MERCK

Milliplex

高通量多因子检测平台

转化医学及精准医学研究的系统化平台

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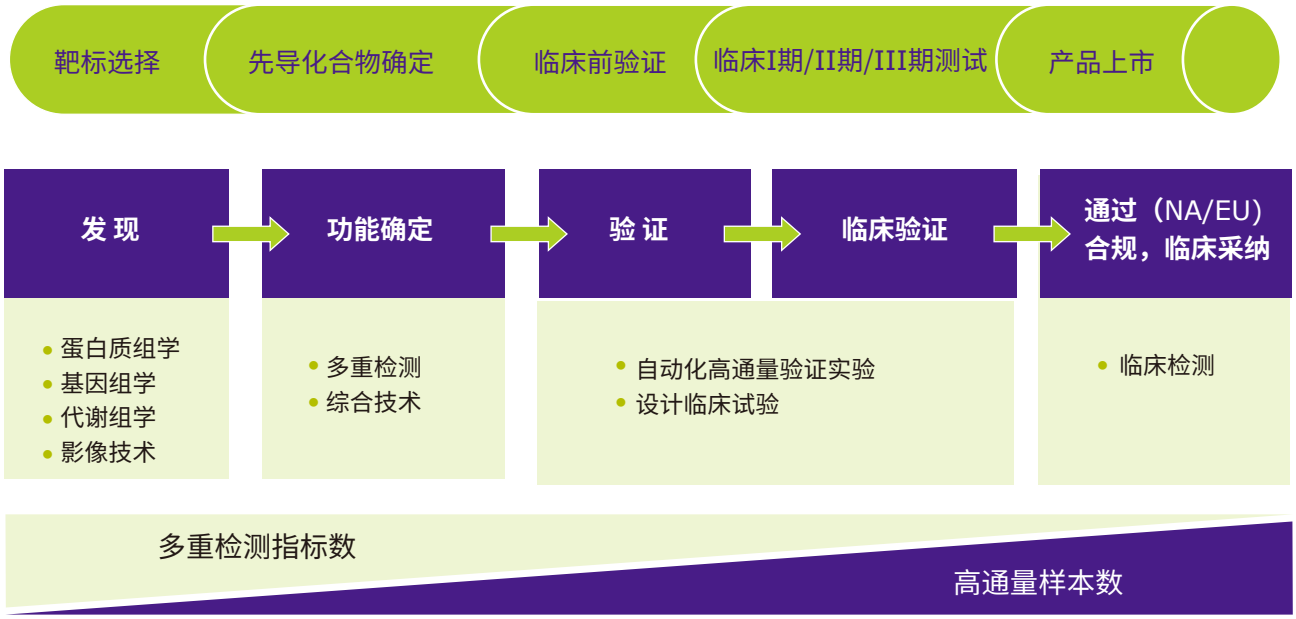
Luminex®
多功能液相芯片分析平台

快速悬浮液相芯片，转化医学全进程研究的系统化平台！

新生物标志物研发都会经历生物标志物的发现、功能确定、标志物在疾病中验证、到临床检测的过程。在研发前期主要通过蛋白组学/基因组学等技术进行高通量指标数的筛选。在Biomarker功能确定、验证、临床验证的转化过程中，需要多重指标和中高通量样本筛选，这就需要多重指标的高通量样本筛选平台。新药发现与生物标志物相同，对先导化合物药效确定到临床测试都需要多重检测的中高通量样本检测平台。Luminex®多功能液相芯片可以提供1-500重指标的96/384孔板检测，是新Biomarker发现之后最佳的筛选平台。为新的治疗方法的转化医学研究提供强有力的技术保障。



Luminex®多重检测技术的核心即xMAP专利的编码微球系统

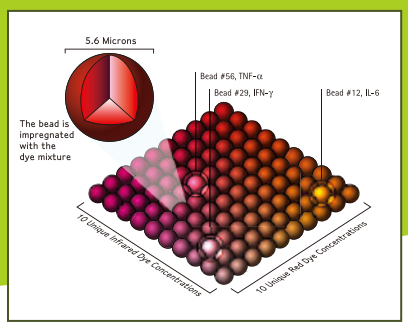
xMAP创新技术真正实现了：

- 多 重 检 测 ： 实现1-500重因子同时检测，为微量样本的精确检测提供技术保障；
- 高 灵 敏 度 ： 精密的光学设计提升检测灵敏度，低至0.04pg/ml；
- 快速/高通量： 96/384孔板自动化高通量检测，每小时数据量可达9,600个结果
- 微 量 样 本 ： 10-50ul的样本量使得跟踪动物模型的阶段性变化成为可能，避免个体差异带来的实验误差。

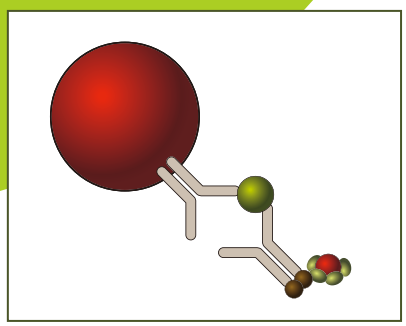
xMAP专利的微球编码技术，创新实现多重精确检测

xMAP技术原理：

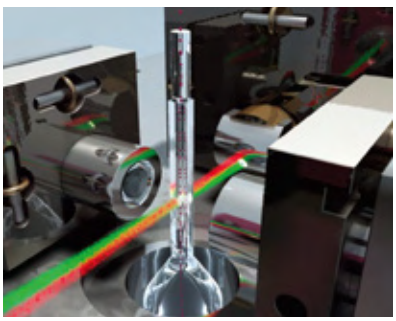
xMAP技术是液相芯片实现多重检测的基础。通过独有的微球表面化学技术，实现了在96/384孔板的每一个单孔中同时检测多个指标的研究。并通过精密的仪器和精确的分析软件获得值得信赖的数据。该平台已被广泛用于抗原-抗体（蛋白生物标志物）免疫分析、核酸研究、酶-底物的酶学研究以及受体-配体识别分析等研究领域。



Luminex®应用其专利技术对每一个微球进行2-3种荧光染料的着色，通过精确的染料比例产生100-500种不同颜色的微珠，每一种颜色的微珠上偶联一种特异性的蛋白抗体。



当偶联了特异性抗体的微珠与样本中的蛋白(Analyte)反应，加入生物素标记的检测抗体。通过PE标记的Streptavidin与生物素的连接放大信号。整个反应结束后形成的复合物包括了微珠的荧光和PE的荧光信号。



仪器在检测时，在液流系统中，微珠快速通过第一束红色激光，对微珠进行ID识别。第二束激光是绿色激光，对PE荧光信号的强弱进行检测。

最后，获取到的光信号将被快速处理成数字信号，经软件分析后计算得到每一种蛋白的含量。

Merck Millipore 联合Luminex®
共同建立多重生物标志物检测金标准

作为Luminex®最早全球的合作伙伴，Merck Millipore始终致力于生物标志物多重检测技术与研发。拥有三十多年深厚的研发经验，Merck Millipore秉持着严谨、专业的态度在基于Luminex®液相芯片平台上创建了生物标志物快速检测的金标准 — Merck Millipore与Luminex®液相悬浮芯片相结合的多重检测平台。拥有这样专业全面的平台，您将更快速的掌握最新的技术、获取更多经验、实现更高效的科学研究。

Merck Millipore 是最早提供 FLEXMAP 3D®, Luminex 200TM, MAGPIX® 以及Milliplex MAP检测的完整平台，满足从实验室到临床全进程转化医学的需要。自2003年，美国国立卫生研究院(NIH)正式提出转化医学研究以提高公民健康状况，转化医学研究就为弥补基础实验研发与临床之间的鸿沟，为新药开发、研究新的治疗方法开辟了一条新途径，是从实验台到临床的双向开发研究过程。Merck Millipore与Luminex ®，为基础研究 — 新药研发 — 新治疗探索的转化医学研究提供了统一的研究平台。

Merck Millipore液相芯片检测平台，
开创生物标志物检测完整平台及一站式服务

FLEXMAP 3D
液相芯片分析仪

Milliplex
平台软件

平台整体服务

检测平台：
Merck Millipore提供所有基于xMAP技术的检测仪器，FLEXMAP 3D®, Luminex200™, MAGPIX®。独特的仪器维护校验、校正系统为客户得到多重精确的数据检测提供了坚实的保障。

软件平台：
Merck Millipore为更准确的数据对比和分析提供Luminex®原厂软件xPONENT®、专业定量分析软件Milliplex Analyst，为您更高效地获得更高效的数据分析提供强有力的保证。为更高效的数据分析和结果对比提供有力的工具。

应用平台：
Merck Millipore是蛋白生物标志物检测的领导者，为多种疾病检测提供广泛的试剂应方案：包括癌症、免疫疾病、心血管疾病、代谢疾病、神经退行性疾病等，以及肾毒性、信号转导研究等。Merck Millipore提供超过8个种属1200种生物标志物的选择。

服务平台：
近40年的研发经验积累，打造了Merck Millipore Biomarker Service金牌服务。十几家Milliplex认证实验室，遍布主要区域，让你享受在身边的高品质服务。

检测平台 —
Luminex® 液相芯片分析仪介绍

1. 灵活地高通量高速检测，药物筛选和验证的高效平台

FLEXMAP-3D® 超群的识别能力，提供500重检测的灵活搭配，配合高速的96/384孔板的自动化进样系统，实现了每小时85,000个数据点检测。为新药的筛选、药效验证及药物毒性的测试提供快速、高效的检测平台。

2. 符合FDA510（K）标准的疾病检测平台

Luminex 200™ 被誉为真正的临床型生物芯片。Luminex200™ 的操作平台支持100重反应；96孔板自动化检测实现了大量样本的检测，可实现每小时9,600个结果检测。独有的xPONENT操作软件系统通过FDA 21CFR认证，提供真实可靠性的数据。

3. 生物标志物验证平台，终结ELISA技术时代

MAGPIX®以最先进的光学激光技术作为仪器检测的光源，在确保仪器检测能力的同时，大大延长了光学系统使用寿命。紧凑式的设计和更友好的操作模式使得MAGPIX®成为个人型的液相芯片，被广泛用于基础科研中。

选择最适合你的一款Luminex液相芯片分析仪

Instrument	FLEXMAP 3D® System	Luminex 100/200™ System	MAGPIX® System
Software	xPONENT® 4.2	xPONENT® 3.1	xPONENT® 4.2
Optic	Lasers/ APDs/ PMTs	Lasers/ APDs/ PMTs	LED/ CCD Camera
Hardware	Flow Cytometry-based	Flow Cytometry-based	Fluorescent Imager
Bead Compatibility	Magnetic and nonmagnetic	Magnetic and nonmagnetic	Magnetic
Multiplex Capacity	500 (80 for MagPlex®)	100 (80 for MagPlex®)	50
Read Time	~20 min/96-well plate	~40 min/96-well plate	~60 min/96-well plate
Applications	Protein/ Nucleic Acid	Protein/ Nucleic Acid	Protein/ Nucleic Acid
Dynamic Range	4.5 logs	3.5 logs	3.5 logs
Microtiter Plate	96-well & 384-well	96-well	96-well
Footprint including PC (linear bench space)	64.8 cm (24")	80.0 cm (32")	64.8 cm (24")
Weight (Analyzer)	77.1 kg (170 lbs)	49 kg (113 lbs)	17.5 kg (38.5 lbs)

Luminex® 液相芯片分析仪配套的校准校验试剂盒和鞘液

Description	Pack Size	Cat. No.
MAGPIX® Drive Fluid	4 pack, 750 mL ea	MPXDF-4PK
Sheath Fluid for Luminex 100/200™ & FLEXMAP 3D® Systems	20 L	SHEATHFLUID
MAGPIX® Calibration Kit	25 uses	40-049
MAGPIX® Performance Verification Kit	25 uses	40-050
Luminex 200™ Calibration Kit (xPONENT®)	25 uses	40-275
Luminex 200™ Performance Verification Kit (xPONENT®)	25 uses	40-276
FLEXMAP 3D® Calibration Kit	25 uses	40-028
FLEXMAP 3D® Performance Verification Kit	25 uses	40-029

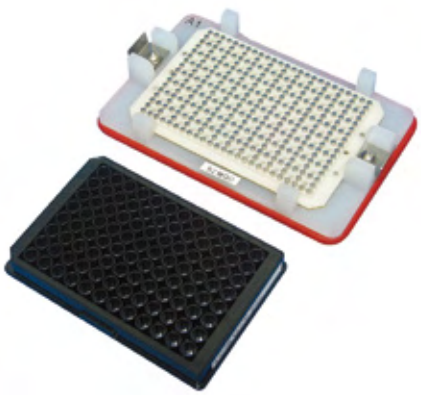
(Cat. No. 40-276)

(Cat. No. MPXDF-4PK)

(Cat. No. 40-049)

手持式磁力架

- 磁力架顶部是白色聚碳酸酯，下面是耐腐蚀的钢板，外面包被聚丙烯材料。
- 可调节的夹片适用于多种微孔板。
- 底座上的O-Ring方便不同大小的手操作时都可以握紧。
- 每个孔周围环绕9个磁铁，提供更强大的磁力，最大程度减少磁珠损失。
- 磁力强度：52 Mega Gauss Oersteds (MGO)



Description	Cat. No.
Handheld Magnetic Separator Block for 96-well Flat Bottom or Conical Well Plates	40-285

软件平台 — Luminex® xPONENT®操作软件和Milliplex™ Analyst数据分析软件

Luminex® xPONENT®操作软件

xPONENT®采用模块化及可视化图形设计，除了可以控制Luminex 200™/FLEXMAP 3D®/ MAGPIX®仪器运行外，同时还可兼容实验室信息管理系统，21CFR Part 11 Compliant及自动化操作系统。为您带来更易于使用的仪器操控体验。配合Merck Millipore强大的数据处理专业软件Milliplex™Analyst，让您获得的海量数据实现快速分析，并生成多种格式的报告。xPONENT®和Milliplex™Analyst的完美结合为您的科研成果带来质和量的飞跃。

xPONENT® 3.1 / xPONENT® 4.0 / xPONENT® 4.2软件，充分发挥Luminex®仪器平台的高通量检测功能

- 模块化设置，一键化完成开机 / 校准 / 校验 / 关机
- 一键导入检测模板，操作简便
- 预设磁珠校准 / 校验程序，与磁珠应用兼容
- 实时在线分析
- 友好直观的操作界面，易于学习和掌握

xPONENT® 软件的功能拓展

- 21 CFR Part 11 认证提供电子签名选择
- 兼容自动化工作站，进一步提升效率
- 兼容LIS/LIMS
- 安全模块升级，提供用户信息安全管理功能

1. 仪器运行与维护：

进入程序主界面后，可直接对仪器进行开、关机维护；调节探针高度、建立检测Protocol以及数据获取。界面友好，操作界面直观。

仪器维护

- CAL试剂盒：
  校正仪器的光学系统包括：微珠分类检测通路，荧光信号检测通路、High PMT/Low PMT 等。
- VER 试剂盒：验证校正结果
  包括：光学系统和液流系统。
- 试剂盒信息CD: 一键输入试剂盒验证信息。
- 自动维护板（Automated maintenance plate, AMP）

2. xPONENT®数据获取：

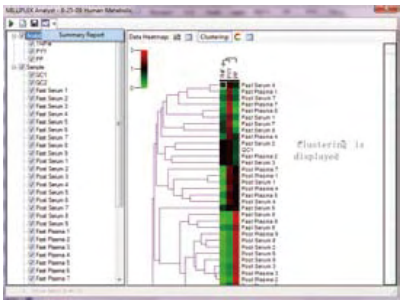
实时监控数据获取情况，显示微珠图谱，并同时显示标准曲线、Median值、CV%和浓度值等。

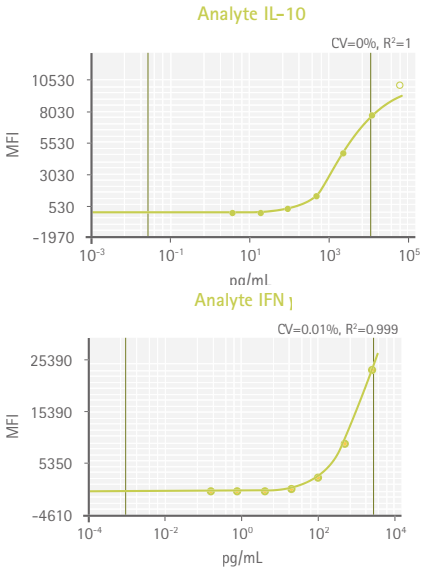
- 兼容聚苯乙烯微珠和磁珠系统
- 分析类型包括：定性、定量和等位基因分析
- 与第三方分析软件兼容
- 在线实时分析
- 灵活的读板设置方式
- 一键输入模板，避免误差。

Milliplex™ Analyst数据分析软件与xPONENT软件组成完美的多重检测分析方案

我们提供最优的软件组合:最强的MULTIPLEX 数据分析软件——MILLIPLEX™ Analyst 5.1搭配Luminex® xPONENT®数据采集软件。MILLIPLEX® Analyst 5.1软件能够更快速高效地管理、追踪和分析多重检测的海量数据,使您的研究工作事半功倍。

Luminex®所有的硬件系统,包括MAGPIX®, Luminex 200™和FLEXMAP 3D® ,在数据采集和分析过程中能够做到无缝衔接。MILLIPLEX™ Analyst 5.1提供多种License选择方案,方便大中小型实验室的使用。利用该软件你能够轻松的获得满足多种格式要求的数据报表。





标准品

Location	Expected pg/mL(i)	MFI(i)	pg/mL(i)	MFI	pg/mL	CV	Recovery
1C1	0.13	45	0.09	46.5	0.13	4.56%	100.37%
1D1		48	0.17				
1E1	0.64	66	0.68	64.5	0.63	3.29%	99.08%
1F1		63	0.59				
1G1	3.2	164	3.48	153.25	3.17	9.92%	99.12%
1H1		142.5	2.86				
1A2	16	592	16.17	610.75	16.74	4.34%	104.6%
1B2		629.5	17.3				
1C2	80	2456	76.33	2578	80.51	6.67%	100.64%
1D2		2699	84.73				
1E2	400	9938	411.35	9154	367.15	12.11%	91.79%
1F2		8370	325.53				
1G2	2000	23685	2131	23298	2031	2.35%	101.53%
1H2		22912	1936				

样品

Location	Sample	MFI(i)	pg/mL(i)	MFI	pg/mL	CV
1A3	QC1	1630	48.75	1599	47.72	2.81%
1B3		1567	46.69			
1C3	QC2	8054	309.44	8581	336.49	8.69%
1D3		9108	364.64			

应用平台

提供超过8个种属1200种生物标志物的选择，涵盖肿瘤、免疫疾病、心血管疾病、代谢疾病、神经退行性疾病等、肾毒性、干细胞、信号转导研究等十几个热门研究领域。

Immunology

Human Cytokine / Chemokine Panel I

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

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 ♦
IFN α2 ♦	MCP-3/CCL7
IFN γ♦	MDC/CCL22
IL-1 α♦	MIP-1 α/CCL3 ♦
IL-1 β♦	MIP-1 β/CCL4 ♦
IL-1Ra ♦	PDGF-AA Δ
IL-2 ♦	PDGF-AB/BB Δ
IL-3 ♦	RANTES/CCL5 ♦ Δ
IL-4 ♦	TGF α
IL-5 ♦	TNF α♦
IL-6 ♦	TNF β /Lymphotoxin α (LTA) ♦
IL-7 ♦	VEGF-A ♦
IL-8/CXCL8 ♦	

Human Cytokine / Chemokine Panel II

(Cat. No. HCYP2MAG-62K)
(Cat. No. HCP2MAG-62K-PX23) 23
(Bulk Cat. No. HCP2MAG62KPX23BK) 23

6Ckine/CCL21/ Exodus-2	I-309/CCL1
BCA-1/CXCL13	LIF
CTACK/CCL27	MCP-2/CCL8
ENA-78/CXCL5	MCP-4/CCL13
Eotaxin-2/CCL24/ MPIF-2	MIP-1 δ/MIP-5/CCL15
Eotaxin-3/CCL26	SCF
IL-16	SDF-1/CXCL12
IL-20	TARC/CCL17
IL-21	TPO
IL-23	TRAIL/TNFSF10
IL-28A/IFN λ2	TSLP
IL-33/NF-HEV (mature)	

Human Cytokine / Chemokine Panel III

(Cat. No. HCYP3MAG-63K)

HCC-1/CCL14 Δ	M-CSF
IL-11	MIG/CXCL9
IL-29/IFN λ1	MIP-3 α/CCL20
I-TAC/CXCL11	MIP-3 β/CCL19
LIX/CXCL6/GCP-2	NAP-2/CXCL7 Δ
Lymphotactin/XCL1	

Human Cytokine/Chemokine Panel IV NEW!

