康的主要疾病之一，一直是生物医学研究的热点，目前针对肿瘤的研究主要集中在肿瘤生长，侵袭和转移，肿瘤免疫治疗，肿瘤微环境等方面。生物标志物的检测已经成为肿瘤科学研究的重要手段，不同类型不同阶段的肿瘤疾病研究都需要对不同的特定肿瘤生物标志物进行检测和评估，因此具备高效的，高灵敏度的，并经过高度验证的检测方法对于确保生物标志物检测的准确性、灵敏度和重现性至关重要。

默克强大的生物标志物检测平台为您提供高通量，可同时检测多个生物标志物的MILLIPLEX®MAP技术平台，还有经过多年验证业内金标准的肿瘤研究相关ELISA检测试剂盒，还有新一代可检测浓度低至飞摩尔级别蛋白的超高灵敏度的SMC™ (Single molecule counting)单分子蛋白免疫检测平台。我们确保以最少的重复次数帮助您得到最为可靠的结果。



# 默克生命科学提供全面适合您的生物标志物检测方案，助力您的肿瘤科学研究

- 默克MILLIPLEX®MAP多重蛋白检测技术平台
- 肿瘤代谢研究领域金标准ELISA试剂盒
- 肿瘤研究创新超高灵敏度SMC™ (Single molecule counting) 单分子技术平台

肿瘤生物标志物研究有不同的研究需求。

在这里,我们将向您介绍成功解决肿瘤生物标志物研究挑战的最佳解决方案

蛋白检测平台	平台特征	定量	灵敏度	样本体积	动态范围	多重检测能力	定制分析支持
<b>Luminex® platform</b>							
	灵活的多重检测平台	是	pg/mL	≤ 25 µL	•••		是
<b>SMCxPRO™ system</b>							
	超高灵敏度检测平台	是	fg/mL	5-100 µL	•••		是
<b>ELISA</b>							
	高品质酶标仪检测平台	是	pg/mL	50-100 µL	••		是

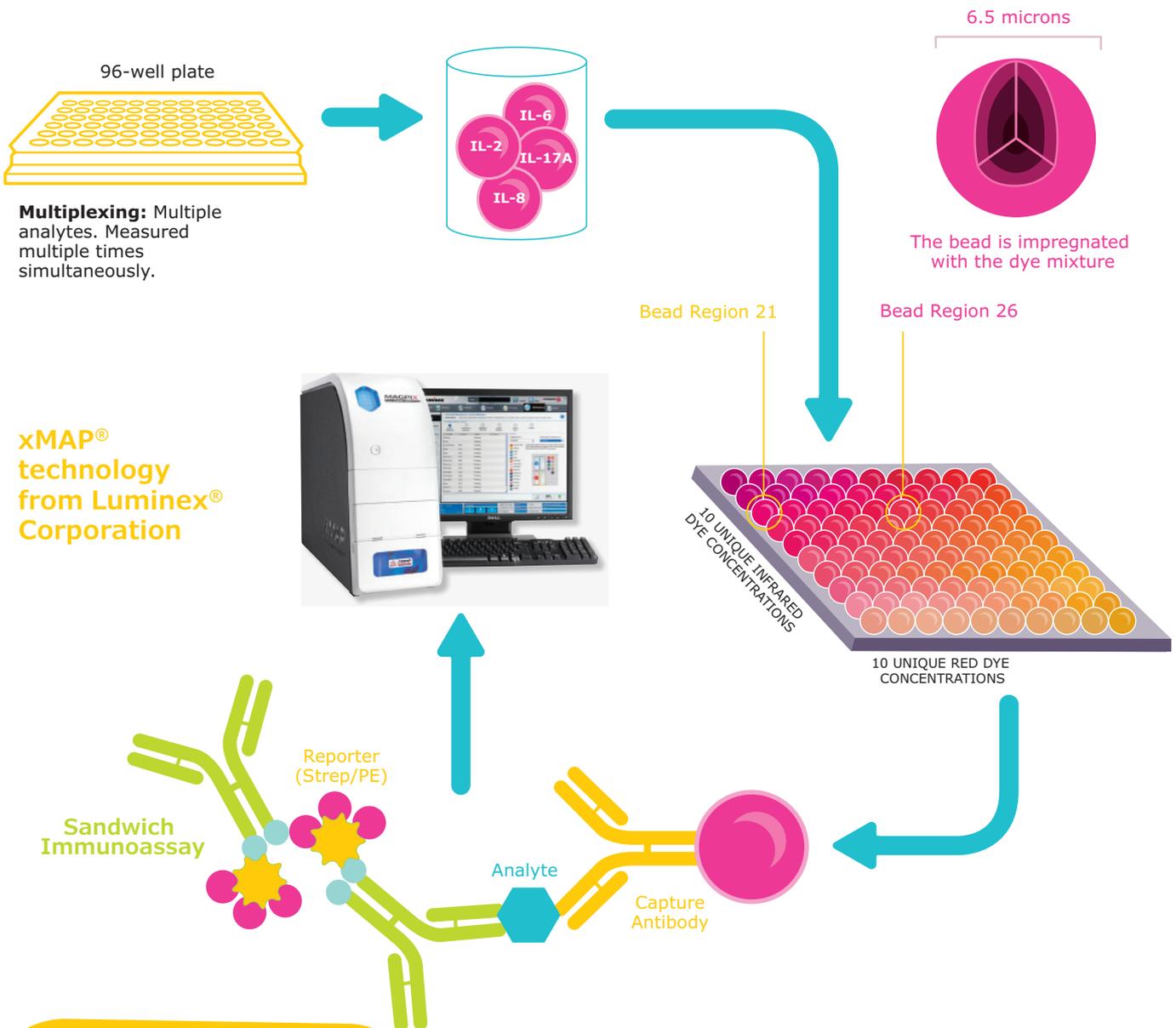
• 性能良好      •• 性能优良      ••• 性能卓越       不推荐       推荐



# MILLIPLEX® MAP原理

MILLIPLEX®MAP 是基于 xMAP® 技术的液相芯片多因子检测产品，该技术采用独特的微球染色技术，通过 2-3 种荧光染料，按照不同比例对微米级的微球进行染色，可获得 1-500 种不同微球组成的液相微球悬浮芯片系统，检测时不同颜色微珠上偶联针对不同待测分析物特异性捕获抗体，通过最终荧光标记的检测抗体双抗夹心原理，使用 Luminex® 平台，轻松实现对单个样本中的多种待测分析物的精确检测。

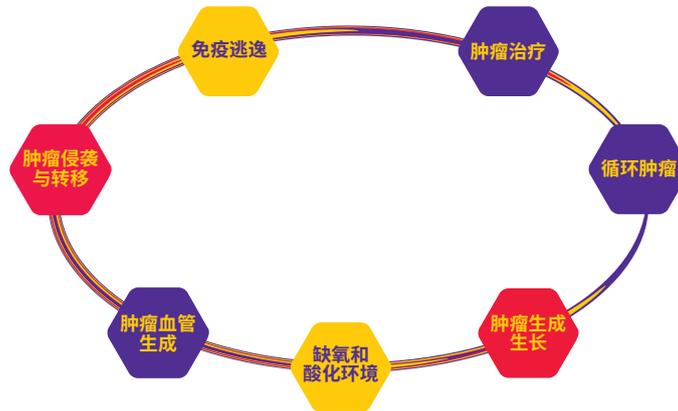
## 原理图示：



更多产品内容请见：  
[MerckMillipore.com/immunoassays](http://MerckMillipore.com/immunoassays)

# 肿瘤微环境

肿瘤微环境是肿瘤细胞赖以生存和发展的复杂环境, 肿瘤微环境由细胞成分和非细胞成分组成。其中细胞成分包括肿瘤细胞本身、炎症细胞、免疫细胞、间充质干细胞、内皮细胞、以及与肿瘤相关的成纤维细胞等; 非细胞成分主要包括细胞因子, 趋化因子等, 共同构成了复杂的肿瘤微环境。细胞成分和非细胞成分共同为肿瘤生长起到支撑的作用。



Hanahan D1, Weinberg RA. Cell. 2011.