(Cat. No. HCYP4MAG-64K)
(Cat. No. HCY4MG-64K-PX21) 21
(Cat. No. HCP4MG64KPX21BK) 21

APRIL/TNFSF13	IL-19
IL-14/ α-Taxilin	IL-24
BAFF/Blys	IL-28B/IFN λ3
BRAK/CXCL14	IL-32 α
CXCL16	IL-34
CCL28	IL-35
HCC-4/CCL16	IL-36/IL-1F8
HMGB1 ⌂	IL-37/IL-1F7
MPIF/CCL23	IL-38/IL-1F10
IFN β	YKL40/1CHI3L1
MIP-4/PARC/CCL18	

Human High Sensitivity T Cell

(Cat. No. HSTCMAG-28SK)
(Cat. No. HSTCMAG28SPMX13) ♦ 13
(Bulk Cat. No. HSTCMAG28PMX13BK) ♦ 13
(Cat. No. HSTCMAG28SPMX21) 21
(Bulk Cat. No. HSTCMAG28PMX21BK) 21

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

Human Soluble Cytokine Receptor

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

sCD30	sRAGE
sEGFR	sTNF RI
sgp130	sTNF RII
sIL-1RI	sVEGFR1/sFlt-1
sIL-1RII	sVEGFR2/sKDR/sFlk-1
sIL-2R α	sVEGFR3/sFlt-4
sIL-4R	
sIL-6R	

Human Th17

(Cat. No. HTH17MAG-14K)
(Cat. No. HT17MG-14K-PX25) 25
(Bulk Cat. No. HT17MAG14PMX25BK) 25

GM-CSF	IL-17E/IL-25
IFN γ	IL-17F
IL-1 β	IL-21
IL-2	IL-22
IL-4	IL-23
IL-5	IL-27
IL-6	IL-28A/IFN λ2
IL-9	IL-31
IL-10	IL-33/NF-HEV (mature)
IL-12 (p70)	MIP-3 α/CCL20
IL-13	TNF α
IL-15	TN β /Lymphotoxin α (LTA)
IL-17A/CTLA8	

Human CD8+ T Cell

(Cat. No. HCD8MAG-15K)
(Cat. No. HCD8MAG15K17PMX) 17
(Bulk Cat. No. HCD8MAG15K17PXBK) 17

sCD137/4-1BB/TNFRSF9	IL-5
sFas	IL-6
sFasL/TNFRSF6	IL-10
GM-CSF	IL-13
Granzyme A	MIP-1 α/CCL3
Granzyme B	MIP-1 β/CCL4
IFN γ	Perforin
IL-2	TNF α
IL-4	

Metabolism / Endocrinology, continued

Human IGF
(Cat. No. HIGFMAG-52K)

IGF-1	IGF-2

Human Pituitary Panel 1
(Cat. No. HPTP1MAG-66K)

ACTH	FSH
Agouti-Related Protein (AgRP)	GH
CNTF	LH
	TSH

Human Pituitary Panel 2
(Cat. No. HPTP2MAG-66K)

BDNF	Prolactin

Cardiovascular

Human CVD Panel 1
(Cat. No. HCVD1MAG-67K)

BNP	FABP4
NT proBNP	LIGHT
CK-MB	Oncostatin (OSM)
LIX/CXCL6/GCP-2	Placental Growth Factor (PLGF)
CXCL16	Troponin I (TnI)
Endocan (ESM-1)	
FABP3	

Human CVD Panel 2
(Cat. No. HCVD2MAG-67K)

ADAMTS13	Myeloperoxidase (MPO)
GDF-15	Myoglobin
D-dimer	Serum Amyloid A
sICAM-1	sP-Selectin
NGAL/Lipocalin-2	sVCAM-1

Human CVD Panel 3 (Acute Phase)
(Cat. No. HCVD3MAG-67K)

α-2-Macroglobulin	Haptoglobin
Adipsin/Factor D	sL-Selectin
α1-Acid Glycoprotein (AGP)	Platelet Factor 4 (PF4)
CRP	Serum Amyloid P
Fetuin A	von Willebrand Factor (vWF)
Fibrinogen	

Human CVD Panel 4
(Cat. No. HCVD4MAG-67K)

sE-Selectin	Pentraxin-3 (PTX3)
Follistatin (FST)	Tissue Factor (TF)
dPAPP-A	Thrombomodulin
sCD31/sPECAM-1	Troponin T (TnT)

Human Apolipoproteins
(Cat. No. APOMAG-62K)

Apo AI	Apo CII
Apo AII	Apo CIII
Apo B	Apo E

Bone

Human Bone
(Cat. No. HBNMAG-51K)

ACTH	Osteocalcin (OC)
DKK1	Osteopontin (OPN)
FGF-23	Osteoprotegerin (OPG)
IL-1β	PTH
IL-6	Sclerostin (SOST)
Insulin	TNFα
Leptin	

Human RANKL - Single Plex
(Cat. No. HRNKLMAG-51K-01)

RANKL

Cancer Biomarkers

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	PSA (total)†
sFasL/TNFRSF6	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
Complement Factor H (CFH)
Extracellular Matrix Protein 1 (ECM1)
Vitamin D Binding Protein
Vitronectin

Human Circulating Cancer Biomarker Panel 3
(Cat. No. HCCBP3MAG-58K)

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

Human Circulating Cancer Biomarker Panel 4 NEW!
(Cat. No. HCCB4MAG-58K)

ALDH1A1
Carbonic Anhydrase 9 (CA9)
CD44
EpCAM
Hepsin
Kallikrein-6
Mesothelin
Midkine
NCAML1/L1CAM/CD171
Transglutaminase 2 (TGM2)

Human Cancer / Metastasis Biomarker Panel 1
(Cat. No. HCMBMAG-22K)

DKK1	Periostin
GDF15	TRAP
Neuron-specific enolase (NSE)	TWEAK
Osteonectin (SPARC)	YKL40/1CHI3L1
Osteoprotegerin (OPG)	

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	

Immunology

Non-Human Primate Cytokine / Chemokine Panel 1

(Cat. No. PRCYTOMAG-40K)
(Cat. No. PCYTMG-40K-PX23) 23
(Bulk Cat. No. PRCYMAG40PMX23BK) 23

sCD40L	IL-12/23 (p40)
G-CSF	IL-13
GM-CSF	IL-15
IFN γ	IL-17A/CTLA8
IL-1 β	IL-18
IL-1Ra	MCP-1/CCL2
IL-2	MIP-1 α/CCL3
IL-4	MIP-1 βCCL4
IL-5	TGF α
IL-6	TNF α
IL-8/CXCL8	VEGF-A
IL-10	

Non-Human Primate Cytokine / Chemokine Panel 2

(Cat. No. PRCYT2MAG40K)
(Cat. No. PRCYTMAG40K-PX24) 24
(Bulk Cat. No. PRCY2MG40PMX24BK) 24
(Cat. No. PRCYTMAG40K-PX25) 25
(Bulk Cat. No. PRCY2MG40PMX25BK 25

sCD137/4-1BB/TNFRSF9	IL-117E/IL-25
Eotaxin/CCL11	IL-21
sFasL/TNFRSF6	IL-22
FGF-2/FGF-basic	IL-23
Fractalkine/CX3CL1	IL-28A/IFN λ2
Granzyme A	IL-31
Granzyme B	IL-33/NF-HEV (mature)
IL-1 α	IP-10/CXCL10
IL-2	MIP-3 α/CCL20
IL-4	Perforin
IL-6	RANTES/CCL5 Δ
IL-16	TNF β /Lymphotoxin α (LTA)
IL-17A/CTLA8	

Metabolism

Non-Human Primate Metabolic Hormone

(Cat. No. NHPMHMAG-45K)

Amylin (active)	Insulin
C-Peptide	Leptin
Ghrelin (active) %	MCP-1/CCL2
GIP (total)	Pancreatic Polypeptide (PP)
GLP-1 (active)	PYY (total)
Glucagon	TNF α
IL-6	

Non-Human Primate Pituitary Panel 1

(Cat. No. NHPPT1MG-46K)

ACTH	GH
Agouti-Related Protein (AgRP)	LH
CNTF	TSH
FSH	

Non-Human Primate Pituitary Panel 2

(Cat. No. NHPPT2MG-46K)

BDNF	Prolactin

Immunology

Mouse Cytokine / Chemokine Panel I

(Cat. No. MCYTOMAG-70K)
(Cat. No. MCYTOMAG-70K-PMX) ♦ 25
(Bulk Cat. No. MCYTMAG70PMX25BK) ♦ 25
(Cat. No. MCYTMAG-70K-PX32) 32
(Bulk Cat. No. MCYTMAG70PMX32BK) 32

Eotaxin/CCL11	IL-13 ♦
G-CSF ♦	IL-15 ♦
GM-CSF ♦	IL-17A/CTLA8 ♦
IFN γ♦	IP-10/CXCL10 ♦
IL-1 α♦	KC/GRO α/CXCL1 ♦
IL-1 β♦	LIF
IL-2 ♦	LIX
IL-3	MCP-1/CCL2 ♦
IL-4 ♦	M-CSF
IL-5 ♦	MIG/CXCL9
IL-6 ♦	MIP-1 α/CCL3 ♦
IL-7 ♦	MIP-1 βCCL4 ♦
IL-9 ♦	MIP-2/CXCL2 ♦
IL-10 ♦	RANTES/CCL5 ♦
IL-12 (p40) ♦	TNF α♦
IL-12 (p70) ♦	VEGF-A

Mouse Cytokine / Chemokine Panel 2

(Cat. No. MECY2MAG-73K)
(Cat. No. MECY2MAG-73KPX) 15
(Bulk Cat. No. MECY2MAG73KPXBK) 15

Erythropoietin (EPO)	IL-17A/F
Exodus-2/CCL21/6Ckine	IL-20
Fractalkine/CX3CL1	MCDC/CCL22
IFN β	MCP-5/CCL12
IFN γ	MIP-3 α/CCL20
IL-11	MIP-3 βCCL19
IL-16	TARC/CCL17
	TIMP-1

Mouse Soluble Cytokine Receptor

(Cat. No. MSCRMAG-42K)

sCD30	sRAGE
sgp130	sTNF RI
sIL-1RI	sTNF RII
sIL-1RII	sVEGFR1/sFlt-1
sIL-2R α	sVEGFR2/sKDR/sFlk-1
sIL-4R	sVEGFR3/sFlt-4
sIL-6R	

Immunology, continued

Mouse Th17
(Cat. No. MTH17MAG-47K)
(Cat. No. MT17MAG47K-PX25) 25
(Bulk Cat. No. MT17MAG47PMX25BK) 25

sCD40L	IL-17E/IL-25
GM-CSF	IL-17F
IFN γ	IL-21
IL-1 β	IL-22
IL-2	IL-23
IL-4	IL-27
IL-5	IL-28B/IFN λ3
IL-6	IL-31
IL-10	IL-33/NF-HEV (mature)
IL-12 (p70)	MIP-3 α/CCL20
IL-13	TNF α
IL-15	TNF β /Lymphotoxin α (LTA)
IL-17A/CTLA8	

Mouse CD8+ T Cell
(Cat. No. MCD8MAG-48K)
(Cat. No. MCD8MAG48K-PX15) 15
(Bulk Cat. No. MCD8MAG48KPX15BK) 15

sCD137/4-1BB/TNFRSF9	IL-5
sFas	IL-6
sFasL/TNFRSF6	IL-10
GM-CSF	IL-13
Granzyme B	MIP-1 βCCL4
IFN γ	RANTES/CCL5
IL-2	TNF α
IL-4	

Mouse MMP Panel 1
Serum/Plasma samples
(Cat. No. MMMP1MAG-79K)

MMP-2	MMP-8
MMP-3	

Mouse MMP Panel 2
Serum/Plasma samples
(Cat. No. MMMP2MAG-79K)

proMMP-9	MMP-12

Mouse MMP Panel 3
Cell culture samples
(Cat. No. MMMP3MAG-79K)

MMP-2	proMMP-9
MMP-3	MMP-12
MMP-8	

Mouse Immunoglobulin Isotyping
(Cat. No. MGAMMAG-300K)

IgA	IgG2b
IgG1	IgG3
IgG2a	IgM

Mouse IgE - Single Plex
(Cat. No. MGAMMAG-300E)

IgE

Metabolism / Endocrinology

Mouse Adipokine
Serum/Plasma samples
(Cat. No. MADKMAG-71K)

IL-6	PAI-1 (total)
Insulin	Resistin
Leptin	TNF α
MCP-1/CCL2	

Mouse Adipocyte
Cell culture samples
(Cat. No. MADCYMAG-72K)

Adiponectin	PAI-1 (total)
IL-6	Resistin
Leptin	TNF α
MCP-1/CCL2	

Mouse Adiponectin - Single Plex
Serum/Plasma samples
(Cat. No. MADPNMAG-70K-01)

Adiponectin

Mouse Metabolic Hormone
(Cat. No. MMHMAG-44K)

Amylin (active)	Leptin
C-Peptide 2	MCP-1/CCL2
Ghrelin (active) %	Pancreatic Polypeptide (PP)
GIP (total)	PYY (total)
GLP-1 (active)	Resistin
Glucagon	TNF α
IL-6	
Insulin	

Mouse IGF Binding Protein
(Cat. No. MIGFBPMAG-43K)

IGFBP1	IGFBP5
IGFBP2	IGFBP6
IGFBP3	IGFBP7

Mouse Pituitary
(Cat. No. MPTMAG-49K)

ACTH	LH
BDNF	Prolactin
FSH	TSH
GH	

Cardiovascular

Mouse CVD1
(Cat. No. MCVD1MAG-77K)

sCD31/sPECAM-1	PAI-1 (total)
sE-Selectin	sP-Selectin
sICAM	Thombomodulin
proMMP-9	

Mouse CVD2
(Cat. No. MCVD2MAG-77K)

sCD40L	Oncostatin-M
CXCL16	Placental Growth Factor (PLGF-2)
Endocan-1	Troponin I (TnI)
Follistatin (FST)	Troponin T (TnT)
LIGHT	

Mouse Acute Phase Panel 1
(Cat. No. MAP1MAG-76K)

NGAL/Lipocalin-2	Serum Amyloid A-3 (SAA-3)
Pentraxin-3 (PTX3)	

Mouse Acute Phase Panel 2
(Cat. No. MAP2MAG-76K)

Adipsin/Factor D	CRP
α-1-Acid Glycoprotein (AGP)	Haptoglobin
α-2-Macroglobulin	Serum Amyloid P

Bone Metabolism

Mouse Bone
(Cat. No. MBNMAG-41K)

ACTH	Osteocalcin (OC) Δ
DKK-1	Osteoprotegerin (OPG)
FGF-23	Sclerostin (SOST)
IL-6	TNF α
Insulin	
Leptin	

Mouse RANKL - Single Plex
(Cat. No. MRNKLMAG-41K-01)

RANKL

Cancer Biomarkers

Mouse Angiogenesis / Growth Factor Panel 1
(Cat. No. MAGPMAG-24K)

sALK-1	IL-6
Amphiregulin	IL-17A/CTLA8
Angiopoietin-2 Δ	KC/CXCL1
Betacellulin Δ	Leptin
sCD31/sPECAM-1 Δ	MCP-1/CCL2
EGF	MIP-1α/CCL3
Endoglin	Placental Growth Factor (PLGF-2)
Endothelin-1	Prolactin
sFasL/TNFRSF6	SDF-1/CXCL12
FGF-2/FGF-basic	TNFα
Follistatin (FST)	VEGF-A
G-CSF	VEGF-C
HGF	VEGF-D
IL-1β	

Neuroscience

Mouse Neuropeptide
(Cat. No. RMNPMAG-83K) n

α-MSH	Orexin A
β-Endorphin	Oxytocin
Neurotensin	Substance P

Toxicity

Mouse Kidney Injury Panel 1
(Cat. No. MKI1MAG-94K)

β-2-Microglobulin	Renin
IP-10/CXCL10	TIMP-1
KIM-1	VEGF-A

Mouse Kidney Injury Panel 2
(Cat. No. MKI2MAG-94K)

Clusterin	NGAL/Lipocalin-2
Cystatin C	Osteopontin (OPN)
EGF	

Immunology

Rat Cytokine / Chemokine
(Cat. No. RECYTMAG-65K)
(Cat. No. RECYMAG65K27PMX) 27
(Bulk Cat. No. RECYMAG65PMX27BK) 27

EGF	IL-10
Eotaxin/CCL11	IL-12 (p70)
Fractalkine /CX3CL1	IL-13
G-CSF	IL-17A/CTLA8
GM-CSF	IL-18
GROα/KC/CINC-1 /CXCL1	IP-10/CXCL10
IFNγ	Leptin
IL-1α	LIX
IL-1β	MCP-1/CCL2
IL-2	MIP-1α/CCL3
IL-4	MIP-2/CCL8
IL-5	RANTES/CCL5
IL-6	TNFα
	VEGF-A

Rat Immunoglobulin Isotyping
(Cat. No. RGAMMAG-302K)

IgA	IgG2b
IgG1	IgG2c
IgG2a	IgM

Rat IgE - Single Plex
(Cat. No. RGAMMAG-302E)

IgE

Metabolism / Endocrinology

Rat Adipokine
Serum/Plasma samples
(Cat. No. RADPKMAG-80K)

IL-1β	MCP-1/CCL2
IL-6	PAI-1 (total)
Insulin	TNFα
Leptin	

Rat Adipocyte
Cell culture samples
(Cat. No. RADPCMAG-82K)

Adiponectin	Leptin
IL-1β	PAI-1 (total)
IL-6	TNFα

Rat Adiponectin - Single Plex
Serum/Plasma samples
(Cat. No. RADPNMAG-81K-01)

Adiponectin

Rat Metabolic Hormone
(Cat. No. RMHMAG-84K)

Amylin (active)	Insulin
C-Peptide 2	Leptin
Ghrelin (active) %	MCP-1/CCL2
GIP (total)	Pancreatic Polypeptide (PP)
GLP-1 (active)	PYY (total)
Glucagon	TNFα
IL-6	

Rat Pituitary
(Cat. No. RPTMAG-86K)

ACTH	LH
BDNF	Prolactin
FSH	TSH
GH	

Rat Stress Hormone
(Cat. No. RSHMAG-69K)

ACTH	Melatonin
Corticosterone	

Rat Thyroid
(Cat. No. RTHYMAG-30K)

T3	TSH
T4	

Cardiovascular

Rat Cardiac Injury Panel 1
(Cat. No. RCI1MAG-87K)

Cardiac Troponin I (cTnI)	FABP3
Cardiac Troponin T (cTnT)	Follistatin-like Protein 1 (FSTL1)
Creatine Kinase Muscle (CKM)	Myosin Light Chain 3 (MYL3)
	TIMP-1

Rat Vascular Injury Panel 1
Serum/Plasma samples
(Cat. No. RV1MAG-26K)

Caveolin-1	PAI-1 (total)
GROα/KC/CINC-1 /CXCL1	TIMP-1
Connective Tissue Growth Factor (CTGF)	TNFα
IL-6	VEGF-A
MCP-1/CCL2	

Rat Vascular Injury Panel 2
Serum/Plasma samples
(Cat. No. RV2MAG-26K)

Adiponectin	von Willebrand Factor (vWF)
sE-Selectin	
sICAM-1	

Cardiovascular, (continued)

Rat Vascular Injury Panel 3
Serum/Plasma samples
(Cat. No. RV3MAG-26K)

α-1-Acid Glycoprotein (AGP)	Fibrinogen Δ
α-2-Macroglobulin (A2M)	Haptoglobin

Bone Metabolism

Rat Bone Panel 1
Serum/Plasma samples
(Cat. No. RBN1MAG-31K)

ACTH	Osteocalcin (OC)
DKK1	Osteoprotegerin (OPG)
FGF-23	PTH
Insulin	Sclerostin (SOST)
Leptin	

Rat Bone Panel 2
Cell culture samples
(Cat. No. RBN2MAG-31K)

ACTH	Osteopontin (OPN)
DKK-1	Osteoprotegerin (OPG)
FGF-23	PTH
Insulin	Sclerostin (SOST)
Leptin	
Osteocalcin (OC)	

Rat RANKL - Single Plex
(Cat. No. RRNKLMAG-31K-01)

RANKL

Neuroscience

Rat Neuropeptide
(Cat. No. RMNPMAG-83K) n

α-MSH	Orexin A
β-Endorphin	Oxytocin
Neurotensin	Substance P

Toxicity

Rat Kidney Toxicity Panel 1
Urine samples
(Cat. No. RKTX1MAG-37K)

Calbindin	KIM-1
Clusterin	Osteopontin (OPN)
GST α	TIMP-1
IP-10/CXCL10	VEGF-A

Rat Kidney Toxicity Panel 2
Urine samples
(Cat. No. RKTX2MAG-37K)

α-1-Acid Glycoprotein (AGP)	Cystatin C
Albumin	EGF
β-2-Microglobulin	NGAL/Lipocalin-2

Rat Liver Injury
(Cat. No. RLI1MAG-92K)

ARG1	5'NT/CD73
GOT1	SDH
GST α	

Immunology

Canine Cytokine / Chemokine
(Cat. No. CCYTOMAG-90K)
(Cat. No. CCYTMG-90K-PX13) 13
(Bulk Cat. No. CCYTMAG90KPX13BK) 13

GM-CSF	IL-15
IFN γ	IL-18
IL-2	IP-10/CXCL10
IL-6	KC-like
IL-7	MCP-1/CCL2
IL-8/CXCL8	TNF α
IL-10	

Metabolism / Endocrinology

Canine Gut Hormone
(Cat. No. CGTMAG-98K)

Amylin (total)	Insulin
Ghrelin (active) %	Leptin
GIP (total)	Pancreatic Polypeptide (PP)
GLP-1 (active)	PYY (total)
Glucagon	

Canine Pituitary
(Cat. No. CPTMAG-96K)

ACTH	LH
BDNF	Prolactin
FSH	TSH
GH	

Toxicity

Canine Kidney Toxicity Expanded Panel 1
Urine samples
(Cat. No. CKT1MAG-97K)

Clusterin	NGAL/Lipocalin-2
Cystatin C	MCP-1/CCL2
KIM-1	Osteopontin (OPN)
IL-8/CXCL8	

Canine Kidney Toxicity Panel 2
Urine samples
(Cat. No. CKT2MAG-97K)

Albumin	RBP4
β-2-Microglobulin	TFF3

Immunology

Feline Cytokine / Chemokine
(Cat. No. FCYTOMAG-20K)
(Cat. No. FCYTMAG-20K-PMX) 19
(Bulk Cat. No. FCYTMAG20KPX19BK) 19

sFas	IL-13
Flt3 Ligand	IL-18
GM-CSF	GRO/KC
IFN γ	MCP-1/CCL2
IL-1 β	PDGF-BB
IL-2	RANTES/CCL5
IL-4	SCF
IL-6	SDF-1/CXCL12
IL-8/CXCL8	TNF α
IL-12 (p40)	

Metabolism / Endocrinology

Feline Metabolic Hormone
(Cat. No. FMHMAG-29K)

Amylin (active)	Insulin
Ghrelin (active) %	Leptin
GIP (total)	Pancreatic Polypeptide (PP)
GLP-1 (active)	PYY (total)
Glucagon	

Immunology

Porcine Cytokine / Chemokine
(Cat. No. PCYTMAG-23K)
(Cat. No. PCYTMG-23K-13PX) 13
(Bulk Cat. No. PCYTMAG23PMX13BK) 13

GM-CSF	IL-6
IFN γ	IL-8/CXCL8
IL-1 α	IL-10
IL-1Ra	IL-12
IL-1 β	IL-18
IL-2	TNF α
IL-4	

Immunology

Equine Cytokine/Chemokine Panel NEW!
(Cat. No. EQCYTMAG-93K)
(Cat. No. EQCYTMG-93KPX23)
(Cat. No. EQCTMG93KPX23BK)

Eotaxin/CCL11	IL-6
FGF-2/FGF-basic	IL-8/CXCL8
Fractalkine/CX3CL1	IL-10
G-CSF	IL-12 (p70)
GM-CSF	IL-13
GRO	IL-17A/CTLA8
IFN γ	IL-18
IL-1 α	IP-10/CXCL10
IL-1 β	MCP-1/CCL22
IL-2	RANTES/CCL5
IL-4	TNF α
IL-5	

Immunology

Multi-species TGF β- Single Plex
(Cat. No. TGFBMAG-64K-01)
(Bulk Cat. No. TGFBMAG-64K-01BK)

TGF β1

Multi-species TGF β- 3 Plex ▼
(Cat. No. TGFBMAG-64K-03)

TGF β1	TGF β3
TGF β2	

Metabolism / Endocrinology

Multi-species Steroid/Thyroid Hormone
(Cat. No. STTHMAG-21K)

Cortisol	T3
Estradiol	T4
Progesterone	

Cellular Metabolism Assays

Human Glycolysis Pathway
(Cat. No. HGPMAG-27K)

Enolase 1 (ENO1)
Glucose-6-Phosphate Isomerase (G7PI)
HIF-1α
Lactate Dehydrogenase A (LDA)
Lactate Dehydrogenase B (LDB)
Pyruvate Kinase Isozyme M2 (PKM2)
Transketolase

Human Oxidative Phosphorylation
(Cat. No. HØXPSMAG-16K) ▼

Complex I (NADH-Ubiquione Oxidoreductase)
Complex II (Succinate Ubiquinone Oxidoreductase)
Complex III (Ubiquione Cytochrome C Oxidoreductase)
Complex IV (Cytochrome C Oxidase)
Complex V (ATP Synthase)
NNT (Nicotinamide Nucleotide Transhydrogenase)

Rat / Mouse Oxidative Phosphorylation
(Cat. No. RMØXPSMAG-17K) ▼

Complex I (NADH-Ubiquinone Oxidoreductase)
Complex III (Ubiquinone Cytochrome C Oxidoreductase)
Complex V (ATP Synthase)

Human Oxidative Stress
(Cat. No. HØXSTMAG-18K) ▼

Catalase
Peroxiredoxin 2 (PRX2/PRDX2)
Superoxide dismutase 1 (SOD1)
Superoxide dismutase 2 (SOD2)
Thioredoxin (TRX1)

Multi-species Pyruvate Dehydrogenase (PDH) Complex
(Cat. No. PDHMAG-13K) ▼

Analyte	Total	Phosphorylated
PDH	3	
PDH		3 (Ser232)
PDH		3 (Ser293)
PDH		3 (Ser300)

Can be plexed with other 2 Plexes
◊ Cannot plex with other phospho Akt
▼ Premix panel only
AB1: Uses Assay Buffer 1
AB2: Uses Assay Buffer 2
● Recommended
● Acceptable
○ Not Recommended
H Human
M Mouse
R Rat

Cell Signaling Phosphoprotein + Total 2 Plex Assays

Akt1 Phospho/Total - 2 Plex
(Coming Soon) AB2 ▼◊

Analyte	Total	Phosphorylated	
Akt1		(Ser473)	H, M, R
Akt1	3		H, M, R

Akt2 Phospho/Total - 2 Plex
(Coming Soon) AB2 ▼◊

Analyte	Total	Phosphorylated	
Akt2		(Ser473)	H, M, R
Akt2	3		H, M, R

Akt3 Phospho/Total - 2 Plex
(Coming Soon) AB2 ▼◊

Analyte	Total	Phosphorylated	
Akt3		(Ser473)	H, M, R
Akt3	3		H, M, R

Akt Phospho/Total – 2 Plex
(Cat. No. 48-618MAG) AB2 ▼◊

Analyte	Total	Phosphorylated	
Akt/PKB		3 (Ser473)	H, M, R
Akt/PKB	3		H, M, R

CREB Phospho/Total – 2 Plex
(Cat. No. 48-628MAG) AB2 ▼

Analyte	Total	Phosphorylated	
CREB		3 (Ser133)	H, M, R
CREB	3		H, M, R

Erk/MAPK 1/2 Phospho/Total – 2 Plex
(Cat. No. 48-619MAG) AB2 ▼

Analyte	Total	Phosphorylated	
Erk/MAPK 1/2		3 (Thr185/Tyr187)	H, M, R
Erk/MAPK 1/2	3		H, M, R

IRS1 Phospho/Total – 2 Plex
(Cat. No. 48-626MAG) AB2 ▼

Analyte	Total	Phosphorylated	
IRS1		3 (Ser636)	H, M
IRS1	3		H, M, R

JNK Phospho/Total – 2 Plex
(Cat. No. 48-622MAG) AB2 ▼

Analyte	Total	Phosphorylated	
JNK/SAPK1		3 (Thr183/Tyr185)	H, M, R
JNK/SAPK1	3		H, M, R

mTOR Phospho/Total – 2 Plex
(Cat. No. 48-625MAG) AB2 ▼

Analyte	Total	Phosphorylated	
mTOR		3 (Ser2448)	H, M, R
mTOR	3		H, M

p38 Phospho/Total – 2 Plex
(Cat. No. 48-624MAG) AB1 or AB2

Analyte	Total	Phosphorylated	
p38/SAPK2A/B		3 (Thr180/Tyr182)	H, M, R
p38/SAPK2A/B	3		H, M, R

STAT3 Phospho/Total – 2 Plex
(Cat. No. 48-623MAG) AB2 ▼

Analyte	Total	Phosphorylated	
STAT3		3 (Tyr705)	H, M, R
STAT3	3		H, M, R

Cell Signaling

Akt / mTOR (Phosphoprotein) – 11 Plex
(Cat. No. 48-611MAG) AB2 ▼

Analyte	Total	Phosphorylated	
Akt/PKB		3 (Ser473)	H, M, R
GSK3 α		3 (Ser21)	H, M, R
GSK3 β		3 (Ser9)	H, M, R
IGF1R		3 (Tyr1135/1136)	H, M
IR		3 (Tyr1162/1163)	H
IRS1		3 (Ser636)	H, R
mTOR		3 (Ser2448)	H, M
p70S6 Kinase		3 (Thr389/412)	H, M, R
PTEN		3 (Ser380)	H, M, R
RPS6		3 (Ser235/236)	H, M, R
TSC2		3 (Ser939)	H, M, R

Akt / mTOR (Total) – 11 Plex
(Cat. No. 48-612MAG) AB2 ▼

Analyte	Total	Phosphorylated	
Akt/PKB	3		H, M, R
GSK3 α	3		H, M, R
GSK3 β	3		H, M, R
IGF1R	3		H, M, R
IR	3		H, R
IRS1	3		H, M, R
mTOR	3		H, M, R
p70S6 Kinase	3		H, M, R
PTEN	3		H, M, R
RPS6	3		H, M, R
TSC2	3		H, M, R

Early Apoptosis – 7 Plex
(Cat. No. 48-669MAG) AB2 ▼

Analyte	Total	Phosphorylated	
Akt/PKB		3 (Ser473)	H, M, R
BAD		3 (Ser112)	H
Bcl-2		3 (Ser70)	H
Active Caspase 8	3		H
Active Caspase 9	3		H
JNK/SAPK1		3 (Thr183/Tyr185)	H, M, R
p53		3 (Ser46)	H

Human Late Apoptosis – 3 Plex
(Cat. No. 48-670MAG) AB1 ▼

Analyte	Total	Phosphorylated	
Active Caspase 3	3		H, M
Cleaved PARP	3		H
GAPDH	3		H

Human DNA Damage / Genotoxicity – 7 Plex
(Cat. No. 48-621MAG) AB1 ▼

Analyte	Total	Phosphorylated	
ATR	3		
Chk1		3 (Ser345)	
Chk2		3 (Thr68)	
H2A.X		3 (Ser139)	
MDM2	3		
p21	3		
p53		3 (Ser15)	

Human Heat Shock Protein – 5 Plex
(Cat. No. 48-615MAG) AB1 ▼

Analyte	Total	Phosphorylated	
HSP27	3		
HSP27		3 (Ser78/Ser82)	
HSP60	3		
HSP70	3		
HSP90 α	3		

MAPK / SAPK (Phosphoprotein) – 10 Plex
(Cat. No. 48-660MAG) AB2 ▼

Analyte	Total	Phosphorylated	
ATF2		3 (Thr71)	H, M
ErK/MAPK 1/2		3 (Thr185/Tyr187)	H, M, R
HSP27		3 (Ser78)	H, M, R
JNK/SAPK1		3 (Thr183/Tyr185)	H, M, R
c-Jun		3 (Ser73)	H
MEK1		3 (Ser222)	H, M, R
MSK1		3 (Ser212)	H, M, R
p38/SAPK2A/B		3 (Thr180/Tyr182)	H
p53		3 (Ser15)	H
STAT1		3 (Tyr701)	H, M

Human Mitogenesis RTK (Phosphoprotein) – 7 Plex
(Cat. No. 48-672MAG) AB1 ▼

Analyte	Total	Phosphorylated
c-Met/HGFR		3 (pan Tyr)
EGFR		3 (pan Tyr)
ErbB2/HER2		3 (pan Tyr)
ErbB3		3 (pan Tyr)
ErbB4		3 (pan Tyr)
IGF1R		3 (pan Tyr)
IR		3 (pan Tyr)

Human Mitogenesis RTK (Total) – 7 Plex

(Cat. No. 48-671MAG) AB1 ▼

Analyte	Total	Phosphorylated
c-Met/HGFR	3	
EGFR	3	
ErbB2/HER2	3	
ErbB3	3	
ErbB4	3	
IGF1R	3	
IR	3	