## 肿瘤标志物研究热门靶点

肺癌	CEA, NSE, CA125, CYFRA21-1, IGFBP3, CA9, ECM-1, CD44
结直肠癌	CA19-9, CEA, FAP, IGFBP3, CD44, EpCAM
胃癌	CEA, CA19-9, CYFRA211, Myeloperoxidase, ECM-1, VEGF, Midkine, CD44, Hepsin
乳腺癌	CA15-3, CEA, CA125, CA19-9, Cathepsin D, ALDH1A1, CA9, Midkine, Hepsin, TGM2
肝癌	AFP, CA19-9, CEA, Serum Ferritin (SF), DKK-1, HSP27, OPN, TGFβ1, IGF- II, HGF, MMPs, NSE, VEGF, Sex Hormone Binding Globulin, ECM-1, EpCAM
甲状腺癌	Galectin-3, VEGF, CEA, CA125, CA19-9, ALDH1A1, Midkine
食管癌	CEA, CYFRA2115, CA19-9, AFP, CRP, PSA, P53, HER-2, PCNA, IL2, IL8, Survivin, MUC-1
宫颈癌	CEA, CA125, CA19-9, HIF-1α, c-Met, Bcl-2, EGFR, CA153, HCGβ, EpCAM, Hepsin
淋巴瘤	VEGF, CA125, CA15-3, Serum Ferritin (SF), CYRA21-1, CEA, NSE, CD44, TNFα
脑癌	GFAP, PCNA, P53, CA9
胰腺癌	Antithrombin III, Mesothelin,
卵巢癌	CA125, APO A1, Serum Ferritin (SF), AFP, HE4, HCGβ, ECM1, Mesothelin, Hepsin
前列腺癌	PSA, Vitamin D Binding Protein, Hepsin

\*该表格内容仅供参考

### Human Circulating Cancer Biomarker Panel 1

(Cat. No. HCCBP1MAG-58K)

α-Fetoprotein (AFP)	IL-8/CXCL8
CA125	Leptin
CA15-3	MIF
CA19-9	Osteopontin (OPN)
CEA	Prolactin
CYFRA21-1	PSA (free) <sup>†</sup>
sFAS/TNFRSF6	PSA (total) <sup>†</sup>
sFasL	SCF
FGF-2/FGF-basic	TGFα
HCGβ	TNFα
HE4	TRAIL/TNFSF10
HGF	VEGF-A
IL-6	

### Human Circulating Cancer Biomarker Panel 2

(Cat. No. HCCBP2MAG-58K)

Antithrombin III	Extracellular Matrix Protein 1 (ECM1)
Complement Factor H (CFH)	Vitamin D Binding Protein

### Human Circulating Cancer Biomarker Panel 3

(Cat. No. HCCBP3MAG-58K)

Cathepsin D	Melanoma Inhibitory Activity (MIA)
Ferritin	Myeloperoxidase (MPO)
Fibroblast Activation Protein (FAP)	Sex Hormone Binding Globulin (SHBG)
Galectin-3	
IGFBP3	

### Human Circulating Cancer Biomarker Panel 4

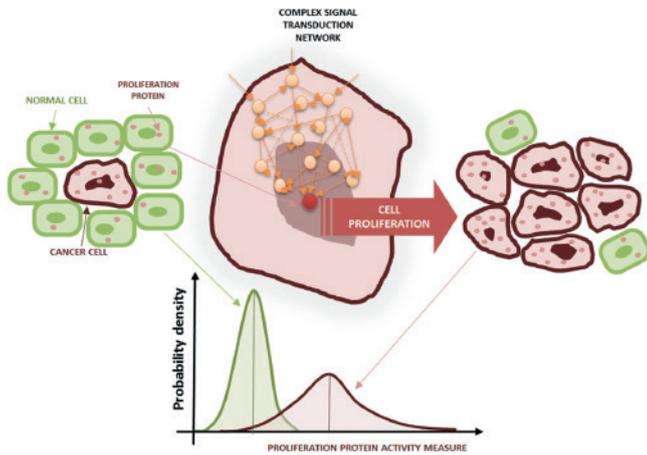
(Cat. No. HCCB4MAG-58K)

ALDH1A1	Kallikrein-6
Carbonic Anhydrase 9 (CA9)	Mesothelin
CD44	Midkine
EpCAM	NCAM1/L1CAM/CD171
Hepsin	Transglutaminase 2 (TGM2)

更多产品内容请见:

[MerckMillipore.com/immunoassays](https://www.MerckMillipore.com/immunoassays)

# 肿瘤生长



Fortunato Bianconi , Elisa Baldelli.  
Bmc Systems Biology,2016.

- 肿瘤细胞凋亡抵抗:肿瘤细胞通过调控凋亡信号(例如 Bcl-2家族),抑制凋亡信号蛋白的表达,促凋亡蛋白失活,以及P53信号途径改变延长其寿命。

## Early Apoptosis – 7 Plex

(Cat. No. 48-669MAG) AB2 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated	
Akt/PKB		√ (Ser473)	H, M, R
BAD		√ (Ser112)	H
Bcl-2		√ (Ser70)	H
Active Caspase 8	√		H
Active Caspase 9	√		H
JNK/SAPK1		√ (Thr183/Tyr185)	H, M, R
p53		√ (Ser46)	H

## Human Bcl-2 Family Apoptosis Panel 1 - 6 Plex

(Cat. No. 48-682MAG) AB1 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated	
BAD	√	√ (Ser112)	H
BAX	√		H
Bcl-xL/BAD (interaction)	√		H
BIM	√		H
Mcl-1/BIM (interaction)	√		H

## Human Bcl-2 Family Apoptosis Panel 2 - 4 Plex

(Cat. No. 48-683MAG) AB1 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated	
Bcl-2	√		H
Bcl-xL	√		H
Mcl-1	√		H
NOXA/Mcl-1 (interaction)	√		H

## Human DNA Damage/Genotoxicity – 7 Plex

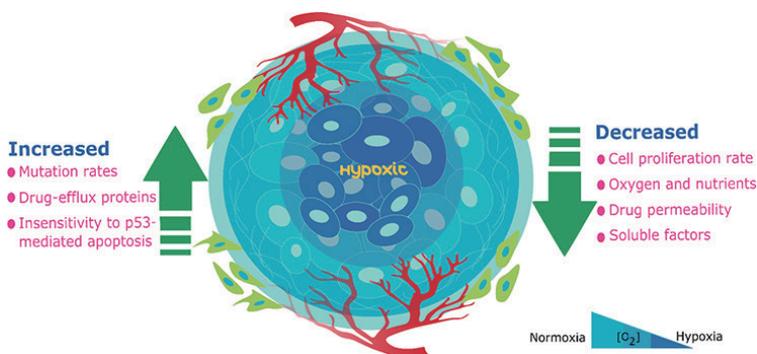
(Cat. No. 48-621MAG) AB1 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated	
ATR	√		H
Chk1		√ (Ser345)	H, M, R
Chk2		√ (Thr68)	H
H2A.X		√ (Ser139)	H, M, R
MDM2	√		H, M, R
p21	√		H
p53		√ (Ser15)	H

更多产品内容请见:

[MerckMillipore.com/immunoassays](https://www.merckmillipore.com/immunoassays)

# 异常的生存环境----缺氧



- 肿瘤组织体积快速扩张,导致一些肿瘤组织逐渐远离提供氧气和营养的血管组织。
- 肿瘤开始大量分泌与促血管生成相关的因子(如HIF-1、VEGF家族等),促使生长出许多的自身专属的新生血管,帮助自身生长以及远端转移。

## Human Cytokine/Chemokine Panel 1

- (Cat. No. HCYTOMAG-60K)
- 29 (Cat. No. HCYTMAG-60K-PX29)
- 29 (Bulk Cat. No. HCYTMAG60PMX29BK)
- 30 (Cat. No. HCYTMAG-60K-PX30) ◆
- 30 (Bulk Cat. No. HCYTMAG60PMX30BK) ◆
- 38 (Cat. No. HCYTMAG-60K-PX38)
- 38 (Bulk Cat. No. HCYTMAG60PMX38BK)
- 41 (Cat. No. HCYTMAG-60K-PX41)
- 41 (Bulk Cat. No. HCYTMAG60PMX41BK)

sCD40L	IL-9
EGF ◆	IL-10 ◆
Eotaxin/CCL11 ◆	IL-12 (p40) ◆
FGF-2/FGF-basic	IL-12 (p70) ◆
Flt3 Ligand	IL-13 ◆
Fractalkine/CX3CL1	IL-15 ◆
G-CSF ◆	IL-17A/CTLA8 ◆
GM-CSF ◆	IP-10/CXCL10 ◆
GRO	MCP-1/CCL2 ◆
IFNα2 ◆	MCP-3/CCL7
IFNγ ◆	MDC/CCL22
IL-1α ◆	MIP-1α/CCL3 ◆
IL-1β ◆	MIP-1β/CCL4 ◆
IL-1Ra ◆	PDGF-AA ▲
IL-2 ◆	PDGF-AB/BB ▲
IL-3 ◆	RANTES/CCL5◆▲
IL-4 ◆	TGFα
IL-5 ◆	TNFα ◆
IL-6 ◆	TNFβ/Lymphotoxin-α
IL-7 ◆	(LTA) ◆
IL-8/CXCL8 ◆	VEGF-A ◆

## Akt/mTOR (Total) – 11 Plex

(Cat. No. 48-612MAG) AB2 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated
Akt/PKB	√	H, M, R
GSK3α	√	H, M, R
GSK3β	√	H, M, R
IGF1R	√	H, M, R
IR	√	H, R
IRS1	√	H, M, R
mTOR	√	H, M, R
p70S6 Kinase	√	H, M, R
PTEN	√	H, M, R
RPS6	√	H, M, R
TSC2	√	H, M, R

## Human Bcl-2 Family Apoptosis Panel 1 - 6 Plex

(Cat. No. 48-682MAG) AB1 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated
BAD	√	√ (Ser112) H
BAX	√	H
Bcl-xL/BAD (interaction)	√	H
BIM	√	H
Mcl-1/BIM (interaction)	√	H

## Human Bcl-2 Family Apoptosis Panel 2 - 4 Plex

(Cat. No. 48-683MAG) AB1 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated
Bcl-2	√	H
Bcl-xL	√	H
Mcl-1	√	H
NOXA/Mcl-1 (interaction)	√	H

## Akt1 Phospho/Total – 2 Plex

(Cat. No. 48-631MAG) AB2 ▼ **NON-CONFIGURABLE KIT**

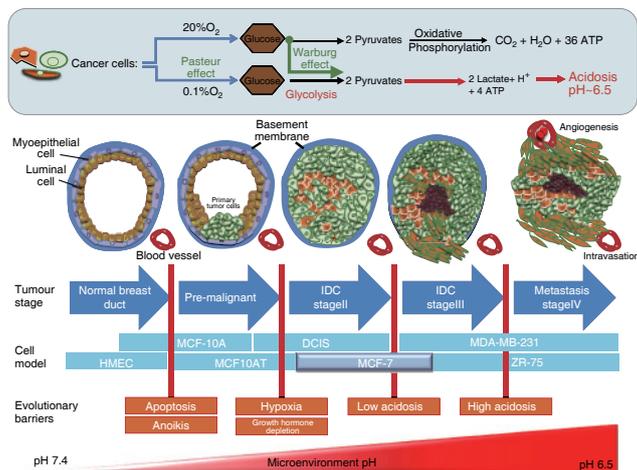
Analyte	Total	Phosphorylated
Akt1		(Ser473) H, M, R
Akt1	√	H, M, R

## NFκB – 6 Plex

(Cat. No. 48-630MAG) AB1 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated
c-Myc	√	H
FADD		√ (Ser194) H
IκBa		√ (Ser32) H
IKKα/β		√ (Ser177/181) H
NFκB		√ (Ser536) H, M
TNFR1	√	H

# 异常的生存环境----酸化



CDamaghi, Mehdi, Tafreshi, Narges K.Nat Commun. 2015.

- 与正常细胞通过氧化方式获取能量的方式不同，肿瘤细胞，只能利用无氧糖酵解产生的能量。因此糖酵解是肿瘤细胞获得能量的主要来源，而糖酵解会产生大量的乳酸，从而导致细胞外酸化，pH值在6.5-6.8之间。

- 酸性微环境对于肿瘤细胞的影响：1改变肿瘤细胞的生物活性2促进血管生成3免疫功能异常。

- 肿瘤细胞通过异常的能量代谢形成和维持一个不利于正常细胞生存的细胞外酸性环境，以维持自身的生存。

## Human MMP Panel 1

(Cat. No. HMMP1MAG-55K)

MMP-3	MMP-13
MMP-12	

## Human MMP Panel 2

(Cat. No. HMMP2MAG-55K)

MMP-1	MMP-9
MMP-2	MMP-10
MMP-7	

## Human TIMP Panel 1 (Serum/Plasma samples)

(Cat. No. HTMP1MAG-54K)

TIMP-1	TIMP-2
--------	--------

## Human TIMP Panel 2 (Cell culture samples)

(Cat. No. HTMP2MAG-54K)

TIMP-1	TIMP-3
TIMP-2	TIMP-4

## Multi-Species TGFβ – Singleplex

(Cat. No. TGFBMAG-64K-01)  
(Bulk Cat. No. TGFBMAG-64K-01BK)

TGFβ1
-------

## Multi-Species TGFβ – 3 Plex ▼

(Cat. No. TGFBMAG-64K-03)

**NON-CONFIGURABLE KIT**

TGFβ1	TGFβ3
TGFβ2	

## Human IGF ■

(Cat. No. HIGFMAG-52K)

IGF-1	IGF-2
-------	-------

## Early Apoptosis – 7 Plex

(Cat. No. 48-669MAG) AB2 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated	
Akt/PKB		√ (Ser473)	H, M, R
BAD		√ (Ser112)	H
Bcl-2		√ (Ser70)	H
Active Caspase 8	√		H
Active Caspase 9	√		H
JNK/SAPK1		√ (Thr183/Tyr185)	H, M, R
p53		√ (Ser46)	H

## Human Bcl-2 Family Apoptosis Panel 1 - 6 Plex

(Cat. No. 48-682MAG) AB1 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated	
BAD	√	√ (Ser112)	H
BAX	√		H
Bcl-xL/BAD (interaction)	√		H
BIM	√		H
Mcl-1/BIM (interaction)	√		H

## Human Bcl-2 Family Apoptosis Panel 2 - 4 Plex

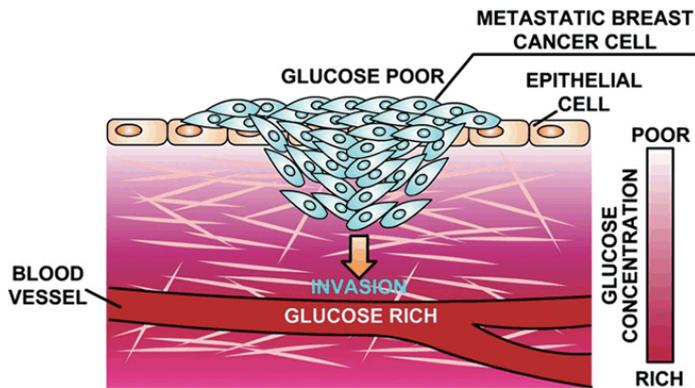
(Cat. No. 48-683MAG) AB1 ▼ **NON-CONFIGURABLE KIT**

Analyte	Total	Phosphorylated	
Bcl-2	√		H
Bcl-xL	√		H
Mcl-1	√		H
NOXA/Mcl-1 (interaction)	√		H

更多产品内容请见：

[MerckMillipore.com/immunoassays](https://www.MerckMillipore.com/immunoassays)

# 肿瘤的转移与侵袭



M. -P. Sablin, S. Faivre .Côlon & Rectum.2010.

- 肿瘤转移是指肿瘤脱离原发生长部位, 通过各种途径的转运, 在集体内原理原发部位的器官/组织继续增殖生长形成同样性质的转移瘤的过程。
- 肿瘤转移是恶性肿瘤最显著的特征之一, 是临床肿瘤病因的主要死因。

## 肿瘤细胞的转移步骤:

- 肿瘤细胞从原发灶脱离
- 肿瘤细胞与细胞外基质ECM发生异质性黏附增加
- ECM降解: 肿瘤细胞分泌蛋白降解酶类降解ECM成分, 形成肿瘤细胞的移动通道, 并以此为诱导血管生成的基础
- 肿瘤细胞运动型增强在粘附讲解的过程中移动, 穿过ECM, 并穿透血管壁的基底膜进入循环

### Human MMP Panel 1

(Cat. No. HMMP1MAG-55K)

MMP-3	MMP-13
MMP-12	

### Human MMP Panel 2

(Cat. No. HMMP2MAG-55K)

MMP-1	MMP-9
MMP-2	MMP-10
MMP-7	

### Human TIMP Panel 2 (Cell culture samples)

(Cat. No. HTMP2MAG-54K)

TIMP-1	TIMP-3
TIMP-2	TIMP-4

### Multi-Species TGFβ – 3 Plex ▼

(Cat. No. TGFBMAG-64K-03)

**NON-CONFIGURABLE KIT**

TGFβ1	TGFβ3
TGFβ2	

### Multi-Species TGFβ – Singleplex

(Cat. No. TGFBMAG-64K-01)

(Bulk Cat. No. TGFBMAG-64K-01BK)

TGFβ1

### Human Sepsis Panel 1

(Cat. No. HSP1MAG-63K)

sFAS/ TNFRSF6	MIF
sFasL	PAI-1 (total)
sICAM-1	sVCAM-1

### Human Circulating Cancer Biomarker Panel 1

(Cat. No. HCCBP1MAG-58K)

α-Fetoprotein (AFP)	IL-8/CXCL8
CA125	Leptin
CA15-3	MIF
CA19-9	Osteopontin (OPN)
CEA	Prolactin
CYFRA21-1	PSA (free)†
sFAS/TNFRSF6	PSA (total)†
sFasL	SCF
FGF-2/FGF-basic	TGFα
HCGβ	TNFα
HE4	TRAIL/TNFSF10
HGF	VEGF-A
IL-6	

### Human Cancer/Metastasis Biomarker Panel 1

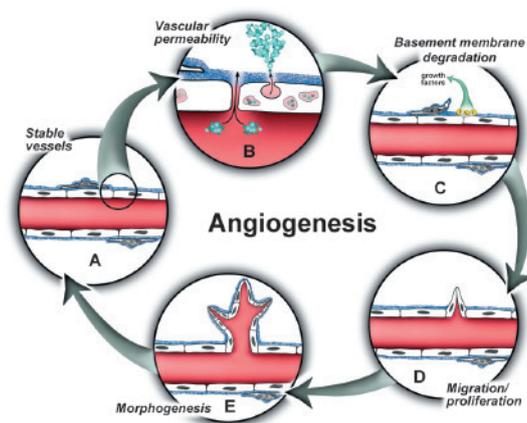
(Cat. No. HCMBMAG-22K)

DKK1	Osteoprotegerin (OPG)
GDF-15	Periostin
Neuron-specific Enolase (NSE)	TRAP5
Osteonectin/SPARC	TWEAK
	YKL40/CHI3L1

更多产品内容请见:

[MerckMillipore.com/immunoassays](https://www.MerckMillipore.com/immunoassays)