Multi-Pathway (Phosphoprotein) – 9 Plex

(Cat. No. 48-680MAG) AB2 ▼

Analyte	Total	Phosphorylated	
Akt/PKB		3 (Ser473)	H, M, R
CREB		3 (Ser133)	H, M, R
Erk/MAPK 1/2		3 (Thr185/Tyr187)	H, M, R
NFκB		3 (Ser536)	H
JNK/SAPK1		3 (Thr183/Tyr185)	H, M, R
p38/SAPK2A/B		3 (Thr180/Tyr182)	H, M, R
p70S6 Kinase		3 (Thr389/412)	H, M, R
STAT3		3 (Ser727)	H, M, R
STAT5A/B		3 (Tyr694/699)	H, M, R

Multi-Pathway (Total) – 9 Plex

(Cat. No. 48-681MAG) AB2

Analyte	Total	Phosphorylated	
Akt/PLB	3		H, M, R
CREB	3		H, M, R
Erk/MAPK 1/2	3		H, M, R
NF B	3		H, M, R
JNK/SAPK1	3		H, M, R
p38/SAPK2A/B	3		H, M, R
p70S6 Kinase	3		H, M, R
STAT3	3		H, M, R
STAT5A/B			H, M, R

NFκB – 6 Plex

(Cat. No. 48-630MAG) AB1 ▼

Analyte	Total	Phosphorylated	
c-Myc	3		H
FADD		3 (Ser194)	H
IκBα		3 (Ser32)	H
IKKα/β		3 (Ser177/Ser181)	H
NFκB		3 (Ser536)	H, M
TNFRI	3		H

Src Family Kinase Active Site (Phosphoprotein) – 8 Plex

(Cat. No. 48-650MAG) AB2 ▼

Analyte	Total	Phosphorylated	
Blk		3 (Tyr389)	H, M, R
Fgr		3 (Tyr412)	H, M, R
Fyn		3 (Tyr420)	H, M, R
Hck		3 (Tyr411)	H, M, R
Lck		3 (Tyr394)	H, R
Lyn		3 (Tyr397)	H, R
Src		3 (Tyr419)	H
Yes		3 (Tyr421)	H, M

STAT (Phosphoprotein) – 5 Plex

(Cat. No. 48-610MAG) AB2 ▼

Analyte	Total	Phosphorylated	
STAT1		3 (Tyr701)	H, M
STAT2		3 (Tyr690)	H
STAT3		3 (Tyr705)	H, M, R
STAT5A/B		3 (Tyr694/699)	H, M, R
STAT6		3 (Tyr641)	H

T-Cell Receptor (Phosphoprotein) – 7 Plex

(Cat. No. 48-690MAG) AB2 ▼

Analyte	Total	Phosphorylated	
CD3 ε		3 (pan Tyr)	H
CREB		3 (Ser133)	H, M, R
Erk/MAPK 1/2		3 (Thr185/Tyr187)	H, M, R
LAT		3 (pan Tyr)	H
Lck		3 (pan Tyr)	H, M, R
Syk		3 (pan Tyr)	H
ZAP-70		3 (pan Tyr)	H

TGF β- 6 Plex

(Cat. No. 48-614MAG) AB2 ▼

Analyte	Total	Phosphorylated	
Akt/PKB		3 (Ser473)	H
Erk/MAPK 1/2		3 (Thr185/Tyr187)	H, M, R
SMAD2		3 (Ser465/467)	H, M, R
SMAD3		3 (Ser423/425)	H, M, R
SMAD4	3		H, M, R
TGF βRII	3		H

Cell Signaling, continued

Human RTK (Phosphoprotein)
(Choose Analytes that Meet your Needs)
Coming Soon

Analyte	Total	Phosphorylated
c-Kit		(pan Tyr)
c-Met/HGFR		(pan Tyr)
EGFR		(pan Tyr)
ErbB2/HER2		(pan Tyr)
ErbB3/HER3		(pan Tyr)
ErbB4/HER4		(pan Tyr)
FGFR1		(pan Tyr)
Flt3		(pan Tyr)
IGF1R		(pan Tyr)
IR		(pan Tyr)
MSCFR		(pan Tyr)
PDGFR α		(pan Tyr)
PDGFR β		(pan Tyr)
TIE1		(pan Tyr)
TIE2		(pan Tyr)
VEGFR1/Flt-1		(pan Tyr)
VEGFR2/KDR/Flk-1		(pan Tyr)
VEGFR3/Flt-4		(pan Tyr)

MAPmate™ Phosphoprotein & Total Single Plex Kits

Plex up to 8 individual MAPmate™ assays together using our Cell Signaling Buffer and Detection Kit or include them in existing MILLIPLEX® MAPCell Signaling Panels to enhance the panel or serve as controls within the guidelines provided in the protocols.

Important MAPmate™ rules

Consult the protocol prior to use.

- All magnetic MAPmate™ assays require the Cell Signaling Buffer & Detection Kit **(48-602MAG)**.
  This kit contains all necessary reagents except the MAPmate™ assay. Both a filter and flat bottom plate are included for convenience
- To select the appropriate buffer for your MAPmate™ assays, please refer to the protocols, this publication or the buffer selection tables on the website

The following MAPmate™ assays should not be plexed together:

- MAPmate™ assays that require different assay buffers
- Phospho-specific and total MAPmate™ pairs, e.g. total GSK3 β and phospho-GSK3 β(Ser9)
- Pan Tyr and site-specific MAPmate™ assays, e.g. phospho-EGF Receptor (pan Tyr) and phospho-STAT1 (Tyr701)
- More than 1 phospho-MAPmate™ assay for a single target, e.g. pAkt, pSTAT3
- GAPDH and βTubulin assays cannot be plexed with kits or MAPmate™ assays containing pan Tyr assays

Magnetic Bead MAPmate™ kits	Cat. No.	Species Homology	AB1	AB2
β-Tubulin (Total)	46-713MAG	H,M,R	●	●
GAPDH (Total)	46-667MAG	H	○	●
Akt/PKB (assay buffer 2) (Ser473)	46-677MAG	H,M,R	●	●
Akt/PKB (assay buffer 2) (Total)	46-675MAG	H,M,R	●	●
BAD (Ser112)	46-694MAG	H,M	●	●
Caspase 3 (Active)	46-604MAG	H,M	●	●
c-Jun (Ser73)	46-622MAG	H,M,R	●	●
c-Kit (total)	46-620MAG	H	●	●
c-Met/HGFR (total)	46-650MAG	H	●	●

Cell Signaling, continued

Magnetic Bead MAPmate™ kits	Cat. No.	Species Homology	AB1	AB2
CREB (Ser133)	46-631MAG	H,M,R	●	●
CREB (Total)	46-632MAG	H,M,R	●	●
EGF Receptor (Total)	46-606MAG	H	●	●
ERK/MAPK 1/2 (Thr185/Tyr187)	46-602MAG	H,M,R	○	●
ERK/MAPK 1/2 (Total)	46-609MAG	H,M,R	●	●
GSK3 β(Ser9)	46-690MAG	H,M,R	●	●
GSK3 β(Total)	46-689MAG	H,M,R	●	●
H2A.X (Ser139)	46-692MAG	H,M	●	●
HSP27 (Ser78)	46-607MAG	H	●	●
HSP27 (Total)	46-608MAG	H	●	●
IκBα(Ser32)	46-643MAG	H	●	●
IκBα(Total)	46-644MAG	H	●	●
JNK/SAPK1 (Thr183/Tyr185)	46-613MAG	H,M	●	●
JNK/SAPK1 (Total)	46-618MAG	H,M	○	●
MEK1 (Ser222)	46-670MAG	H,M,R	●	●
MEK1 (Total)	46-669MAG	H,M	●	●
mTOR (Ser2448)	46-686MAG	H,M,R	●	●
mTOR (Total)	46-685MAG	H,M,R	●	●
NFκB (Ser536)	46-702MAG	H	●	●
NFκB (Total)	46-701MAG	H	●	●
p21 (Total)	46-621MAG	H	●	●
p38/SAPK2A/B (Thr180/Tyr182)	46-610MAG	H,M,R	○	●
p38/SAPK2A/B (Total)	46-612MAG	H,M,R	○	●
p53 (Ser15)	46-663MAG	H	●	●
p53 (Total)	46-662MAG	H	●	●
p70S6K (Thr389/412)	46-629MAG	H,M,R	●	●
p70S6K (Total)	46-630MAG	H,M,R	●	●
Cleaved PARP (Total)	46-656MAG	H	●	●
PTEN (Total)	46-678MAG	H,M,R	●	●
RPS6 (Ser235/Ser236)	46-714MAG	H,M,R	●	●
RPS6 (Total)	46-715MAG	H,M,R	●	●
Src (Tyr419)	46-710MAG	H,M,R	●	●
STAT1 (Tyr701)	46-655MAG	H,M	●	●
STAT1 (Total)	46-654MAG	H,M	●	●
STAT3 (Ser727)	46-624MAG	H,M,R	●	●
STAT3 (Tyr705)	46-623MAG	H,M,R	●	●
STAT3 (Total)	46-625MAG	H,M,R	●	●
STAT5A/B (Tyr694/Tyr699)	46-641MAG	H,M,R	●	●

Lysates

Lysate Description	Cat. No.
A431: EGF	47-210
A549: Camptothecin	47-218
Daudi: IL-4	47-217
HEK293: Serum	47-233
HeLa: IFNα	47-226
HeLa: Lambda Phosphatase	47-229
HeLa: TNFα+CalA	47-230
HeLa: Unstim	47-205
HeLa:HS/Ars	47-211
HepG2: DCA	47-232
HepG2: Insulin	47-227
HepG2: TGF β	47-235
HepG2: Unstim (1)	47-231
HepG2: Unstim(2)	47-234

Lysate Description	Cat. No.
HepG2: Unstim(3)	47-239
HL-60: PVD	47-225
HUVEC: Serum	47-238
Jurkat: Anisomycin	47-207
Jurkat: H_2O_2	47-208
Jurkat: Paclitaxel	47-220
Jurkat: Unstim	47-206
MCF7: IGF-1	47-216
MCF-7: Unstim	47-242
NIH3T3: Anisomycin	47-219
NTERA-2: Unstim	47-241
Ramos: PVD	47-224
Rat Heart Lysate	50-100

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- BMS检测服务中心实验室拥有全套的Luminex液相芯片检测系统平台：包括MAGPIX, Luminex 200及最高端的FlexMAP 3D液相芯片检测平台。
- BMS检测服务中心实验室专职技术人员经过严格的认证获得提供服务能力的资质。
- BMS检测服务中心实验室严格按照标准流程操作和管理，保证各环节完善的质量把控和追溯性。
- BMS检测服务中心实验室在收到客户样本和试剂盒并确认之后，在2周内完成检测服务提供结果报告，并跟踪检测服务质量。
- 默克密理博BMS检测服务产品货号：

服务产品货号	检测平台	特点
CNBMSLX200	Luminex 200 仪器检测	高灵敏度和检测动力学范围；常规结果数据形式
CNBMSMAGPIX	MAGPIX 仪器检测	高灵敏度和检测动力学范围；常规结果数据形式
CNBMSFM3D	FlexMap3D 仪器检测	更高的灵敏度和检测动力学范围；更多结果数据形式

MAGPIX® System

Luminex 200™ System

FLEXMAP 3D® System

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- 析服务(Whole-Assay)
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- 务。
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- 片检测服务。
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Milliplex™高通量多因子检测平台在不同研究领域中的应用

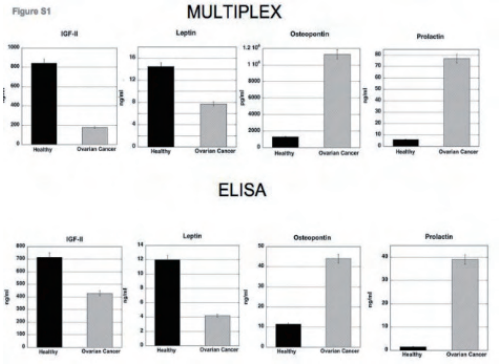
• 肿瘤研究

肿瘤早期诊断

Milliplex多因子检测平台在卵巢癌早期诊断中应用

Diagnostic Markers for Early Detection of Ovarian Cancer

Irene V, Ziding F, Gary L, et al. Diagnostic markers for early detection of ovarian cancer.[J]. Clinical Cancer Research An Official Journal of the American Association for Cancer Research, 2008, 14(4):1065-1072. IF:8.19



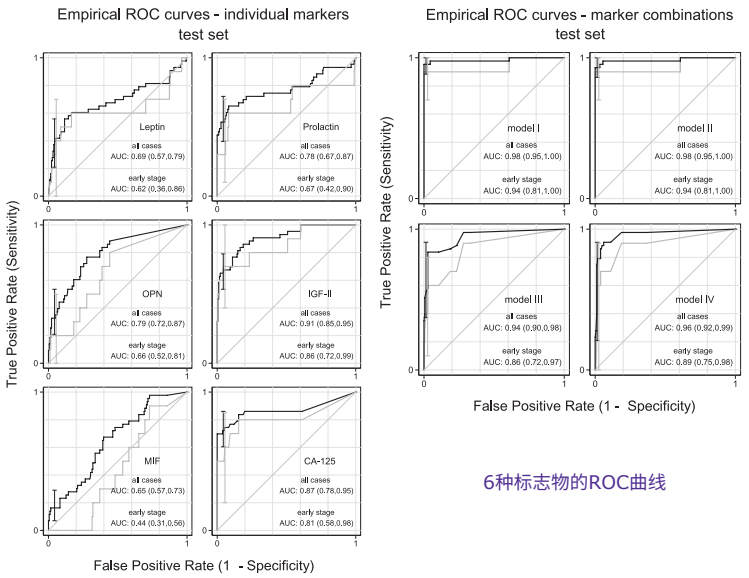
Milliplex 与 ELISA比较，
对于所有标志物的检测呈现很好一致性

研究背景：

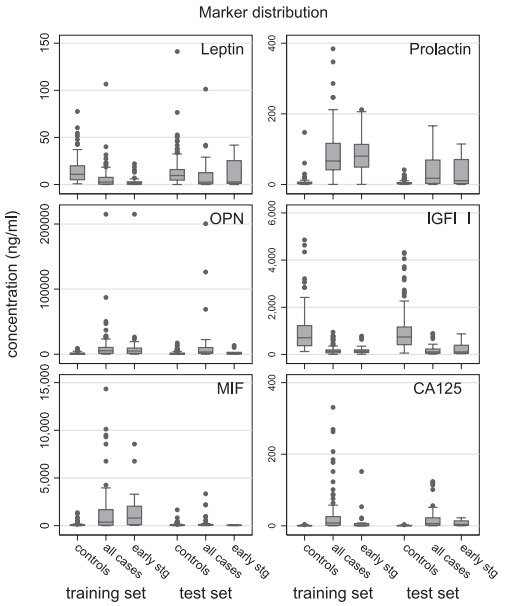
卵巢癌(ovarian cancer)的早期检测能够显著降低疾病的致死率。

实验设计：

362例健康对照和156例确诊卵巢癌样本分为两组（检测组和验证组），使用Milliplex技术检测血清样本中6种蛋白因子leptin, prolactin, MIF, osteopontin, IGF-II和CA-125表达水平。



6种标志物的ROC曲线



6种血清标志物的表达水平

结果和意义：

1:非侵入性方法（血清）对肿瘤进行早期诊断。

2:多种因子联合检测提高了检测特异性。

3:Milliplex和ELISA 在不同因子的检测上数据具有很高一致性，反应出相同的趋势。

4:6种标志物联合检测的诊断价值（灵敏度95.3%，特异性 99.4%）显著高于CA-125（灵敏度72%，特异性95%）检测效果。

小M有话说

Milliplex高通量蛋白因子检测平台具有高效筛选卵巢癌高危（high risk）人群的潜力，能够有效用于疾病诊断标志物的筛选，符合当前转化医学的需求。Milliplex技术在转化医学研究中具有如下3种独特优势和价值：

1、在一次操作中可以检测80例样本，每例样本仅需25-50ul便可同时进行超过40种标志物的筛选，有效的节约样本（尤其对神经科学中脑脊液样本，或眼科学中的泪液样本等），同时也能够显著提高筛选效率；

2、使用血清样本而非获取病人病理性的活检组织相对来说对病人是无创伤的方法，能够显著降低病人在检测中的痛苦。

3、肿瘤高危病人的早期诊断能够显著降低肿瘤带来的致死率，实现对疾病的极早治疗，有效提高病人的生活质量，延长病人的生命。因此，Milliplex技术具有很高的临床应用价值，能够将基础研究获得的生物标志物快速实现向临床医学的转化，是当前转化医学重要的研究方向之一。研究也显示，Milliplex高通量蛋白检测技术和传统ELISA方法在检测结果中具有高度一致性，也保证了该技术在临床检测中的准确性和可靠性。

肿瘤风险评估

肺癌炎症标志物和预后风险评估及与吸烟的相关性

Circulating inflammation Markers and Prospective risk for lung cancer

Shiels, M. S., et al. (2013). "Circulating inflammation markers and prospective risk for lung cancer." J Natl Cancer Inst 105(24): 1871-1880.