# 血管生成



B A, Bryan, P A, D'Amore .Cellular and molecular life sciences : CMLS).2007

- 肿瘤血管生成在肿瘤的生长和转移中起着重要的作用,是肿瘤生长、侵袭、转移和复发的先决条件。目前发现的血管生成开关开启的调控子有VEGF家族、IL8、TGF $\beta$ 、PDGF、FGF、EGF、TGF、MMP家族、TIMP家族、TNF $\alpha$ 、HIF-1 $\alpha$ 等。
- 肿瘤新生血管形成主要有以下三个步骤:
  - ①肿瘤血管生成的启动:肿瘤细胞自发性增殖,导致局部缺血缺氧,刺激血管生成的同时产生多种促血管生成因子,这些因子刺激产生大量蛋白酶,从而降解基膜并形成新生血管的芽胚
  - ②血管内皮细胞的增殖和迁移:血管内皮细胞在各种促血管生长因子的作用下迅速增殖并向肿瘤组织定向迁移
  - ③肿瘤新生血管的成熟:新增殖的血管内皮细胞进一步与血管外基质和周围的间质细胞相互作用,形成完整的血管结构

## Human Angiogenesis/Growth Factor Panel 1

(Cat. No. HAGP1MAG-12K)

Angiopoietin-2	HB-EGF
BMP-9	HGF
EGF	IL-8/CXCL8
Endoglin	Leptin
Endothelin-1	Placental Growth Factor (PLGF)
FGF-1/FGF-acidic	VEGF-A
FGF-2/FGF-basic	VEGF-C
Follistatin (FST)	VEGF-D
G-CSF	

## Human MMP Panel 1

(Cat. No. HMMP1MAG-55K)

MMP-3	MMP-13
MMP-12	

## Human MMP Panel 2

(Cat. No. HMMP2MAG-55K)

MMP-1	MMP-9
MMP-2	MMP-10
MMP-7	

## Human TIMP Panel 1 (Serum/Plasma samples)

(Cat. No. HTMP1MAG-54K)

TIMP-1	TIMP-2
--------	--------

## Human TIMP Panel 2 (Cell culture samples)

(Cat. No. HTMP2MAG-54K)

TIMP-1	TIMP-3
TIMP-2	TIMP-4

## Human Angiogenesis Panel 2

(Cat. No. HANG2MAG-12K)

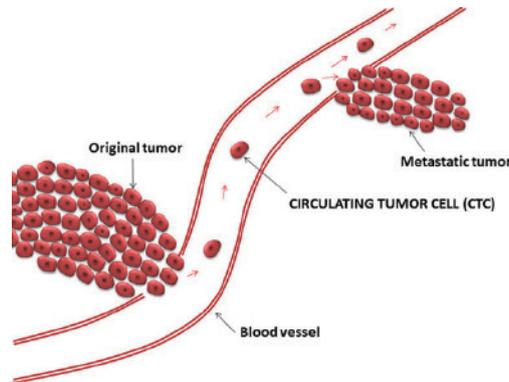
Angiostatin/Kringle	sIL-6R $\alpha$
sAXL	sNeuropilin-1 (sNRP-1)
sCD31/sPECAM-1	Osteopontin (OPN)
sc-Kit/sStem Cell Factor Receptor (SCFR)	PDGF-AB/BB
sE-Selectin	Tenascin-C (TN-C)
sEGFR/sHER1/sErbB1	Thrombospondin-2 (TSP-2)
sHER2/sEGFR2/sErbB2	sTIE-2
sHER3/sEGFR3/sErbB3	suPAR
sHGFR/sc-Met	sVEGFR1/sFlt-1
	sVEGFR2/sKDR/sFlk-1
	sVEGFR3/sFlt-4

更多产品内容请见:

[MerckMillipore.com/immunoassays](https://www.MerckMillipore.com/immunoassays)

# 循环肿瘤

循环肿瘤细胞 (circulating tumor cell) 简称CTC, 通常把进入人体外周血的肿瘤细胞称为循环肿瘤细胞



Thore Hillig, AnnBritt Nygaard. *Apmis Acta Pathologica Microbiologica Et Immunologica Scandinavica*. 2014.

- 进入血液循环的肿瘤细胞在运送过程中大多数都被杀死破坏。只有极少数转移倾向极高的细胞相互聚集形成微小癌栓并在循环系统中存活下来
- 在循环中幸存的癌细胞到达特定的继发组织或器官时, 通过黏附作用特异地锚定在毛细血管壁上, 并穿透管壁逸出血管进入周围组织。这些肿瘤细胞逃避宿主的局部非特异免疫杀伤作用, 在各类生长因子的作用下增殖生长, 最终形成转移肿瘤灶

## Human Circulating Cancer Biomarker Panel 1

(Cat. No. HCCBP1MAG-58K)

α-Fetoprotein (AFP)	IL-8/CXCL8
CA125	Leptin
CA15-3	MIF
CA19-9	Osteopontin (OPN)
CEA	Prolactin
CYFRA21-1	PSA (free)†
sFAS/TNFRSF6	PSA (total)†
sFasL	SCF
FGF-2/FGF-basic	TGFα
HCGβ	TNFα
HE4	TRAIL/TNFSF10
HGF	VEGF-A
IL-6	

## Human Circulating Cancer Biomarker Panel 2

(Cat. No. HCCBP2MAG-58K)

Antithrombin III	Extracellular Matrix Protein 1 (ECM1)
Complement Factor H (CFH)	Vitamin D Binding Protein

## Human Circulating Cancer Biomarker Panel 3

(Cat. No. HCCBP3MAG-58K)

Cathepsin D	Melanoma Inhibitory Activity (MIA)
Ferritin	Myeloperoxidase (MPO)
Fibroblast Activation Protein (FAP)	Sex Hormone Binding Globulin (SHBG)
Galectin-3	
IGFBP3	

## Human Circulating Cancer Biomarker Panel 4

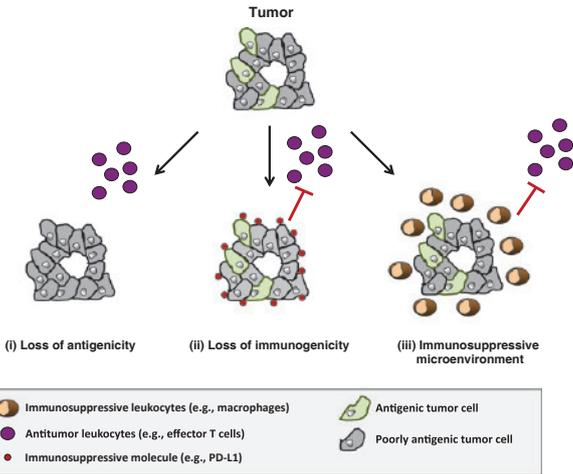
(Cat. No. HCCB4MAG-58K)

ALDH1A1	Kallikrein-6
Carbonic Anhydrase 9 (CA9)	Mesothelin
CD44	Midkine
EpCAM	NCAM1/L1CAM/CD171
Hepsin	Transglutaminase 2 (TGM2)

更多产品内容请见:

[MerckMillipore.com/immunoassays](http://MerckMillipore.com/immunoassays)

# 免疫逃逸



Beatty, G. L., Gladney, W. L. .Clinical Cancer Research.2015.

## 免疫逃逸:

肿瘤免疫逃逸 (Tumor escape) 是指肿瘤细胞通过多种机制逃避机体免疫系统识别和攻击, 从而得以在体内生存和增殖的现象。

- 抑制/逃脱肿瘤免疫反应: 肿瘤可分泌抑制因子及酶来逃避免疫清除, 包括TGF-β、IL-10, IL-6、PGE2, VEGF, GM-CSF等。

## Human Immuno-Oncology Checkpoint Protein

(Cat. No. HCKPMAG-11K)

BTLA	GITRL
CD27	HVEM
CD28	ICOS
CD40	LAG-3
CD80/B7-1	PD-1
CD86/B7-2	PD-L1
CTLA-4/CD152	TIM-3
GITR	TLR-2

## Human Cytokine/Chemokine Panel II

- (Cat. No. HCP2MAG-62K)
- 23 (Cat. No. HCP2MAG-62K-PX23)
- 23 (Bulk Cat. No. HCP2MAG62KPX23BK)

6Ckine/CCL21/Exodus-2	IL-28A/IFNλ2
BCA-1/CXCL13	IL-33/NF-HEV (mature)
CTACK/CCL27	LIF
ENA-78/CXCL5	MCP-2/CCL8
Eotaxin-2/CCL24/MPIF-2	MCP-4/CCL13
Eotaxin-3/CCL26	MIP-1δ/MIP-5/CCL15
I-309/CCL1	SCF
IL-16	SDF-1/CXCL12
IL-20	TARC/CCL17
IL-21	TPO
IL-23	TRAIL/TNFSF10
	TSLP

## Human Cytokine/Chemokine Panel I

- (Cat. No. HCYTMAG-60K)
- 29 (Cat. No. HCYTMAG-60K-PX29)
- 29 (Bulk Cat. No. HCYTMAG60PMX29BK)
- 30 (Cat. No. HCYTMAG-60K-PX30) ◆
- 30 (Bulk Cat. No. HCYTMAG60PMX30BK) ◆
- 38 (Cat. No. HCYTMAG-60K-PX38)
- 38 (Bulk Cat. No. HCYTMAG60PMX38BK)
- 41 (Cat. No. HCYTMAG-60K-PX41)
- 41 (Bulk Cat. No. HCYTMAG60PMX41BK)

sCD40L	IL-9
EGF ◆	IL-10 ◆
Eotaxin/CCL11 ◆	IL-12 (p40) ◆
FGF-2/FGF-basic	IL-12 (p70) ◆
Flt3 Ligand	IL-13 ◆
Fractalkine/CX3CL1	IL-15 ◆
G-CSF ◆	IL-17A/CTLA8 ◆
GM-CSF ◆	IP-10/CXCL10 ◆
GRO	MCP-1/CCL2 ◆
IFNα2 ◆	MCP-3/CCL7
IFNγ ◆	MDC/CCL22
IL-1α ◆	MIP-1α/CCL3 ◆
IL-1β ◆	MIP-1β/CCL4 ◆
IL-1Ra ◆	PDGF-AA ▲
IL-2 ◆	PDGF-AB/BB ▲
IL-3 ◆	RANTES/CCL5◆◆
IL-4 ◆	TGFα
IL-5 ◆	TNFα ◆
IL-6 ◆	TNFβ/Lymphotoxin-α (LTA) ◆
IL-7 ◆	VEGF-A ◆
IL-8/CXCL8 ◆	

## Human Cytokine/Chemokine Panel III

(Cat. No. HCP3MAG-63K)

HCC-1/CCL14 ▲	M-CSF
IL-11	MIG/CXCL9
IL-29/IFNλ1	MIP-3α/CCL20
I-TAC/CXCL11	MIP-3β/CCL19
LIX/CXCL6/GCP-2	NAP-2/CXCL7 ▲
Lymphotoxin/XCL1	

## Human Cytokine/Chemokine Panel IV

- (Cat. No. HCP4MAG-64K)
- 21 (Cat. No. HCY4MG-64K-PX21)
- 21 (Cat. No. HCP4MG64KPX21BK)

APRIL/TNFSF13	IL-28B/IFNλ3
BAFF/Blys	IL-32α
BRAK/CXCL14	IL-34
CCL28	IL-35
CXCL16	IL-36β/IL-1F8
HCC-4/CCL16	IL-37/IL-1F7
HMGB1 ●	IL-38/IL-1F10
IFNβ	MIP-4/PARC/CCL18
IL-14/α-Taxilin	MPIF/CCL23
IL-19	YKL40/CHI3L1
IL-24	

## Human High Sensitivity T Cell

- (Cat. No. HSTCMAG-28SK)
- 15 (Cat. No. HSTCMAG28SPMX13) ◆
- 15 (Bulk Cat. No. HSTCMAG28SPMX13BK) ◆
- 21 (Cat. No. HSTCMAG28SPMX21)
- 21 (Bulk Cat. No. HSTCMAG28SPMX21BK)

Fractalkine/CX3CL1	IL-12 (p70) ◆
GM-CSF ◆	IL-13 ◆
IFNγ ◆	IL-17A/CTLA8
IL-1β ◆	IL-21
IL-2 ◆	IL-23
IL-4 ◆	I-TAC/CXCL11
IL-5 ◆	MIP-1α/CCL3
IL-6 ◆	MIP-1β/CCL4
IL-7 ◆	MIP-3α/CCL20
IL-8/CXCL8 ◆	TNFα ◆
IL-10 ◆	

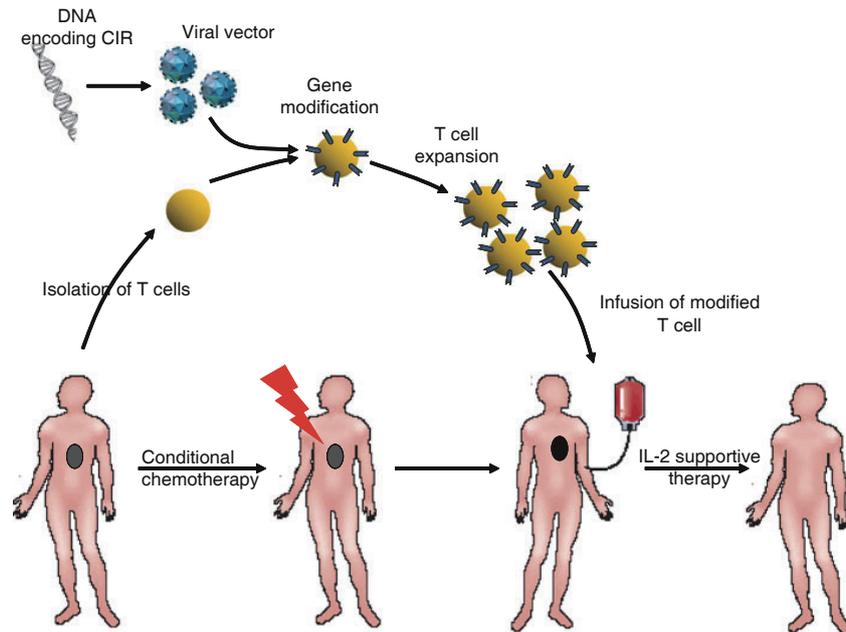
更多产品内容请见:

[MerckMillipore.com/immunoassays](http://MerckMillipore.com/immunoassays)

# 肿瘤免疫治疗

## CAR-T治疗

CAR-T全称是 chimeric antigen receptor T cells, 嵌合抗原受体T细胞免疫疗法。CAR-T的原理就是通过基因工程手段修饰人的T细胞, 使其表达嵌合抗原受体(chimeric antigen receptor, CAR), 即将识别肿瘤细胞表面抗原的抗体与激活T细胞所需的信号分子连接, 以此增强T细胞对肿瘤的特异性杀伤。



Lipowska-Bhalla, Grazyna.  
Cancer Immunology, Immunotherapy.2012.

## CART治疗引起的副作用:

### 1: 细胞因子释放综合征: 细胞因子风暴

细胞因子释放综合征 (CRS) 是一种因细胞因子的显著升高引起的系统性炎症反应, 同时伴有 CARTs 的迅速体内活化及增殖, 通常在首次输注后数天内发生。其初始的标志性临床表现: 发热、流感样症状, 可迅速进展为血管扩张性休克、毛细血管渗漏及呼吸功能损伤等重度 CRS (sCRS) 的表现

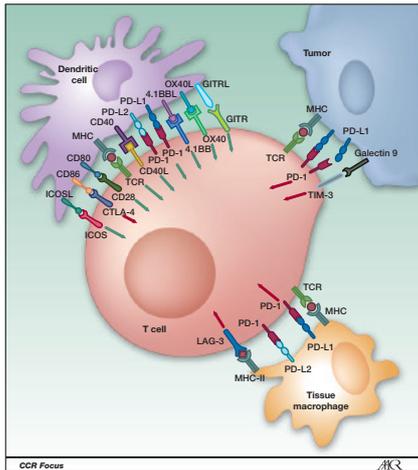
### 2: 神经毒性反应

神经毒性包括谵妄、脑病及抽搐, 由系统性、大量的炎症因子穿过血脑屏障或直接在中枢神经系统产生引起

更多产品内容请见:

[MerckMillipore.com/immunoassays](https://www.MerckMillipore.com/immunoassays)

# 肿瘤免疫治疗



Patrick A Ott, F Stephen Hodi.  
Clinical Cancer Research.2013.

## 免疫检查点抑制剂

- T细胞时刻准备着杀死肿瘤细胞, 但是该过程往往受到共刺激信号中的负性调控信号所约束。负性调控信号即为-免疫检查点(immune checkpoint)。
- 免疫检查点实质是免疫细胞会产生抑制自身的蛋白质小分子, 为了防止过度的免疫反应和保护周围的其他正常细胞免受伤害。
- 肿瘤细胞往往利用这种抑制作用, 抑制免疫细胞的活性, 从而逃脱免疫细胞的追杀而存活下来。

### Human CVD Panel 3 (Acute Phase)

(Cat. No. HCVD3MAG-67K)

α-1-Acid Glycoprotein (AGP)	Haptoglobin
α-2-Macroglobulin	sL-Selectin
Adipsin/Factor D	Platelet Factor 4 (PF4)/CXCL4
CRP	Serum Amyloid P (SAP)
Fetuin A	von Willebrand Factor (vWF)
Fibrinogen	

### Human Soluble Cytokine Receptor

(Cat. No. HSCRMAG-32K)  
 14 (Cat. No. HSCRMAG32KPX14)  
 14 (Bulk Cat. No. HSCRMAG32PMX14BK)

sCD30	sIL-6R
sEGFR/sHER1/ErbB1	sRAGE
sGP130	sTNF RI
sIL-1RI	sTNF RII
sIL-1RII	sVEGFR1/sFlt-1
sIL-2Rα	sVEGFR2/sKDR/sFlk-1
sIL-4R	sVEGFR3/sFlt-4

### Human IgE – Singleplex

(Cat. No. HGAMMAG-303E)

IgE
-----

### Human Circadian Stress

(Cat. No. HNCSMAG-35K)

Cortisol	Melatonin
----------	-----------

### Human Amyloid Beta and Tau (CSF samples)

(Cat. No. HNABTMAG-68K)