研究背景：

虽然有大量关于肺癌炎症因子病原学的报道，但是很少有用流行病学系统的结合肺癌病人血清炎症因子的研究。

实验设计：

Milliplex多因子分析平台检测526例肺癌样本和592例对照样本血清中77种炎症标志物表达水平，使用Conditional logistic回归和weighted Cox模型评估优势比（odds ratios，ORs）和累积风险分析。

基于4种独立的炎症因子评估非吸烟人群，
曾经吸烟史人群和当前吸烟人群肺癌的10年累积发病风险

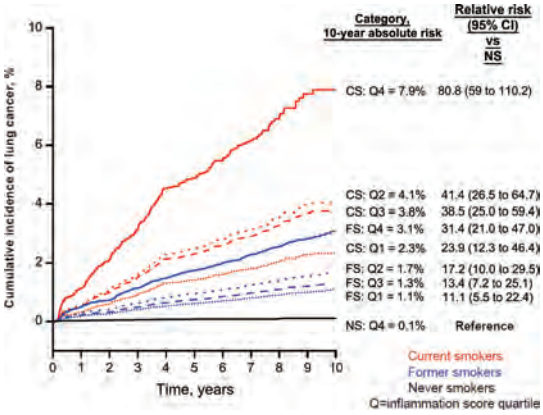


Table1. Characteristics of lung cancer case patients and control subjects

Characteristic	Control subjects (n=592)	Lung cancer case patients (n=526)	P*
Age at randomization, years			—†
<59	104 (17.6)	96 (18.3)	
60–64	167 (28.2)	146 (27.8)	
65–69	192 (32.4)	177 (33.7)	
≥70	129 (21.8)	107 (20.3)	
Sex			—†
Female	212 (35.8)	168 (31.9)	
Male	380 (64.2)	358 (68.1)	
Smoking status			—†
Never	99 (16.7)	33 (6.3)	
Former	294 (49.7)	294 (55.9)	
Current	199 (33.6)	199 (37.8)	
Pack-years smoked			—†
Never smokers	99 (16.7)	33 (6.3)	
<30	124 (21.0)	125 (23.8)	
30–40	128 (21.6)	128 (24.3)	
40–50	42 (7.1)	41 (7.8)	
≥50	199 (33.6)	199 (37.8)	
Years since quitting smoking			—†
Not applicable	298 (50.3)	232 (44.1)	
<15	187 (31.6)	187 (35.6)	
≥15	107 (18.1)	107 (20.3)	
Race			.11
White	538 (90.9)	467 (88.8)	
Black	28 (4.7)	40 (7.6)	
Other	26 (4.4)	19 (3.6)	
Education			.02
≤12 years/completed high school	199 (33.6)	211 (40.1)	
>12 years	393 (66.4)	315 (59.9)	
Body mass index, kg/m²			.53
<25	198 (33.5)	195 (37.1)	
25–29.9	270 (45.6)	224 (42.6)	
≥30	114 (19.3)	101 (19.2)	
Missing	10 (1.7)	6 (1.1)	
History of emphysema or chronic bronchitis			<.0001
No	532 (89.9)	428 (81.4)	
Yes	60 (10.1)	98 (18.6)	
History of coronary heart disease or heart attack			.14
No	519 (87.7)	445 (84.6)	
Yes	73 (12.3)	81 (15.4)	
Family history of lung cancer			<.0001
No	508 (85.8)	398 (75.7)	
Yes	77 (13.0)	123 (23.4)	
Missing	7 (1.2)	5 (1.0)	
Regularly uses aspirin/ibuprofen			.66
No	218 (36.8)	187 (35.6)	
Yes	374 (63.2)	339 (64.5)	

肺癌样本和对照样本基本信息

结果与意义：

1：11种标志物（CRP，SAA, sTNFRII], IL-1RA, IL-7, TGF-A, ENA 78/CXCL5, MIG/CXCL9, BCA-1/CXCL13, TARC/CCL17, MDC/CCL22）与肺癌发病风险显著相关；

2：建立风险分析模型，使用4种因子（CRP, BCA-1/CXCL13, MDC/CCL22和IL-1RA）能够有效区分曾经具有吸烟史的人群与当前正在吸烟人群对于肺癌的10年累积发病风险。

小M有话说

针对当前存在致病机制、发病症状复杂多样的情况，单个指标无法对疾病进行特异准确的预测评估的现状。使用多种指标对于肿瘤综合分析更易发现与肿瘤的密切关系，对疾病评估也更加准确客观。因此使用Milliplex技术对多个指标联合分析也能够进一步提高肿瘤的检测效率，并有效区分不同人群的肿瘤发病风险，符合当前精准医学希望能够对疾病或病人进一步分期、分级、分类或分型的要求，从而建立个体化的用药方案和治疗指南。

肿瘤分期评估

宫颈鳞癌患者血清蛋白谱的改变与肿瘤分期的相关性

Twelve Serum Proteins Progressively Increase With Disease Stage in Squamous Cell Cervical Cancer Patients

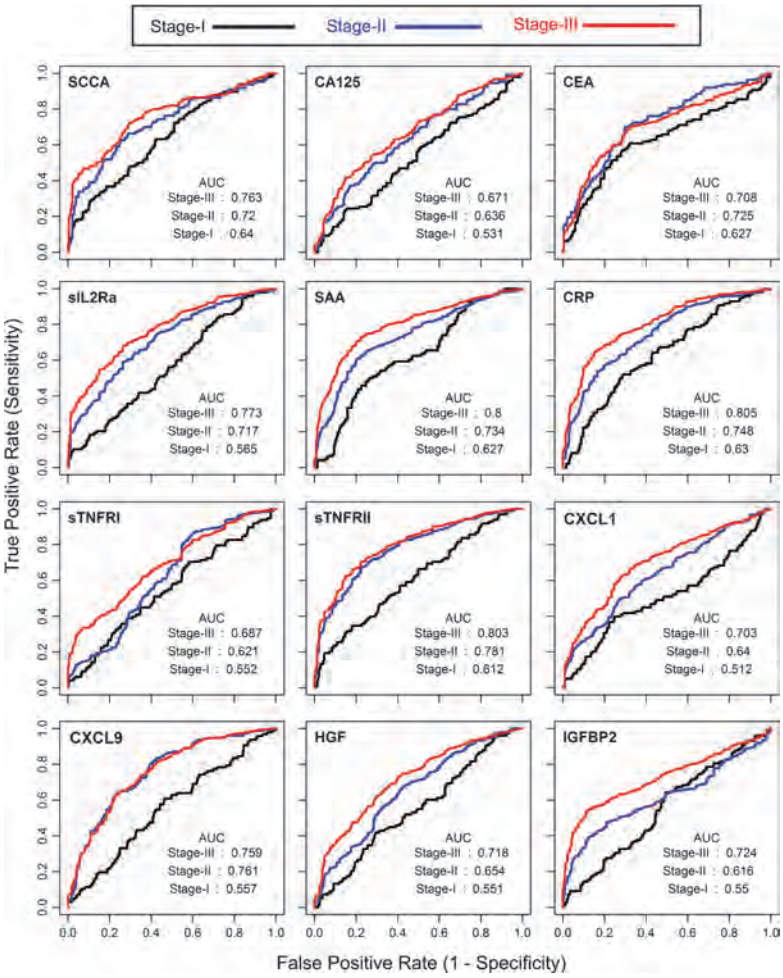
Zhi W, Ferris D, Sharma A, et al. Int J Gynecol Cancer. 2014;24(6):1085-92.

研究背景：

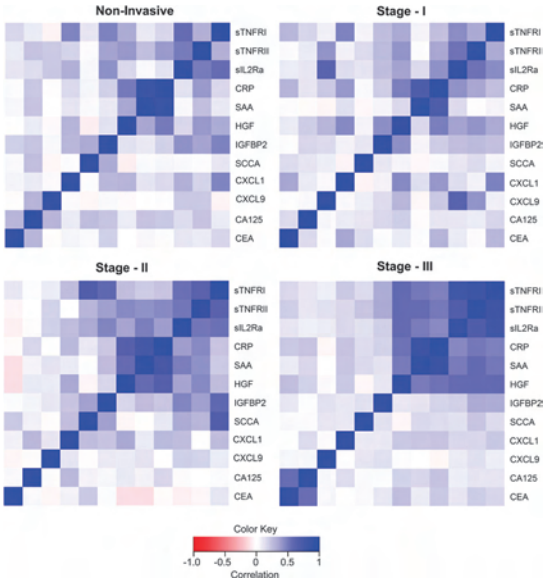
鉴定宫颈鳞状细胞癌血清蛋白变化图谱用于疾病致病机理的阐明及发现疾病新的治疗或干预的靶标。

实验设计：

鉴定宫颈鳞状细胞癌血清蛋白变化图谱用于疾病致病机理的阐明及发现疾病新的治疗或干预的靶标。



宫颈鳞状细胞癌I、II、III期和癌前病变患者
12种血清蛋白ROC曲线比较。



宫颈鳞状细胞癌I、II、III期和癌前病变患者
12种蛋白在血清水平的相互关系。

结果与意义：

1：发现了12种蛋白（SAA, CRP, sTNFRI，sTNFRII,sIL2R, CXCL1, CXCL9, HGF, SCCA, ILGFBP2,CA125 和CEA）血清浓度和AUC（曲线下面积）随着疾病的进展显著升高。

2：显著升高的蛋白和多种致病机制相关，如炎症反应和免疫、血管形成、生长促进、转移。

3：快速发现大量的血清蛋白在不同病人的不同阶段显著不同。

小M有话说

Milliplex多因子联合检测技术不仅能够用于上述介绍的肿瘤早期诊断和风险评估，也可以根据选择研究疾病发病阶段的不同用于转化医学的不同方向（高危评估，早期预警/诊断，检测定位，预后判断，复发监测）的研究，甚至深入疾病机理进行探讨。

肿瘤转移研究

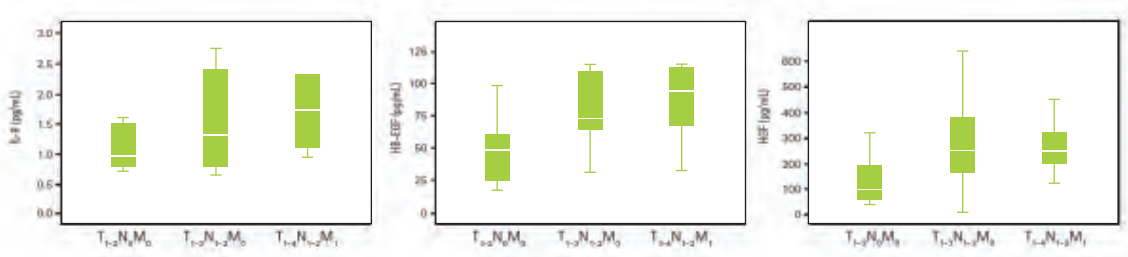
血管生成相关因子与非小细胞肺癌转移的相关性研究

A multi-analyte serum test for the detection of non-small cell lung cancer.

Farlow, E.C., Vercillo, M.S., Coon, J.S., et al. British Journal of Cancer 2010; 103(8):1221.

实验设计：

用Milliplex多因子检测平台对38例非小细胞肺癌不同病程阶段的病人样品17种血管生成相关因子同时检测。其中12位患者记为T1-2N0M0（"无转移"），12位为T1-3N1-2M0（"局部转移"），14位T1-4N1-2M1（"有长程转移"）。



不同标志物在不同肿瘤阶段的表达水平

	$T_{1-2}N_0M_0$		$T_{1-3}N_{1-2}M_0$		$T_{1-4}N_{1-2}M_1$	
	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	14,2650	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

不同标志物在不同阶段的表达水平

结果与意义：

1：与"无转移"现象的病人（T1-2N 0M 0）相比，发生远程转移的病人(T1-4N 1-2M 1)血清中 IL-8，HGF 和 HB-EGF 明显升高，能够用于肿瘤转移的检测。

2：非侵入方法检测减少病人痛苦。

小M有话说

该研究特色是通过Milliplex技术仅对疾病样本进行（而非传统研究中同时使用疾病组和健康组），这样获得的标志物能够特异性用于肿瘤转移的评估，从而为病人提供个性化用药治疗，是当前转化医学和精准医学研究的重要应用方向。

肿瘤预后评估

Milliplex 多因子检测平台在肝细胞癌(HCC)预后评估中的应用

Using multiple cytokines to predict hepatocellular carcinoma recurrence in two patient cohorts.

Chen, Z. Y., et al. (2014). Br J Cancer 110(3): 733-740.

研究背景:

细胞因子和肝细胞癌(hepatocellular carcinoma,HCC)的致病机理,发展和预后具有密切的关系。

实验设计:

179例肝癌血清样本分为两组(检测组和验证组),用Milliplex高通量技术平台检测血清样本中39种细胞因子。

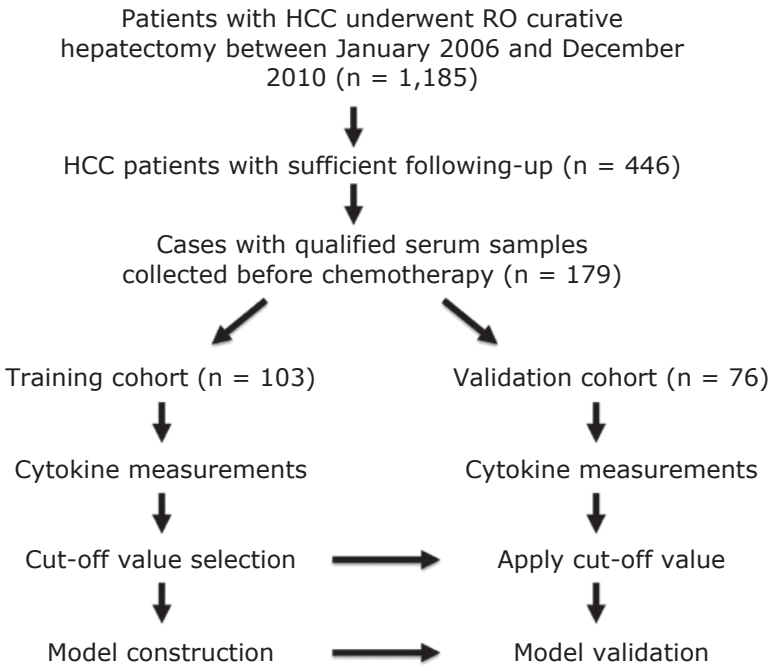


Figure 1. A schematic overview of patient selection. The schematic summarises the cases for construction and validation of the classifier.

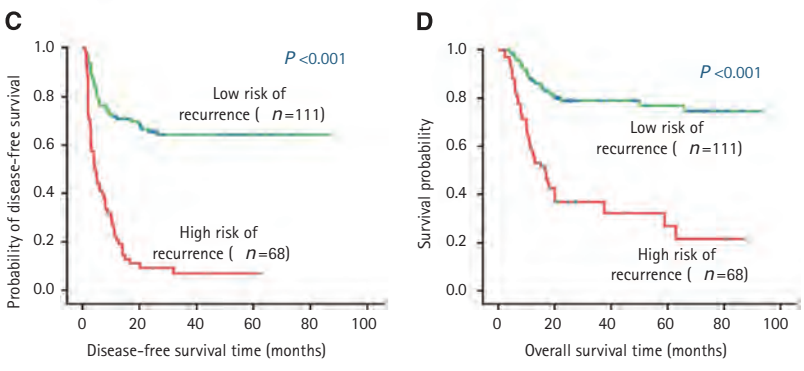
疾病样本选择与分组

结果与意义:

1:发现6种重要的预后因子用来预测无病存活率(disease-free survival,DFS)和总体存活率(overall survival,OS),FGF-2, GRO, IL-8, IP-10, VEGF, IFN-a2。

2:整合6种因子和3个临床特征,开发出一种新型的细胞因子为基础的预后分类模型(CBPC) 预测复发和3年总体存活率(训练组:灵敏度 0.648,特异性0.918;验证组:灵敏度0.585,特异性 0.857)。IFN-a2是唯一的单独的疾病预后因子。

3:以细胞因子为基础的预后分类模型(CBPC)能够作为新的筛选方法鉴定术后复发高风险和总体存活时间短的肝癌病人,从而开展以细胞因子为靶标的治疗。



应用:CBPC能提高对HCC病人风险的评估

小M有话说

Milliplex技术平台对于肿瘤转化医学和精准医学的典型应用。该类型研究虽然操作简单,整篇文章仅使用Milliplex一项技术,但是完全满足科学研究中的可行性和创新性需求。

如果进一步深挖数据,该文章也具有很高的可持续性研究价值:首先,该篇文章通过多个因子建立了肝癌新的疾病预测模型,后续能够进一步扩大样本建立疾病的新的评价体系和标准;其次,发现的疾病特异性细胞因子也具有潜在作为疾病诊断标志物的价值,后续能够用于新型疾病诊断试剂盒的开发;另外,文章发现的疾病显著性相关的细胞因子也是肝癌治疗的潜在靶标,后续可以开发特异性抗体或抑制剂等治疗药物;最后,也可以以疾病相关细胞因子为基础,进行疾病机制和上下游信号通路分子的分析,从而深入疾病机理研究。

肿瘤机制研究(信号通路)

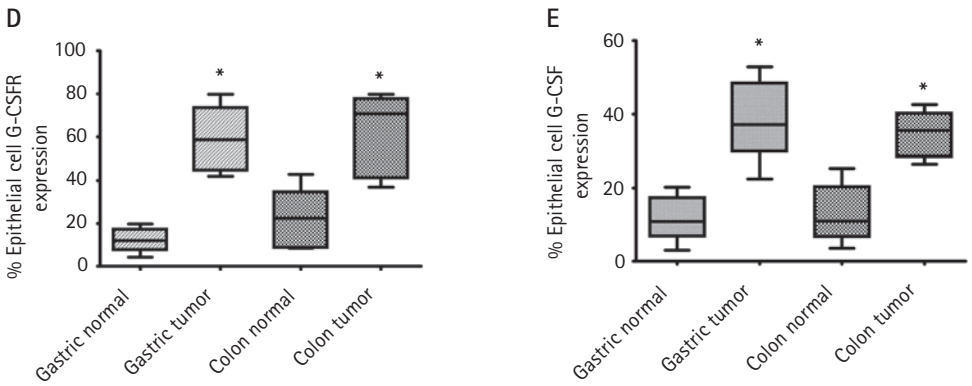
G-CSF and G-CSFR在胃肠癌中高表达促进肿瘤细胞增殖和迁移

G-CSF and G-CSFR are highly expressed in human gastric and colon cancers and promote carcinoma cell proliferation and migration.