Amyloid beta 1-40	pTau (Thr181)
Amyloid beta 1-42	Tau (total)

### Human Cytokine/Chemokine Panel I

(Cat. No. HCYTOMAG-60K)  
 29 (Cat. No. HCYTMAG-60K-PX29)  
 29 (Bulk Cat. No. HCYTMAG60PMX29BK)  
 30 (Cat. No. HCYTMAG-60K-PX30) ◆  
 30 (Bulk Cat. No. HCYTMAG60PMX30BK) ◆◆  
 38 (Cat. No. HCYTMAG-60K-PX38)  
 38 (Bulk Cat. No. HCYTMAG60PMX38BK)  
 41 (Cat. No. HCYTMAG-60K-PX41)  
 41 (Bulk Cat. No. HCYTMAG60PMX41BK)

sCD40L	IL-9
EGF ◆	IL-10 ◆
Eotaxin/CCL11 ◆	IL-12 (p40) ◆
FGF-2/FGF-basic	IL-12 (p70) ◆
Flt3 Ligand	IL-13 ◆
Fractalkine/CX3CL1	IL-15 ◆
G-CSF ◆	IL-17A/CTLA8 ◆
GM-CSF ◆	IP-10/CXCL10 ◆
GRO	MCP-1/CCL2 ◆
IFNα2 ◆	MCP-3/CCL7
IFNγ ◆	MDC/CCL22
IL-1α ◆	MIP-1α/CCL3 ◆
IL-1β ◆	MIP-1β/CCL4 ◆
IL-1Ra ◆	PDGF-AA ▲
IL-2 ◆	PDGF-AB/BB ▲
IL-3 ◆	RANTES/CCL5 ◆▲
IL-4 ◆	TGFα
IL-5 ◆	TNFα ◆
IL-6 ◆	TNFβ/Lymphotoxin-α (LTA) ◆
IL-7 ◆	VEGF-A ◆
IL-8/CXCL8 ◆	

### Human Neuroscience Panel 1 (CSF samples)

(Cat. No. HNS1MAG-95K)

α-Synuclein	PARK5/UCLH1
Glial Fibrillary Acidic Protein (GFAP)	PARK7/DJ1
Neuron-specific Enolase (NSE)	Transglutaminase 2 (TGM2)

### Human Neurodegenerative Disease Panel 1

(Cat. No. HNDG1MAG-36K)

α-2-Macroglobulin	Complement Factor C3
Apo AI	
Apo CIII	Complement Factor H (CFH)
Apo E	

### Human Neurodegenerative Disease Panel 3

(Cat. No. HNDG3MAG-36K)

BDNF	PAI-1 (total)
Cathepsin D	PDGF-AA
sICAM-1	PDGF-AB/BB
Myeloperoxidase (MPO)	RANTES/CCL5
sNCAM	sVCAM-1

### Human Neurological Disorders Panel 3

(Cat. No. HND3MAG-39K)

Angiotensinogen (AGT)	Osteopontin (OPN)
Contactin-1	Soluble Superoxide Dismutase 1 (sSOD1)
Fetuin A	Soluble Superoxide Dismutase 2 (sSOD2)
Kallikrein-6	

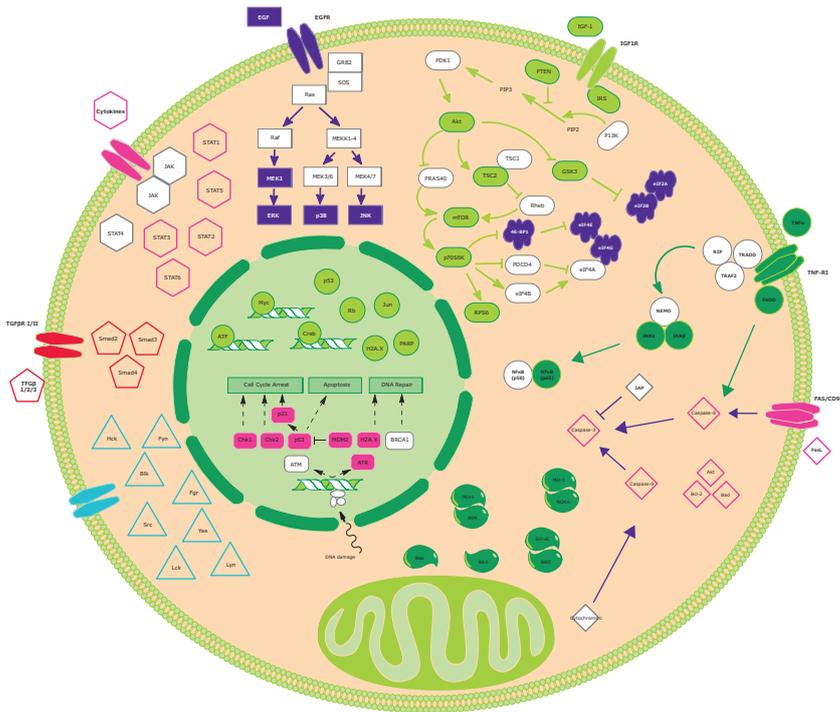
### Human Immuno-Oncology Checkpoint Protein

(Cat. No. HCKPMAG-11K)

BTLA	GITRL
CD27	HVEM
CD28	ICOS
CD40	LAG-3
CD80/B7-1	PD-1
CD86/B7-2	PD-L1
CTLA-4/CD152	TIM-3
GITR	TLR-2

## 参考文献

Title	Journal	Year
Two-Dimensional Regulation of CAR-T Cell Therapy with Orthogonal Switches	Molecular Therapy	2019
CD40 Ligand-Modified Chimeric Antigen Receptor T Cells Enhance Antitumor Function by Eliciting an Endogenous Antitumor Response	Cancer Cell	2019
The Adaptor Protein CARD9 Protects against Colon Cancer by Restricting Mycobiota-Mediated Expansion of Myeloid-Derived Suppressor Cells	Immunity	2018
Fibroblast Heterogeneity and Immunosuppressive Environment in Human Breast Cancer	Cancer Cell	2018
RIP1 Kinase Drives Macrophage-Mediated Adaptive Immune Tolerance in Pancreatic Cancer	Cancer Cell	2018
STIM1 and STIM2 Mediate Cancer-Induced Inflammation in T Cell Acute Lymphoblastic Leukemia	Cell Reports	2018
In vivo fate and activity of second versus third-generation D19-specific CAR-T cells in B-cell non-Hodgkin lymphomas	Molecular Therapy	2018
Development and evaluation of an optimal human single chain variable fragment derived BCMA targeted CAR T cell vector	Molecular Therapy	2018
Dual Targeting of Oncogenic Activation and Inflammatory Signaling Increases Therapeutic Efficacy in Myeloproliferative Neoplasms	Cancer Cell	2017
Phase I Escalating-Dose Trial of CAR-T Therapy Targeting CEA+ Metastatic Colorectal Cancers	Molecular Therapy	2017
Circulating Inflammation Markers and Prospective Risk for Lung Cancer	Journal of the National Cancer Institute	2013
Safety and persistence of adoptively transferred autologous CD19-targeted T cells in patients with relapsed or chemotherapy refractory B-cell leukemias	Blood	2011



Protein Symbol	MILLIPLEX® MAP Panel	Species	Cat. No.
	RTK* Human Soluble Cytokine Receptor Human Angiogenesis Panel 2	H H H	HPRTKMAG-01K HSCRMAG-32K HANG2MAG-12K
	Src Family Kinase Active Site*	H	48-650MAG
	TGFβ Pathway* TGFβ1 Singleplex TGFβ-1,-2,-3	H H,M,R H,M,R	48-614MAG TGFβMAG-64K-01 TGFβMAG-64K-03
	STAT (Phosphoprotein)* Human Angiogenesis Panel 1 Human Circulating Cancer Biomarker Panel 1	H H H	48-610MAG HAGP1MAG-12K HCCBP1MAG-58K
	MAPK/SAPK (Phosphoprotein)* Multi-Pathway (Phosphoprotein)* Multi-Pathway (Total) Human Cytokine Panel 1 Human Angiogenesis Panel 1 Human Circulating Cancer Biomarker Panel 1	H H H,M,R H H H	48-660MAG 48-680MAG 48-681MAG HCYTOMAG-60K HAGP1MAG-12K HCCBP1MAG-58K
	Akt/mTOR (Phosphoprotein)* Akt/mTOR (Total)*	H H,R	48-611MAG 48-612MAG
	Protein Translation	H,M,R	48-655MAG
	NFκB* Human Cytokine Panel 1	H H	48-630MAG HCYTOMAG-60K
	Early Apoptosis* Human Circulating Cancer Biomarker Panel 1	H H	48-669MAG HCCBP1MAG-58K
	Bcl-2 Family Apoptosis Panel 1 Bcl-2 Family Apoptosis Panel 2	H H	48-682MAG 48-683MAG
	DNA Damage/Genotoxicity*	H	48-621MAG

\*For individual analyte species cross-reactivity, please refer to our website.

更多内容请见:

[MerckMillipore.com/immunoassays](https://www.merckmillipore.com/immunoassays)

# 应用举例

## 使用多重蛋白检测平台检测非小细胞肺癌早期肿瘤转移中参与血管生成相关生物标志物

Jeffrey A. Borgia, Ph.D; Daniel Rinewalt, M.D.; Cristina Fhied, M.S.; and Michael J. Liptay, M.D.; Rush University Medical Center

肿瘤血管生成是肿瘤生长和转移过程中一个标志性的阶段,主要用于传递各种营养物质,肿瘤生长和转移所需的各种生长因子,氧气等。血管生成是一个复杂的生物学过程,包括血管内皮细胞的增殖,出芽,迁移等。这一过程受到血管生成因子(VEGF, FGF, PDGF, TGF)和血管抑制因子(thrombospondin, angiostatin, endostatin)共同参与调节<sup>1,2</sup>。作为启动血管生成的“开关”,两者达到平衡,血管生成不被启动,但是在肿瘤组织中,破坏了这种复杂的动态平衡,导致新生血管异常生长,结构和功能同时也是发生异常改变。研究众多肿瘤血管生成中相关分子在肿瘤血管生成中所扮演的角色,从而达到控制肿瘤成长和转移的目的,对于肿瘤治疗至关重要。

### 材料和方法

**样本:**38个非小细胞肺癌的患者的血清,其中20名患者处于T<sub>1-2</sub>N<sub>0</sub>M<sub>0</sub>期(没有发生转移),12名患者处于T<sub>1-3</sub>N<sub>1-2</sub>M<sub>0</sub>(局部转移),14名患者为T<sub>1-4</sub>N<sub>1-2</sub>M<sub>1</sub>(发生远端转移)<sup>3</sup>。所有患者没有接受过化学或者放射治疗。

**材料:**使用来自默克公司的多重蛋白检测试剂盒Human Angiogenesis/Growth Factor Magnetic Bead Panel 1 (Cat. No. HAGP1MAG-12K),检测17种血管生成的相关因子:Angiopoietin-2, BMP-9, EGF, Endoglin, Endothelin-1, FGF-1 (acidic FGF), FGF-2 (basic FGF), Follistatin, G-CSF, HB-EGF, HGF, IL-8, Leptin, PLGF, VEGF-A, VEGF-C, 和 VEGF-D。

实验中所有因子检测均使用96孔板模式按产品说明书操作。使用Luminex 200系统(Luminex Corporation, Austin, TX)采集荧光数据进行检测,数据分析使用默克公司MILLIPLEX Analyst 5.1软件进行分析。统计采用非配对t检验计算双尾p值。

### 结果:

使用MILLIPLEX<sup>®</sup> map Human Angiogenesis/Growth Factor Magnetic Bead Panel 1试剂盒测定38名非小细胞肺癌不同阶段种17种血管生成标志物的表达情况。从数据中可以看到,远端转移的病人血清中的IL-8, HGF, HBEGF表达与没有发生转移的病人相比显著升高(Table 1)。该数据与实验室之前实验结果保持一致,即测定与血管生成信号通路相关的生长因子和其他信号分子的变化<sup>4</sup>。

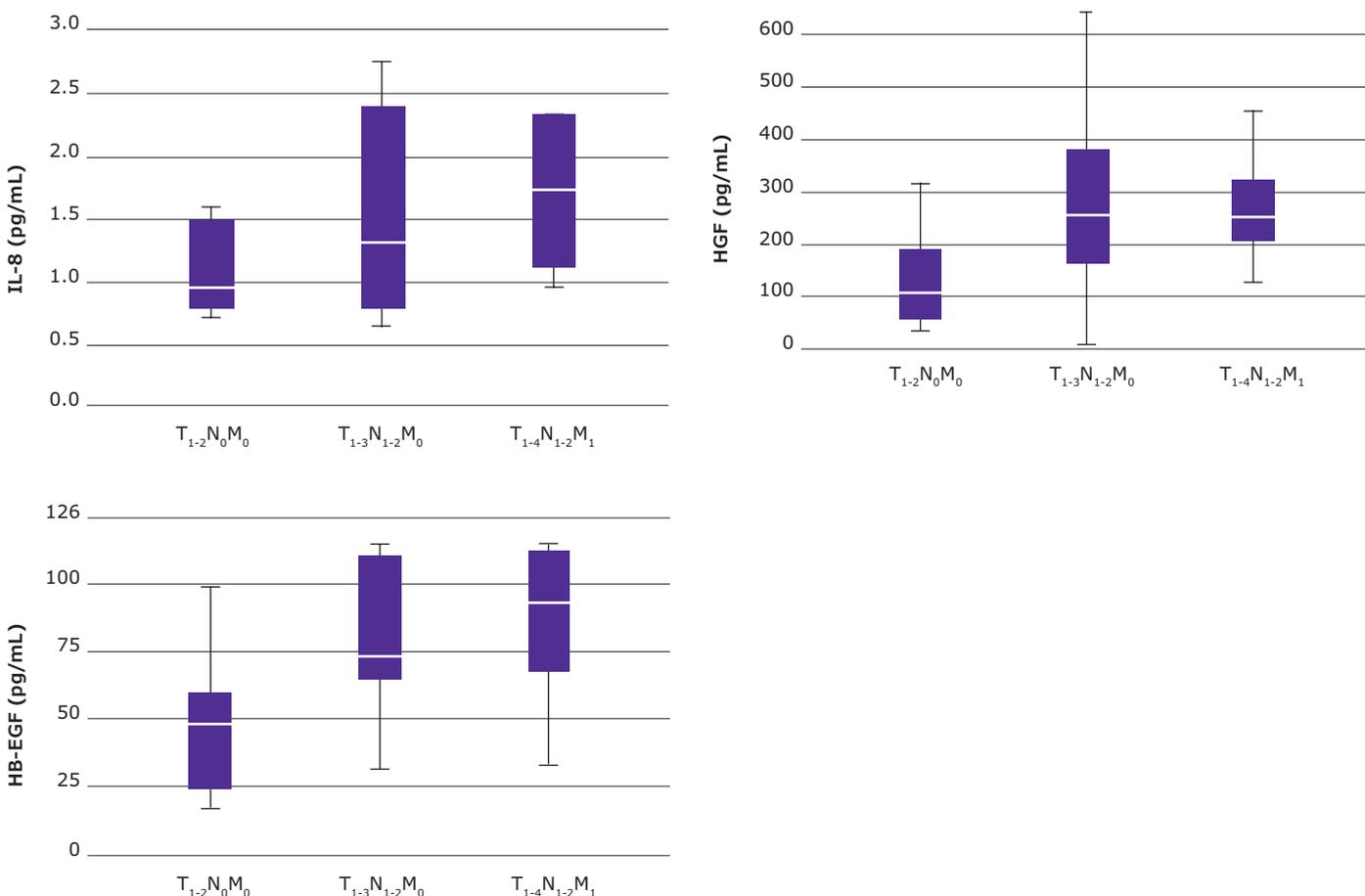
### Tips

利用高通量,小样本量方式筛查大批与血管生成相关的生长因子以及其他参与调节血管生成相关因子尤为关键。我们利用了基于Luminex<sup>®</sup> xMAP<sup>®</sup> 多重检测平台的MILLIPLEX<sup>®</sup> map 血管生成/生长因子试剂盒,同时检测38个非小细胞肺癌不同阶段的病人中17个可能参与了血管生成相关因子,以研究他们在整个血管生成相关信号通路中的作用。

	T <sub>1-2</sub> N <sub>0</sub> M <sub>0</sub>		T <sub>1-3</sub> N <sub>1-2</sub> M <sub>0</sub>		T <sub>1-4</sub> N <sub>1-2</sub> M <sub>1</sub>	
	Range	Median	Range	Median	Range	Median
Angiopoietin-2	607 - 2,181	1,628.00	616 - 4,422	1398.00	770 - 14,250	1,816.00
BMP-9	56.7 - 352.6	98.30	15.9 - 480.2	110.40	15.9 - 428.3	162.90
EGF	3.34 - 62.18	17.6	3.34 - 153.39	38.77	3.3 - 76.4	12.53
Endoglin	203.6 - 2,112	613.7	96 - 1,074.6	649.20	236 - 2,398	497.93
Endothelin-1	2.6 - 12.7	8.19	2.6 - 113.2	2.59	2.6 - 10.9	5.24
FGF-1	0.21 - 19.0	4.71	0.21 - 8,404	2.41	0.21 - 54.0	4.00
FGF-2	41.1 - 330.3	41.10	41.1 - 425.7	41.10	41.1 - 133.2	41.10
Follistatin	175.0 - 2,052	848.40	204.9 - 2,824	839.70	228.2 - 1,353	599.10
G-CSF	2.80 - 108.8	4.26	2.80 - 91.4	2.80	2.80 - 370.8	2.80
HB-EGF	16.2 - 99.1	48.20	31 - 500.5	79.60	32.7 - 198.9	93.00
HGF	34.6 - 316.2	108.40	11.9 - 1,473.3	259.40	129.3 - 1960	253.40
IL-8	0.71 - 1.6	0.95	0.65 - 6.61	1.42	0.96 - 25.4	1.71
Leptin	10,620 - 51,383.4	14,265	1,572 - 24,840	6,585	1,241 - 36,763	9,554
PLGF	0.05 - 16.4	8.88	0.69 - 73.6	5.61	1.41 - 18.2	6.30
VEGF-A	4.5 - 770.5	43.80	15.4 - 1418.4	160.6	6.7 - 978.2	227.4
VEGF-C	1.63 - 65.5	27.40	1.63 - 1,264.1	47.20	1.63 - 61.5	35.30
VEGF-D	0.53 - 27.3	9.30	0.53 - 230.6	3.33	0.53 - 34.3	2.90