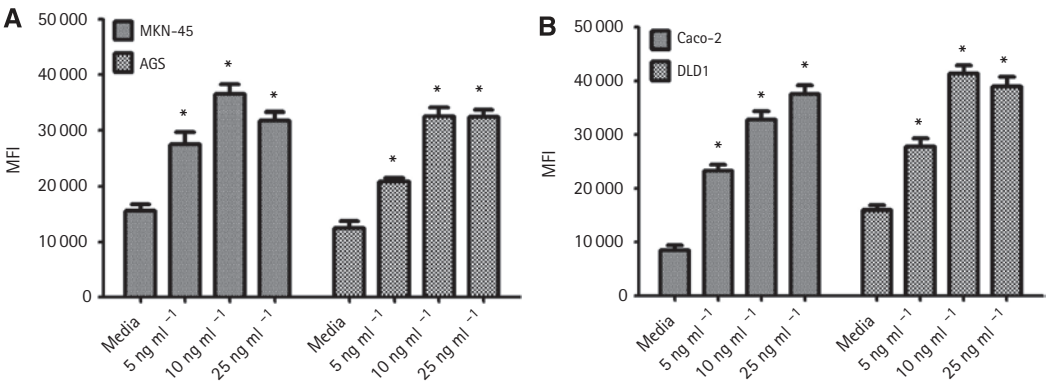
Morris K T, Khan H ,, Ahmad A ,, et al. G-CSF and G-CSFR are highly expressed in human gastric and colon cancers and promote carcinoma cell proliferation and migration.[J]. British Journal of Cancer, 2014, 110(5):1211-1220.

实验设计:

细胞水平通过RT-PCR,流式细胞仪(Guava easyCyte 8HT flow cytometer from Millipore),信号通路检测(MAPmates phospho-ERK1/2 and RSK from Millipore Milliplex),增殖(ERK和RSK抑制剂来自Millipore)和迁移实验研究G-CSF和G-CSFR在肿瘤细胞的表达以及对胃肠癌细胞增殖,迁移和信号的影响。



G-CSF和G-CSFR在人肿瘤细胞和胃肠上皮细胞中高表达



G-CSF诱导ERK1/2 和RSK 信号通路

小M有话说

Milliplex技术不仅仅能够用于转化医学的快速研究,也能够应用于基础医学,生命科学的机制研究,在该文章中能够快速发现疾病相关的信号通路,避免传统研究中需要购买多种信号通路抗体,并需要进行大量Western blot操作或需要进行大量Q-PCR实验,花费较长的时间精力进行信号通路的筛选和分析,为你的研究提供更高的效率。

此外,默克不仅能够提供Milliplex多因子检测平台,也能为肿瘤研究以及生命科学的研究提供全面系统的高品质研究工具和解决方案。该研究中还使用了默克公司的Guava流式细胞仪和信号通路小分子抑制剂。

结果与意义:

1:G-CSFR在90%的人胃肠肿瘤细胞中高表达,G-CSF在基质成纤维细胞和肿瘤细胞中高表达。高表达G-CSF的肿瘤细胞增加增殖和迁移能力,肿瘤细胞的亚群表达"干细胞样"(stem-like)标志物,这种影响均依赖ERK1/2和RSK1磷酸化作用。

2:G-CSF/R axis 促进胃肠肿瘤的形成,是潜在的重要的肿瘤治疗靶标。

• 代谢研究

心血管疾病

hsCRP的表达和颈动脉粥样硬化炎症因子的关系（阴性实验结果）

Plasma levels of high-sensitive CRP do not correlate with inflammatory activity in carotid atherosclerotic plaques.

Grufman, H., et al. (2014). "Plasma levels of high-sensitive C-reactive protein do not correlate with inflammatory activity in carotid atherosclerotic plaques." J Intern Med 275(2): 127-133.

研究背景：

有研究显示血清CRP的升高增加心血管疾病的风险。

实验设计：

Milliplex 技术检测160例动脉内膜切除术例血浆样本中IL-6, IL-10, MCP-1和TNF-alpha. Plaque使用抗CD68抗体染色斑块巨噬细胞含量。

Table 3 Associations between hsCRP and other inflammatory markers in plasma and carotid plaques

	All plaques (n = 160)	Asymptomatic plaques (n = 73)	Symptomatic plaques (n = 87)
Plasma lipids and WBCs			
Triglycerides (mmol L^{-1})	ns	ns	ns
HDL (mmol L^{-1})	ns	ns	ns
LDL (mmol L^{-1})	ns	ns	ns
WBC count (10^6 mL^{-1})	0.25***	ns	0.30**
Plasma cytokines			
IL-6 (pg mL^{-1})	0.22**	ns	0.25*
IL-10 (pg mL^{-1})	ns	ns	ns
TNF-a (pg mL^{-1})	0.17*	ns	ns
MCP-1 (pg mL^{-1})	ns	ns	ns
Plaque cytokines			
IL-6 (pg g^{-1} plaque tissue)	ns	ns	ns
IL-10 (pg g^{-1} plaque tissue)	ns	ns	ns
TNF-a (pg g^{-1} plaque tissue)	ns	ns	ns
MCP-1 (pg g^{-1} plaque tissue)	ns	ns	ns
Plaque staining			
a-actin	ns	ns	ns
CD68	ns	ns	ns
Oil Red O	ns	ns	ns

WBC, white blood cell; ns, nonsignificant. P = 0.05, *P < 0.05, ** P < 0.01 and *** P < 0.005. Plaque staining for smooth muscle cells (a-actin), macrophages (CD68) and lipids (Oil Red O) were measured as percentage of total plaque area.

结果与意义：

1：在血浆hsCRP浓度和血小板细胞因子水平或巨噬细胞含量无显著相关性。

2：当前的研究显示不建议将hsCRP作为血小板炎症的标志物，hsCRP的升高很可能是亚临床系统性信号（subclinical systemic）

小M有话说

很多老师在研究前会对自己的结果有一个理论预期，如果实际结果和理论预期不一致，往往不会讲这些结果进行发表。但是对于这些阴性结果如果分析发现是真实准确的数据，即使为"阴性"，也具有重要参考价值，也能够发表高分期刊。

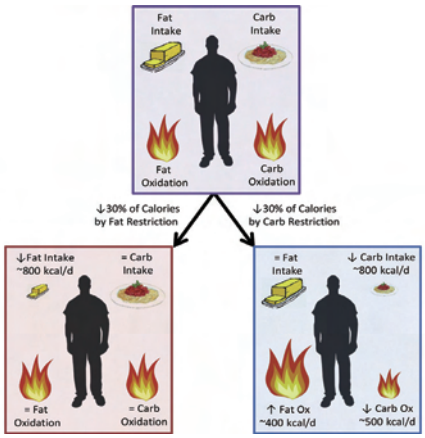
在医学研究中，往往不经意或是微小的操作差异就会造成研究结果的巨大差异，甚至得出相反的结果。尤其对于临床性质的科学研究而言更为重要，比如样本的纳入排除标准，样本的基本临床信息（年龄，性别，生理生化指标，伴发疾病等）和样本病理信息（分级，分期等）的准确性，以及样本本身保存，冻融次数，溶血情况，血脂含量等对于研究结果都有一定的影响，所以在研究中我们既要保证样本信息的准确性也要保证信息记录的完整性，如果你在使用Milliplex技术中对样本的处理存在疑惑，可以和我们的技术及时沟通，这样能够充分保证研究结果的真实准确，哪怕获得的数据是"阴性"的，也具有非常重要的发表价值。

肥胖研究

减脂：限糖还是限脂肪？

Calorie for Calorie, Dietary Fat Restriction Results in More Body Fat Loss than Carbohydrate Restriction in People with Obesity

Hall K, Bemis T, Brychta R, et al. Calorie for Calorie, Dietary Fat Restriction Results in More Body Fat Loss than Carbohydrate Restriction in People with Obesity[J]. Cell Metabolism, 2015, 22(3):427-436. (IF:17.565)



研究方法示意图

实验设计：

19例肥胖症患者进行2周实验。食物中摄入的热量比基础膳食热量低了30%。这少吃的30%热量，在第一阶段都只来自糖，而第二阶段则都只来自于脂肪。同时使用Milliplex技术检测血浆ghrelin, GLP-1, pancreatic polypeptide (PP),PYY,leptin,MCP-1, C-peptide, insulin和 GIP(human metabolic hormone panel,HMHMAG-34K)和血浆adiponectin, resistin, and PAI-1 (human serum adipokine panel A, HADK1-61K-A).

Table 4. Overnight-Fasted Plasma Hormone and Metabolite Levels

All Subjects	Baseline	N	D RC diet	p value	N	D RF diet	p value	N	p value (RC versus RF)
Glucose (mg/dl)	87.5 ± 1.2	19	-2.69 ± 1.7	0.13	19	-7.1± 1.7	0.0008	17	0.025
Glycerol (mg/l)	9.77 ± 1.3	19	1.35 ± 1.5	0.39	19	-0.328± 1.6	0.84	17	0.32
BHB (mM)	0.0682 ± 0.009	19	0.0883 ± 0.014	＜0.0001	19	0.00569± 0.015	0.71	17	＜0.0001
Cholesterol (mg/dl)	179 ± 5.8	18	-8.47 ± 2.8	0.01	15	-19.1± 2.6	＜0.0001	16	0.024
TG (mg/dl)	101 ± 11	18	-17.5 ± 5	0.0044	15	-4.3± 4.8	0.39	16	0.012
LDL (mg/dl)	114 ± 4.2	18	-1.77 ± 2.6	0.52	15	-11.4± 2.5	0.0006	16	0.032
HDL (mg/dl)	44.8 ± 2.4	18	-2.67 ± 0.66	0.0013	16	-7.27± 0.62	＜0.0001	16	＜0.0001
Leptin (ng/ml)	21.5 ± 2.7	19	-3.89 ± 0.81	0.0002	19	-2.89± 0.86	0.0039	17	0.39
Ghrelin (pg/ml)	23.7 ± 1.6	19	7.18 ± 2.9	0.026	18	-3.58± 3.2	0.28	15	0.022
MCP1 (pg/ml)	150 ± 11	19	1.96 ± 4.9	0.69	19	2.41± 5.1	0.64	17	0.95
GIP (pg/ml)	30.9 ± 3.7	19	4.42 ± 3.2	0.18	19	-4.94± 3.3	0.16	17	0.021
GLP1 (pg/ml)	37.8 ± 4.4	19	0.543 ± 0.75	0.48	19	0.628± 0.79	0.44	17	0.95
C-peptide (ng/ml)	1.42 ± 0.13	19	-0.133 ± 0.045	0.009	19	-0.179± 0.047	0.0017	17	0.52
PYY (pg/ml)	125 ± 15	17	4.44 ± 2.8	0.14	17	-1.38± 3.1	0.66	15	0.24
Insulin (pg/ml)	12.6 ± 2	19	-2.76 ± 0.77	0.0024	18	-2.04± 0.8	0.021	17	0.48
PP (ng/ml)	54.6 ± 24	19	-1.02 ± 5.6	0.86	18	0.511± 6	0.93	16	0.88
Adiponectin (mg/dl)	0.978 ± 0.13	17	-0.118 ± 0.035	0.0037	17	-0.126± 0.035	0.0024	17	0.73
Resistin (ng/ml)	56.2 ± 13	17	8.99 ± 3.7	0.028	17	4.2± 3.8	0.28	17	0.26
PAI1 (ng/ml)	36 ± 6.6	17	-3.47 ± 3.3	0.31	17	-7.12± 3.3	0.048	17	0.25
Cortisol (pg/ml)	4,490 ± 690	19	703 ± 540	0.21	19	-494± 570	0.4	17	0.074
CRP (mg/l)	1.18 ± 0.2	17	-0.018 ± 0.11	0.87	16	-0.0887± 0.12	0.46	14	0.55
HOMA-IR	2.72 ± 0.43	19	-0.489 ± 0.15	0.0054	18	-0.541± 0.15	0.0028	17	0.8

等能量限糖(RC)和限脂(RF)饮食中，过夜禁食血浆激素和代谢水平。

结果与意义：

1：限制糖分的摄入能显著促进体内脂肪氧化（约403千卡/天），限制脂肪摄入则做不到。但是，通过限制脂肪摄入所引起的脂肪损失（89 ± 6 克/天）却明显高于限制糖所带来的效果（53 ± 6 克/天），减少相同热量摄入，从脂肪里减和从糖分里减少，对身体起到的作用截然不同的。跟限制糖比起来，限制脂肪的摄入在减脂方面的效果可能优越一点。限制糖分的摄入能显著促进体内脂肪氧化（约403千卡/天），限制脂肪摄入则做不到。但是，通过限制脂肪摄入所引起的脂肪损失（89 ± 6 克/天）却明显高于限制糖所带来的效果（53 ± 6 克/天），减少相同热量摄入，从脂肪里减和从糖分里减少，对身体起到的作用截然不同的。跟限制糖比起来，限制脂肪的摄入在减脂方面的效果可能优越一点。

2：Milliplex检测结果显示RC（限糖）和RF（限脂）饮食都会出现血浆 C-peptide, insulin, insulin resistance, leptin, adiponectin, total cholesterol 和HDL的显著降低. RF饮食中血浆HDL和总胆固醇降低程度更大, LDL下降仅在RF 饮食中出现. 血浆TG 下降仅在RC 饮食出现. 血浆b-hydroxybutyrate and ghrelin升高仅在RC 饮食出现. 血浆GIP在RC 饮食升高和RF饮食降低.

3：尽管结果得到了数学模型的支持，但同样的模型也预测，随着时间的延续，这样的差异将趋于减少。样本并不多，无法给想要减肥的人群一个更加精准的新方向。

小M有话说

肥胖患者激素和代谢水平的变化能够为减肥提供更加针对性的指导，本篇研究的核心内容就是少吃肉比少吃糖减肥效果更好一些，但是如果真正减肥可能还是那句老话"少动嘴，多动腿"。

胃肠短路手术降低炎症与血栓标志物

Roux-en-Y Gastric Bypass Decreases Pro-inflammatory and Thrombotic Biomarkers in Individuals with Extreme Obesity

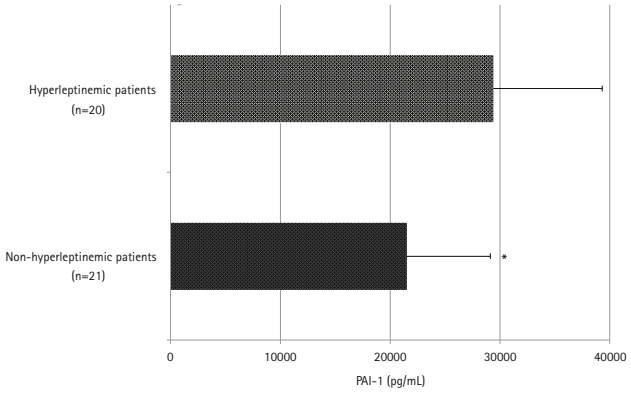
Netto B D M, Bettini S C, Clemente A P G, et al. Decreases Pro-inflammatory and Thrombotic Biomarkers in Individuals with Extreme Obesity[J]. Obesity Surgery, 2014, 25(6):1010-1018.

研究背景：

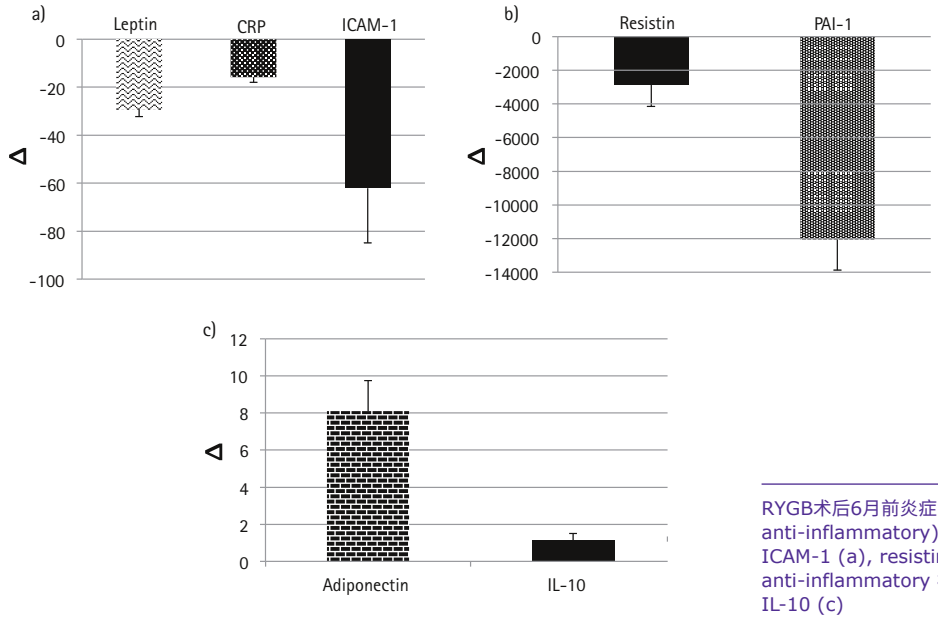
炎症导致肥胖患者体内胰岛素抵抗和内皮功能失调，引发心血管疾病. 本研究评价胃肠短路手术（RYGB）后体重降低早期效应(炎症和血栓状态)。

实验设计：

41例经历RYGB手术过度肥胖患者，进行手术前和术后6个月的人体测量(Anthropometric)和临床状态，炎症标志物检测。



RYGB术前伴有高Leptin血症的病态肥胖和非Leptin血症的病态肥胖样本PAI-1浓度



RYGB术后6月前炎症因子和抗炎因子水平(pro- and anti-inflammatory)的变化 Leptin (a), CRP (a), ICAM-1 (a), resistin (b), and PAI-1 (b). anti-inflammatory 标志物变化, adiponectin and IL-10 (c)

结果与意义：

1：Plasminogen activator inhibitor-1 (PAI-1)浓度在伴有Leptin血症（hyperleptinemia）肥胖个体高于非Leptin血症个体。相对于基线值，术后BMI降低（12.9 kg/m2）。腰围显著降低（126.2 to 101.4 cm）。血浆总胆固醇, LDL , TG 和 Glu也降低。前炎症标志物也发现降低：PAI-1 55.9±6.0 %, CRP 18.8±3.4 %, ICAM-1 89.9±5.7 %, leptin 27.9±3.2%和 resistin 69.3 ±5.8%。

2：TNF-α和leptin/adiponectin比率显著降低。抗炎细胞因子adiponectin和IL-10 显著升高。

3：发现伴有Leptin血症的肥胖个体有更高水平的PAI-1表达。

肝病

HBV病毒竟能"训练"胎儿免疫应答?