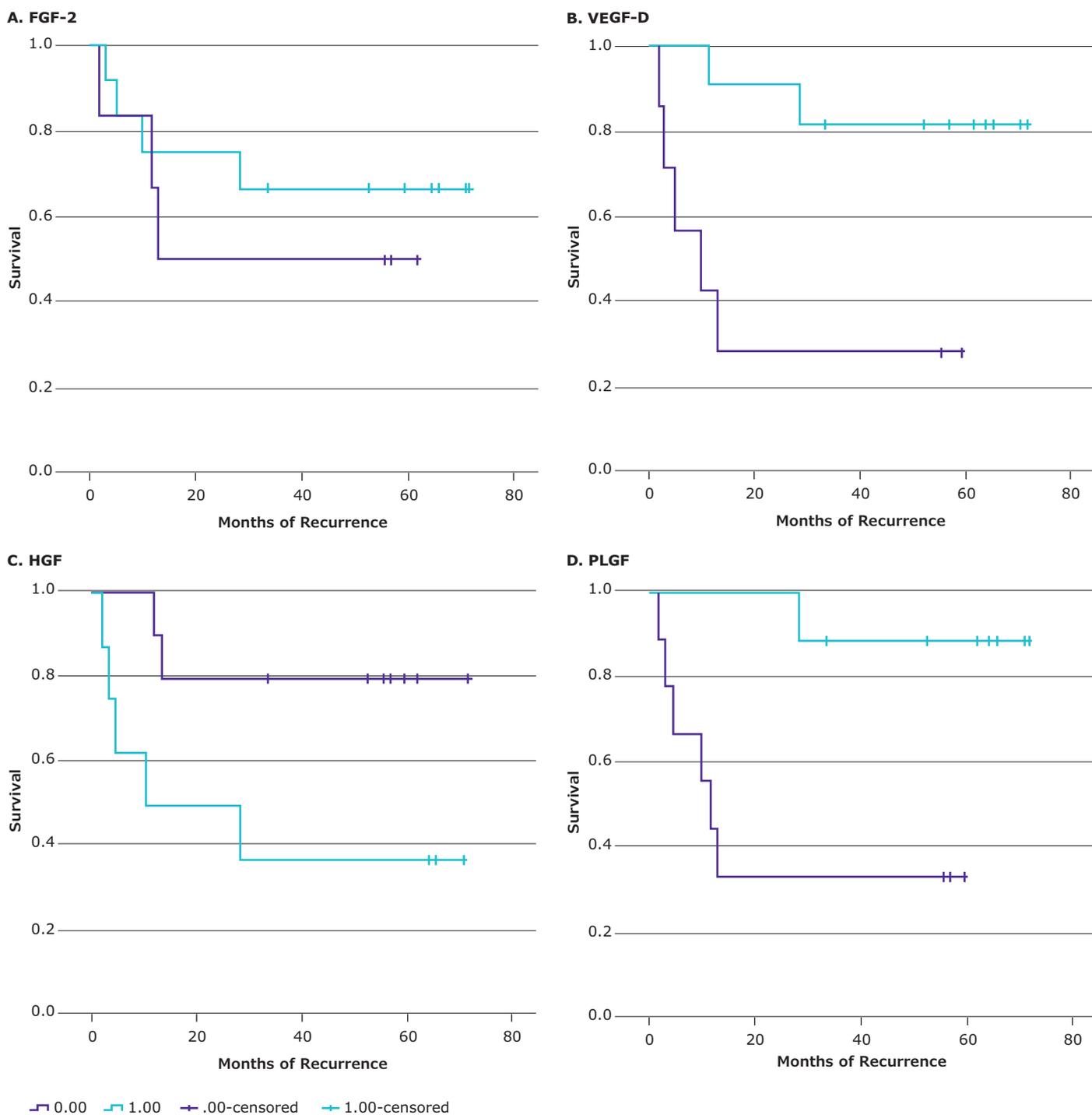
**Table1:** 使用MILLIPLEX® map Human Angiogenesis/Growth Factor Magnetic Bead分析 Panel分析3组非小细胞肺癌患者与血管生成相关因子 (所有因子单位为pg/ml)

用Mann-whitney检验方法,我们发现许多生物标志物与疾病进展相关 (Figure1,例如EGF, PLGF, VEGF-A, VEGF-C)。然而,由于参与这一研究的患者数量较少,因此没有达到研究的意义。而且,我们观察到的模式只是对转移进展的早期阶段的了解。



**Figure1.** IL-8, HB-EGF和HGF在发生转移的非小细胞癌中的患者表达很高。T<sub>1-2</sub>N<sub>0</sub>M<sub>0</sub> 代表没有发生转移, T<sub>1-3</sub>N<sub>1-2</sub>M<sub>0</sub> 代表发生向局部淋巴结转移, T<sub>1-4</sub>N<sub>1-2</sub>M<sub>1</sub>代表发生远端转移或者弥散。进行检测分析。各组均取平均值, p值为: T<sub>1-2</sub>N<sub>0</sub>M<sub>0</sub> versus T<sub>1-4</sub>N<sub>1-2</sub>M<sub>1</sub>, IL-8, p=0.001; T<sub>1-2</sub>N<sub>0</sub>M<sub>0</sub> versus T<sub>1-4</sub>N<sub>1-2</sub>M<sub>1</sub>, HGF, p=0.004; T<sub>1-2</sub>N<sub>0</sub>M<sub>0</sub> versus T<sub>1-4</sub>N<sub>1-2</sub>M<sub>1</sub>, HB-EGF, p=0.004; T<sub>1-2</sub>N<sub>0</sub>M<sub>0</sub> versus T<sub>1-3</sub>N<sub>1-2</sub>M<sub>0</sub>, HB-EGF, P=0.005。需要注意的是所有的异常值和极端值已经在图中被剔除。

鉴于之前的研究结果,我们决定将研究重点放在 $T_{1-2}N_0M_0$ 和 $T_{1-3}N_{1-2}M_0$ 这两个阶段,具体来说,我们评估了与生物标志物浓度相关的复发中位生存期,使用每个生物标志物的平均浓度作为阈值 (Figure 2)。其中有9个生物标志物的log-rank检验P值小于0.05。Figure2中没有展示BMP-9, Follistatin, HB-EGF,Angiopoietin-2, VEGF-C。



**Figure 2.** Kaplan-Meier生存曲线。通过比较17种生物标志物在 $T_{1-2}N_0M_0$ 和 $T_{1-3}N_{1-2}M_0$ 两组中的复发情况,我们发现Kaplan-Meier曲线 (A) FGF-2 [ $p=0.049$ ], (B) VEGF-D [ $p=0.009$ ], (C) HGF [ $p<0.001$ ], (D) PLGF [ $p=0.010$ ]。紫色的线代表病人所检测浓度低于所检测的平均浓度,而青色线代表大于平均浓度

## 结论

用MILLIPLEX® map 血管生成/生长因子试剂盒帮助我们发现FGF-2,VEGF-D,HGF,PLGF等可能与肿瘤转移过程中的血管生成相关。

## 参考文献

1. Winder, T., Lenz, H. Vascular endothelial growth factor and epidermal growth factor signaling pathways as therapeutic targets for colorectal cancer. *Gastroenterology*. 2010; 138(6): 2163 – 76.
2. Carmeliet, P., Jain, R.K. Molecular mechanisms and clinical applications of angiogenesis. *Nature*. 2011; 473(7347): 298 – 307.
3. Rami-Porta, R., Crowley, J.J., Goldstraw, P. The revised TNM staging system for lung cancer. *Ann Thorac Cardiovasc Surg* 200v9;15(1): 4 – 9.
4. Farlow, E.C., Vercillo, M.S., Coon, J.S., et al. A multi-analyte serum test for the detection of non-small cell lung cancer. *British Journal of Cancer* 2010; 103(8): 1221.

#### 上海

上海市浦东新区东育路227弄3号  
前滩世贸中心(二期)C栋15-18层  
电话: (021)20338288  
传真: (021)50803042  
邮编: 200126

#### 北京

北京市朝阳区将台路甲2号  
诺金中心25层  
电话: (010)59072688  
传真: (010)59072699  
邮编: 100016

#### 广州

广州市天河区冼村路5号  
凯华国际中心1201-1204  
电话: (020)32255333  
传真: (021)32255380  
邮编: 510000

#### 成都

成都市锦江区人民南路二段1号  
仁恒置地广场1706室  
电话: (028)80740222  
传真: (028)80740227  
邮编: 610061



本资料中所有内容(包括但不限于产品图片、公司logo等)为德国默克集团所有, 未经允许, 任何人或实体不得擅自使用或转载。  
默克生命科学技术服务热线: 400 620 3333 或 400 889 1988转2号线  
中国技术服务中心: [tscn@merckgroup.com](mailto:tscn@merckgroup.com)  
更多详情, 敬请登陆: [www.merckmillipore.com](http://www.merckmillipore.com)  
资料编号: MK\_BR4093SM 05/19