Trained immunity in newborn infants of HBV-infected mothersIF 11.47

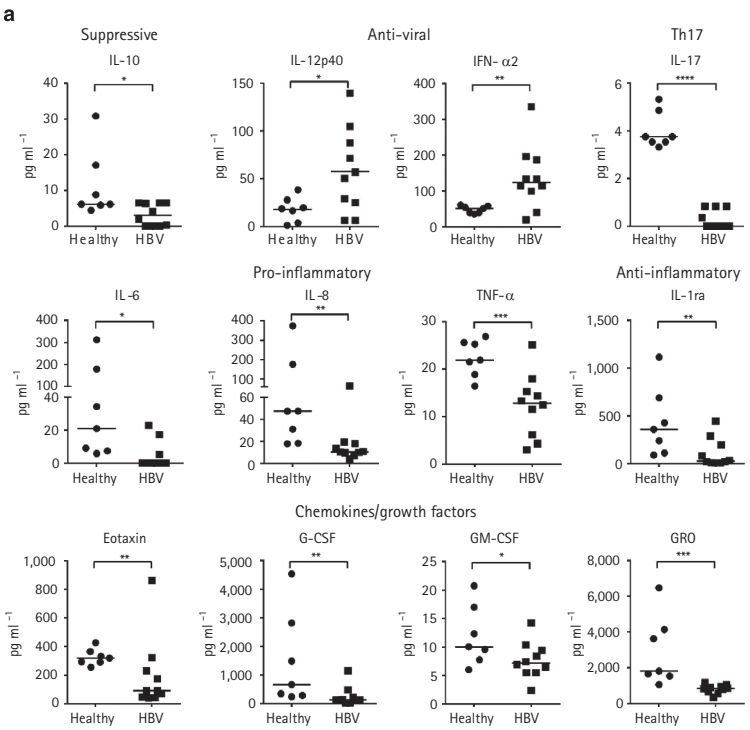
Hong M, Sandalova E, Low D, et al. Trained immunity in newborn infants of HBV-infected mothers.[J]. Nature Communications, 2015, 6.

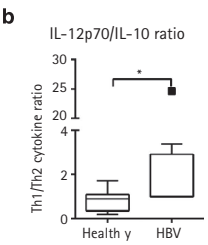
研究背景:

新生儿是HBV慢性感染的一个大的受害群体,通常研究认为,乙肝病毒利用新生儿免疫系统的不成熟,通过诱导宿主产生免疫耐受建立持续的慢性感染状态。

实验设计:

在其研究中,使用Milliplex(MAP Human Cytokine/ Chemokine Magnetic Bead Panel—Premixed 42 Plex)检测血浆和培养细胞上清中细胞因子浓度。





High levels of IL-12p40 and IFN-a2, and low levels of IL-10 and pro-inflammatory cytokines in the CB of Asian HBVt mothers. (a) CB plasma cytokines were determined by multiplex assay in seven healthy controls and ten HBVt mothers. Horizontal line represents the median.
(b) Ratio of Th1/Th2 cytokine (IL-12p70/IL-10) in healthy and HBV-exposed CB.

结果与意义:

1:出生前接触HBV病毒能够诱导胎儿建立一种"被训练"的免疫状态,这种"训练"能够促进胎儿固有免疫细胞成熟以及Th1细胞的发育,这一过程会进一步增强脐带血中免疫细胞应答细菌感染的能力。研究发现这些"训练"效应与细胞因子环境改变有关,主要存在IL-10水平较低,同时在多数情况下还伴随高水平的IL-12p40和IFN-α2等情况。

2:研究结果揭示了HBV病毒与天然宿主之间存在的潜在共生关系,并着重提出在出生前接触病毒,会诱导胎儿免疫系统产生高度可塑性。

小M有话说

该研究完全颠覆了大家对乙肝感染传统观念,有助于大家对这种流行疾病的认识。有助于理解出生前HBV暴露如何形成新生儿的总体免疫反应,并转变我们看待乙肝病毒的方式。尽管HBV会在以后的生活中导致疾病,但在生命早期它实际上可能对人类有益。

什么叫训练免疫:检查HBV阳性母亲脐带血中的免疫细胞,发现无论是先天免疫细胞,还是适应性免疫细胞,都更加有活性和成熟,并且能更好应对细菌挑战,这种现象称为"训练免疫"(trained immunity)。

文章作者表示感染慢性HBV的年轻成年人(年龄在14至30岁)没有免疫耐受性,他们具有的免疫细胞不能够抵御病毒。下一步,他计划检测HBV感染在儿科患者中的影响(2-12岁),以确定免疫系统如何响应病毒,将为慢性乙肝的治疗(从青少年或更早)奠定基础。

• 免疫研究

传染性疾病研究

新型免疫标志物可预测携带肺结核(TB)的HIV患者的早死及并发症风险

Immunological profiling of tuberculosis-associated immune reconstitution inflammatory syndrome and non-immune reconstitution inflammatory syndrome death in HIV-infected adults with pulmonary tuberculosis starting antiretroviral therapy: a prospective observational cohort studyIF 22.433

Ravimohan, S., et al. (2015). "Immunological profiling of tuberculosis-associated immune reconstitution inflammatory syndrome and non-immune reconstitution inflammatory syndrome death in HIV-infected adults with pulmonary tuberculosis starting antiretroviral therapy: a prospective observational cohort study." Lancet Infect Dis 15(4): 429-438

研究背景:

共感染的晚期HIV/TB患者有结核关联的免疫重建炎症综合征(tuberculosis-associated immune reconstitution inflammatory syndrome,TB-IRIS)风险,在抗病毒(antiretroviral therapy,ART)治疗后很快死亡。TB-IRIS与ART后细胞免疫反应快速恢复相关,比较早期死亡患者和TB-IRIC患者之间免疫反应及生物标志物特性的差异。

实验设计:

201例来自博茨瓦纳的患者使用Milliplex技术检测29种血浆生物标志物。基于ART治疗后6个月的记录结果将病人为4组:TB-IRIS组,早期死亡组,存活组(无TB-IRIS),进行抗逆转录病毒疗法前后的反应情况的评估。

	Control (n=118)	TB-associated IRIS (n=32)*	p value†	p_{corr}†	Death (n=17)	p value‡	p_{corr}‡
EGF	146·9 (55·6–235·3)	92·7 (46·3–201·5)	0·17	0·28	78·6 (38·7–156·5)	0·10	0·36
VEGF	123 (76·1–181·7)	106·2 (65·4–160·2)	0·21	0·30	173·3 (97·4– 219·6)	0·28	0·50
G-CSF	124·1 (86·6–174·1)	88·4 (65·3–132·8)	0·01§	0·04§	138·4 (97·7–243·1)	0·29	0·50
GM-CS	34·5 (20·0–51·4)	18·3 (12·2–31·9)	0·0008§	0·02§	46·9 (35·5–66·1)	0·03§	0·20
IL-1RA	78·7 (39·8–153·7)	90·4 (34·2–200·0)	0·74	0·74	115·5 (50·8–160·2)	0·25	0·50
IL-1α	20·1 (9·4–57·3)	9·4 (9·4–44·7)	0·20	0·30	44·2 (9·4–109·5)	0·32	0·52
IL-1β	1·2 (0·8–3·9)	0·8 (0·8–3·2)	0·16	0·28	1·6 (0·8–1·9)	0·77	0·80
IL-2	2·4 (1·0–7·3)	1·0 (1·0–3·0)	0·02§	0·07	3·7 (1·0–11·4)	0·40	0·58
IL-3	3·7 (1·3–9·1)	1·5 (0·7–5·9)	0·007§	0·04§	2·8 (1·5–13·2)	0·69	0·75
IL-5	2·8 (1·5–6·5)	3·0 (1·1–4·8)	0·62	0·70	3·1 (0·5–7·7)	0·97	0·97
IL-6	14·7 (7·5–28·1)	10·3 (5·0–21·3)	0·04§	0·12	19·8 (11·8–33·2)	0·11	0·36
IL-7	21·0 (14·1–29·4)	15·8 (12·2–22·7)	0·14	0·28	23·0 (19·0–47·5)	0·15	0·36
IL-8	16·8 (9·6–28·6)	14·6 (6·8–20·8)	0·15	0·28	22·2 (11·9–38·8)	0·14	0·36
IL-10	18·8 (11·0–32·5)	14·5 (8·3–21·3)	0·07	0·17	39·8 (13·1–98·2)	0·03§	0·20
IL-12p40	15·0 (7·4–36·0)	7·4 (7·4–12·0)	0·002§	0·03§	20·7 (7·4–27·9)	0·65	0·74
IL-12p70	9·8 (5·8–18·7)	6·3 (3·4–12·0)	0·01§	0·04§	11·4 (8·1–19·0)	0·49	0·66
IL-15	4·3 (1·2–10·0)	1·7 (1·2–4·8)	0·02§	0·07	5·8 (2·5–13·3)	0·27	0·50
IL-17a	3·3 (1·6–5·9)	1·4 (0·7–3·8)	0·005§	0·04§	4·2 (2·4–6·2)	0·35	0·54
IFNα	53·3 (29·8–98·6)	71·8 (31·1–110·0)	0·36	0·49	57·4 (35·4–91·4)	0·55	0·68
IFNγ	18·8 (9·2–35·9)	16·3 (5·0–34·9)	0·56	0·66	20·2 (9·3–43·4)	0·64	0·74
IP-10	3390 (2298–4267)	4185 (2827–5931)	0·06	0·16	3935 (2964–5203)	0·12	0·36
MCP-1	548·7 (388·4–779·4)	649·3 (378·2–841·6)	0·71	0·74	832·2 (652·3–1331·2)	0·003§	0·08
MIP-1α	13·3 (5·7–22·9)	10·4 (6·8–15·4)	0·41	0·53	19·7 (8·2–25·0)	0·14	0·36
MIP-1β	66·9 (47·1–112·2)	63·7 (39·1–106·9)	0·45	0·56	99·2 (49·3–114·3)	0·51	0·66
Eotaxin	146·5 (119·6–191·8)	180·0 (132·9–220·0)	0·08	0·17	189·8 (140·6–258·7)	0·06	0·31
TNFα	41·4 (28·9–63·0)	38·2 (27·0–60·5)	0·65	0·71	56·6 (44·9–74·8)	0·02§	0·20

Data are median pg/mL (IQR). TB=tuberculosis. IRIS=immune reconstitution inflammatory syndrome. p_{corr}=Benjamini-Hochberg-corrected p value. EGF=epidermal growth factor. VEGF=vascular endothelial growth factor. G-CSF=granulocyte colony-stimulating factor. GM-CSF=granulocyte-macrophage colony-stimulating factor. IL=interleukin. IFN=interferon. IP=FNγ induced protein. MCP=monocyte chemoattractant protein. MIP=macrophage inflammatory protein. TNF=tumour necrosis factor. *Includes one patient who had TB-associated IRIS and died. †p and p_{corr} values comparing controls with patients with TB-associated IRIS. ‡p and p_{corr} values comparing controls with deaths. §Significant associations.

Table 3: Baseline biomarker concentrations associated with TB-associated IRIS and early mortality in patients with advanced HIV and TB starting antiretroviral therapy

接受ART治疗的晚期HIV/TB患者中TB-IRIS和早期死亡组病人的细胞因子基线浓度

	TB-associated IRIS*	Death†
GM-CSF	0·15 (0·05–0·48)‡	3·0 (0·49–18·9)
IL-2	0·41 (0·18–0·96)‡	1·4 (0·54–3·4)
IL-3	0·39 (0·17–0·86)‡	1·1 (0·41–2·8)
IL-12p40	0·32 (0·14–0·75)‡	1·4 (0·48–4·2)
IL-12p70	0·28 (0·12–0·69)‡	1·4 (0·46–4·6)
IL-15	0·39 (0·18–0·86)‡	2·0 (0·72–5·3)
IL-17a	0·33 (0·14–0·78)‡	1·7 (0·58–5·1)
IL-6	0·40 (0·18–0·89)‡	2·8 (0·93–8·4)
IL-10	0·5 (0·21–1·2)	3·5 (0·89–13·5)
MCP-1	1·5 (0·49–4·5)	9·0 (1·0–80·0)‡
TNFα	0·99 (0·32–3·0)	7·8 (1·1–55·2)‡
Eotaxin	5·4 (0·78–36·5)	3·6 (0·58–22·5)
G-CSF	0·53 (0·20–1·4)	3·6 (0·61–21·0)
IP-10	4·0 (0·84–19·3)	2·9 (0·50–16·8)

Data are adjusted odds ratio (95% CI). Log_{10} transformed baseline values of biomarkers that were associated with TB-associated IRIS or death at p<0·10 in unadjusted analyses (see table 3) were used to establish association with paradoxical TB-associated IRIS and death in a logistic regression model. TB=tuberculosis. IRIS=immune reconstitution inflammatory syndrome. GM-CSF=granulocyte-macrophage colony-stimulating factor. IL=interleukin. MCP=monocyte chemoattractant protein. TNF=tumour necrosis factor. G-CSF=granulocyte colony-stimulating factor. IP=IFNγ induced protein. *TB-associated IRIS associations are adjusted for body-mass index and nevirapine use. †Models included CD4 cell count before antiretroviral therapy, female sex, and presence of baseline opportunistic infections. ‡Independent association between biomarker and outcome.

Table 2: Relation of baseline biomarker concentrations to TB-associated IRIS and early mortality in patients with advanced HIV and tuberculosis starting antiretroviral therapy

接受ART治疗4周后的晚期HIV/TB患者中TB-IRIS和早期死亡组病人的细胞因子浓度浓度变化

结果与意义:

1:TB-IRIS组在pre-ART有较低的IL-6浓度. 然而早期死亡组在pre-ART有较高的 MCP-1和TNFα浓度. ART治疗后,TB-IRIS组IL-6和TNFα浓度和对照相比进一步增加. 死亡组和对照组相比G-CSF, IL-12p40和IL-15因子浓度进一步增加. 在ART中,CD4 细胞数量在对照组和TB-IRIS相似, 但是在死亡组中数量降低。

2:阐明晚期HIV/TB患者在ART治疗前后TB-IRIS和死亡人群明确的免疫学profiles.抗逆转录病毒疗法的患者机体中鉴别出了新型的免疫生物标志物,可帮助预测携带肺结核(TB)的HIV患者的早死及并发症风险。对于开发新型疗法从而降低患者机体炎症,同时还可以促进患者的免疫恢复提供了新的研究线索。

3:患者机体中较低水平的IL-6,IL-15及GM-CSF和其患IRIS的风险增加直接相关,高水平的MCP-1及TNF-α和患者的死亡风险增加直接相关。然而IRIS及早期死亡的患者在进行抗逆转录病毒疗法开始后的免疫反应和炎性反应会明显增加,包括IL-6,TNF-α及G-CSF在内的四种生物标志物也和患者的TB-IRIS风险增加存在独立相关的关系,而另外五种生物标志物则和患者死亡风险增加相关,包括IL-1RA和G-CSF。

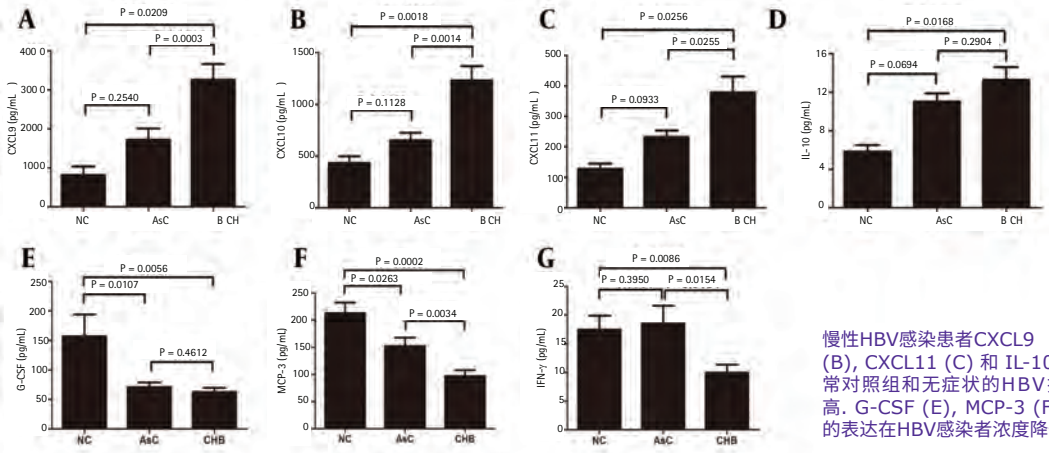
乙肝和炎症因子的相关性研究

Expression profiles of circulating cytokines, chemokines and immune cells in patients with hepatitis B virus infection. Lian, J. Q., et al. (2014).

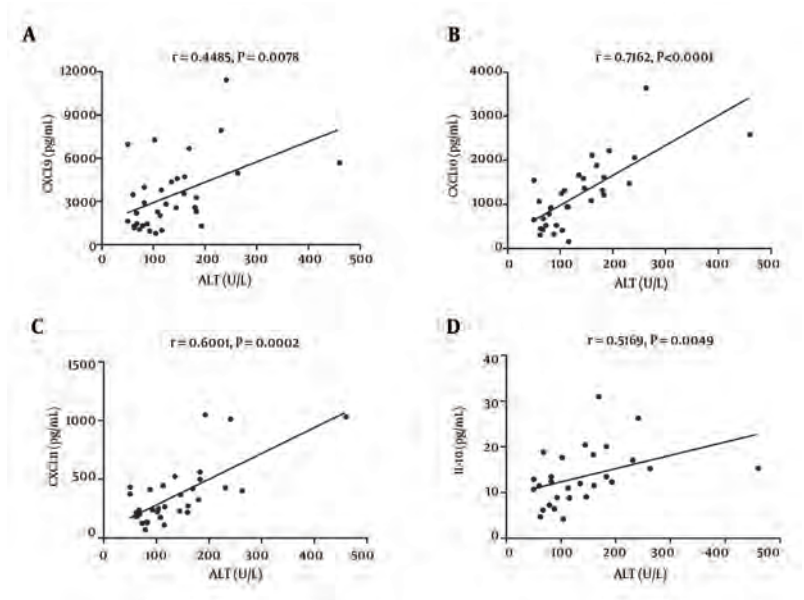
Hepat Mon 14(6): e18892.

实验设计：

用流式细胞仪和Milliplex多因子检测平台对69例位慢性乙肝患者的5种免疫细胞亚群和46细胞因子/趋化因子进行检测。



慢性HBV感染患者CXCL9 (A), CXCL10 (B), CXCL11 (C) 和 IL-10 (D)的浓度与正常对照组和无症状的HBV携带者组相比升高. G-CSF (E), MCP-3 (F) 和 IFN-γ (G) 的表达在HBV感染者浓度降低



HBV患者的CXCL9 (A), CXCL10 (B), CXCL11 (C), and IL-10 (D) 表达和血清ALT正相关.

结果与意义：

1:CXCL9, CXCL10, CXCL11 和 IL-10在HBV人群升高,与ALT阳性相关;G-CSF, MCP-3 和 IFN-γgamma在HBV人群表达降低,与病毒学研究结果(virological findings)或肝炎症(liver inflammation)无相关性。

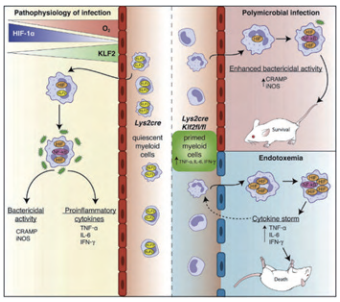
2:CXCR3相关趋化因子与慢性HBV肝炎症具有相关性,, MCP-3和G-CSF被HBV感染infection抑制。 细胞因子和趋化因子表达模式更好的理解慢性 HBV 感染的发病机理infection pathogenesis。

先天性免疫

鉴定先天性免疫反应中重要调控因子KLF-2

The Myeloid Transcription Factor KLF2 Regulates the Host Response to Polymicrobial Infection and Endotoxic Shock Mahabeleshwar G, Kawanami D, Sharma N, et al. The Myeloid Transcription Factor KLF2 Regulates the Host Response to Polymicrobial Infection and Endotoxic Shock[J].

Immunity, 2011, 34(5):715–728.

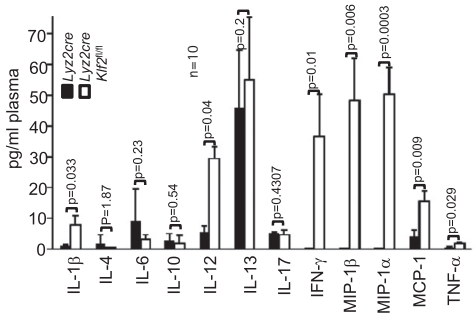


实验设计：

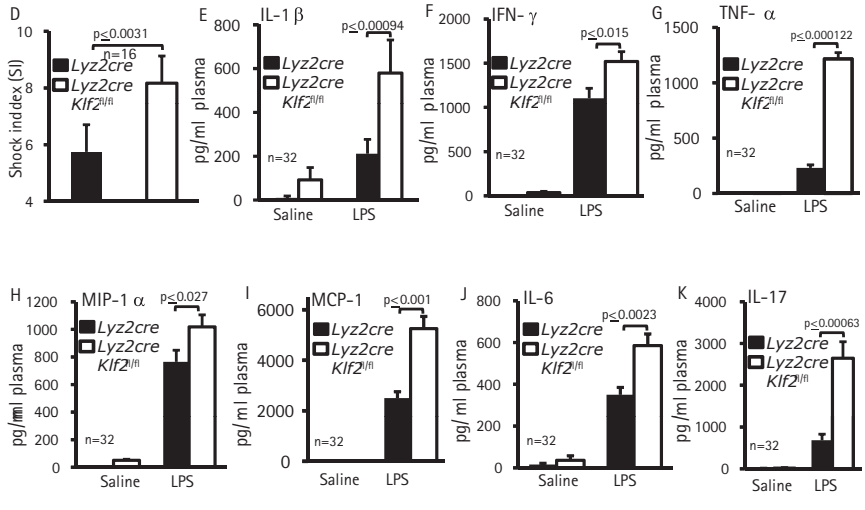
用流式细胞仪和Milliplex多因子检测平台对69例位慢性乙肝患者的5种免疫细胞亚群和 46 细胞因子/趋化因子进行检测。

研究亮点：

- KLF2 deficiency confers a proinflammatory phenotype to myeloid cells
- Myeloid KLF2 deficiency renders animals resistant to polymicrobial infection
- Myeloid KLF2 deficiency renders animals susceptible to endotoxic shock
- KLF2 negatively regulates the NF-κB-HIF-1α axis in macrophages



(A)MILLIPLEX MAP mouse cytokine-chemokine panel分析Lyz2cre and Lyz2cre Klf2fl/fl 小鼠血浆炎症细胞因子



(E–K) LPS (21 mg/kg)刺激年龄和性别匹配的Lyz2cre and Lyz2cre Klf2fl/fl 小鼠. 4 hr后分别收集LPS 或对照组刺激的血浆样本. MILLIPLEX MAP mouse cytokine and chemokine panel分析炎症细胞因子

结果与意义：

1:鉴定Kruppel-like transcription factor 2 (KLF2)作为骨髓细胞激活的潜在调控因子

2:人败血症中发现骨髓细胞暴露在低氧/细菌中诱导HIF-1a,同时KLF2表达降低,KLF2是NF-kB-dependent HIF-1转录的潜在抑制因子,在多种微生物感染及内毒素血症中具有关键作用

3:KLF2是骨髓细胞激活的补充抑制因子,在先天性免疫反应必需的调控因子;

小M有话说

研究使用Milliplex对小鼠血浆细胞因子进行检测。使用Milliplex在小鼠等少量及珍贵样本的检测中具有明显的优势:每只小鼠血浆/血清无法提供足够体积样本进行多因子及多时间点的筛选,如果使用传统的ELISA,WB或/和荧光定量检测中需要使用大量体积的样本,给实验分组和动物饲养带来很多不便,此外传统方法对于大量数目样本的筛选也是难以想象的工作强度,同时多次实验操作会对结果的重复性和稳定性带来影响。因此使用Milliplex能够在此类研究中显著提高研究效率,并有效保证研究结果的准确性和稳定性。

过敏性疾病研究

儿童严重哮喘分子表型

The molecular phenotype of severe asthma in children.

Fitzpatrick A M, Melinda H, Fernando H, et al. Journal of Allergy & Clinical Immunology, 2010, 125(4):851–857.e18.

实验设计：

使用Milliplex多因子检测平台检测53例哮喘儿童和30例成年的支气管肺泡灌洗液 (BAL) 和肺泡巨噬细胞裂解液(AM)中的23种细胞因子/趋化因子表达水平。

	Adult control (n = 30)	Moderate asthma (n = 22)	Severe asthma (n = 31)
IL-1 β	0 (0–0.01)	0.07 ± 0.07$^{\alpha}$ (0–0.23)	0.06 ± 0.07$^{\alpha}$ (0–0.36)
IL-2	0.05 ± 0.08 (0–0.37)	0.07 ± 0.05 (0–0.21)	0.08 ± 0.11 (0–0.62)
IL-4	0.53 ± 0.73 (0–2.76)	0.65 ± 0.84 (0–2.40)	0.55 ± 0.74 (0–2.08)
IL-5	0.06 ± 0.16 (0–0.75)	0.29 ± 0.56 (0–2.03)	0.39 ± 1.03 (0–4.53)
IL-6	0.59 ± 0.48 (0.18–2.11)	5.60 ± 3.73$^{\alpha}$ (1.23–17.09)	8.27 ± 11.65$^{\alpha}$ (0.93–56.15)
IL-7	0.76 ± 1.69 (0–8.52)	1.24 ± 1.30 (0.03–6.55)	0.94 ± 0.98 (0.01–4.53)
IL-10	0.01 ± 0.03 (0–0.15)	0.81 ± 1.86 (0–8.19)	0.69 ± 1.46 (0–7.33)
IL-12 (p70)	0.04 ± 0.06 (0–0.19)	0.10 ± 0.11 (0–0.39)	0.14 ± 0.18 (0–0.81)
IL-13	0.02 ± 0.12 (0–0.55)	0.62 ± 0.52$^{\alpha}$ (0–2.32)	1.04 ± 1.40$^{\alpha}$ (0–5.96)
IFN γ	0.03 ± 0.13 (0–0.60)	0.26 ± 0.38 (0–1.41)	0.14 ± 0.21 (0–0.91)
GM-CSF	0.21 ± 0.21 (0–0.75)	0.34 ± 0.29 (0–1.00)	0.22 ± 0.25 (0–1.32)
TNF α	0.19 ± 0.17 (0.04–0.74)	0.51 ± 0.91 (0.04–4.44)	1.47 ± 5.04 (0.06–25.71)

支气管肺泡灌洗液(BAL fluid)细胞因子浓度(pg/mL)

	Adult control (n = 30)	Moderate asthma (n = 22)	Severe asthma (n = 31)
GRO (CXCL1)	455 ± 391 (126–1596)	3054 ± 1971$^{\alpha}$ (166–10,000)	2657 ± 1615$^{\alpha}$ (111–6363)
IL-8 (CXCL8)	2.8 ± 2.9 (0.7–11.7)	28.3 ± 26.6$^{\alpha}$ (4.0–104)	45.2 ± 49.1$^{\alpha}$ (6.1–245)
IP-10 (CXCL10)	248 ± 284 (16–1294)	762 ± 637$^{\alpha}$ (114–2674)	1302 ± 2145$^{\alpha}$ (46–10,000)
MCP-1 (CCL2)	27.6 ± 19.5 (8.3–82.5)	43.5 ± 34.2 (5.9–1494)	177 ± 603 (3.52–2934)
MIP-1 α (CCL-3)	1.2 ± 1.2 (0–2.9)	5.3 ± 8.8 (0–37.8)	57.9 ± 268 (0–1288)
MIP-1 β (CCL-4)	3.0 ± 3.2 (0–15.0)	20.8 ± 23.6$^{\alpha}$ (1.6–106)	19.1 ± 32.3$^{\alpha}$ (0–161)
RANTES (CCL5)	25.6 ± 49.1 (0.04–199)	108 ± 78.2$^{\alpha}$ (15.1–266)	201 ± 235$^{\alpha}$ (7.6–1145)
MCP-3 (CCL7)	0 (0)	8.7 ± 7.8$^{\alpha}$ (0–27.9)	12.2 ± 15.3$^{\alpha}$ (0–73.5)
Eotaxin (CCL11)	0.1 ± 0.4 (0–1.5)	0.8 ± 2.9 (0–13.4)	6.8 ± 29.9 (0–144)
MDC (CCL22)	34.3 ± 24.2 (0–85.9)	57.4 ± 26.5$^{\alpha}$ (16.6–106)	90.8 ± 98.2$^{\alpha}$ (6.1–357)
Fractalkine (CX3CL1)	60.7 ± 26.8 (20.7–132)	142 ± 88.1$^{\alpha}$ (0–358)	141 ± 79.4$^{\alpha}$ (0–312)

支气管肺泡灌洗液(BAL fluid)趋化因子浓度 (pg/mL)

结果与意义：

1：在支气管肺泡灌洗液中，IL-13 和 IL-6 在哮喘组和对照组之间有显著区别，GRO，RANTES，IL-12，IFNγ和IL-10在不同程度哮喘病人中表达水平存在差异。

2：在肺泡巨噬细胞裂解液中，IL-6 在哮喘组和对照组中具有最显著的差异。

3：通过Milliplex多因子检测平台进行多因子联检，可以对不同程度的儿童哮喘进行分类，结果可能有助于儿童靶向治疗方法的发展。

自身免疫性疾病

风湿性关节炎(rheumatoid arthritis,RA)细胞因子表达

Cytokine expression and cytokine-based T cell profiling in South Indian rheumatoid arthritis Mariaselvam C M, Aoki M, Salah S, et al.

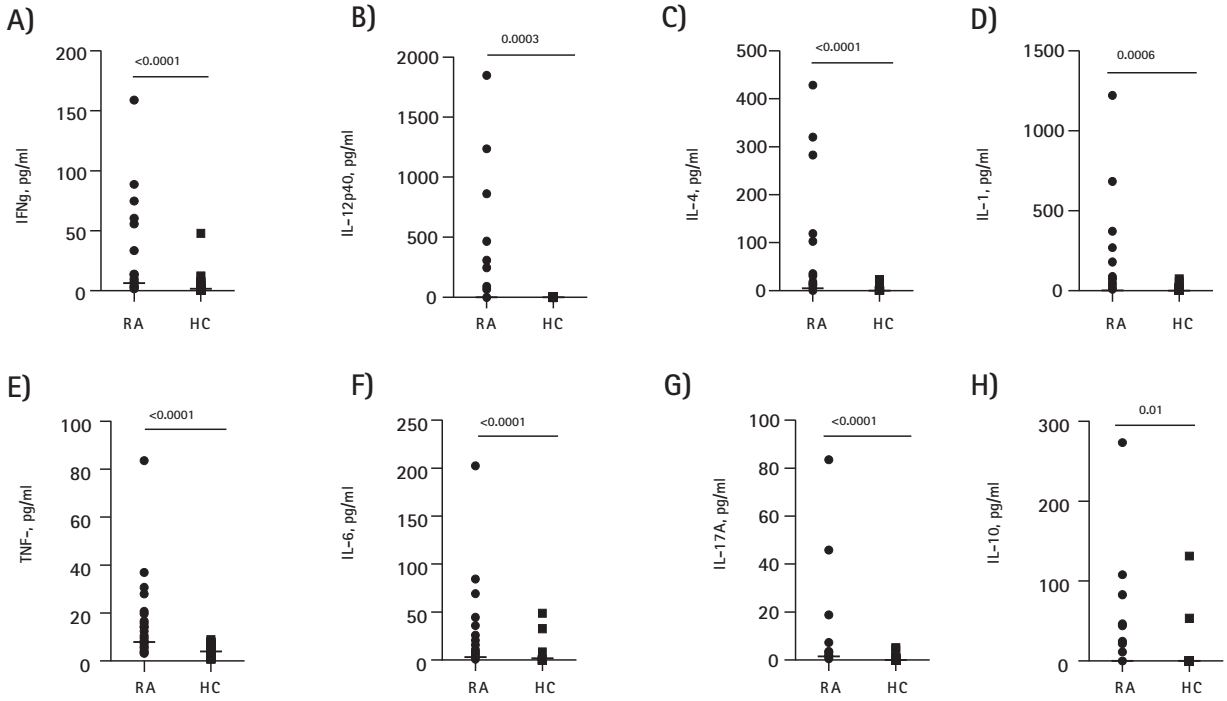
Cytokine expression and cytokine-based T cell profiling in South Indian rheumatoid arthritis[J]. Immunobiology, 2014, 219(10):772–777.

目标研究背景:

检测风湿性关节炎(Rheumatoid arthritis,RA)细胞因子,发现潜在生物标志物。

实验设计:

48例RA 病人和49例健康对照样本,初步使用qPCR分析Th1, Th2, Th17 和 Tregs 细胞特异性的细胞因子和转录因子,进一步使用Milliplex技术检测因子的血浆蛋白表达水平。



RA患者和对照外周血血清细胞因子比较

结果与意义:

1:发现RA患者 T-bet (for Th1),GATA-3 (for Th2),FoxP3 (for Tregs),IFN-γ和IL-10基因表达水平显著低于健康对照。RA患者IL-12p40和TNF-α转录水平高于健康对照。RA患者血浆蛋白水平普遍高于对照组样本。

2:虽然在这些细胞和分子研究进程中没有获得一种特定标志物具有显著的诊断和预后价值,但是发现转录因子与血浆细胞因子的变化显示RA患者T细胞亚群存在潜在的失调,具有显著的炎症表型。

移植研究

CXCR3配体早期预测T细胞介导的肾移植后急性排斥

Serum levels of CXCR3 ligands predict T cell-mediated acute rejection after kidney transplantation.

Huang H, Xu X, Yao C, et al. [J]. Molecular Medicine Reports, 2014, 9(1):45-50.

实验设计：

肾移植后1个月进行肾组织活检，其中32例样本具有T细胞介导的急性排斥，38例样本稳定。收集急性排斥和稳定的血清样本，用Milliplex高通量多因子技术检测平台检测其中的CXCR3 配体，MIG，IP-10和I-TAC的表达水平。

Table II. Levels of chemokines (median, pg/ml) in the serum of patients following transplantation.

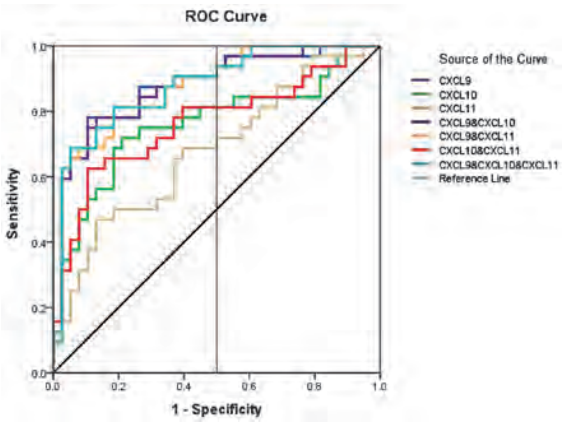
Type of chemokine	Patients		
	Acute rejection	Stable function	P-value
MIG	4,271	1,148	<0.0001
IP-10	686.7	332.2	0.0002
I-TAC	44.32	22.92	0.0103

移植后病人血清趋化因子水平(median, pg/ml)

Table III. The calculated area under the curve (AUC) for chemokine levels.

Type of chemokine	AUC	SD	P-value	95% CI
MIG	0.877	0.043	<0.0001	0.794-0.961
IP-10	0.760	0.061	<0.0001	0.641-0.879
I-TAC	0.679	0.064	0.010	0.553-0.806
MIG + IP-10	0.876	0.042	<0.0001	0.793-0.959
MIG + I-TAC	0.875	0.042	<0.0001	0.793-0.957
IP-10 + I-TAC	0.765	0.060	<0.0001	0.648-0.882
MIG + IP-10 + I-TAC	0.878	0.041	<0.0001	0.797-0.959

趋化因子的曲线下面积(AUC) 计算



趋化因子水平的ROC (Receiver-operating characteristic) 曲线.

结果与意义：

1：急性排斥的血清样本MIG (4,271 pg/ml), IP-10 (686.7 pg/ml) 和 I-TAC (44.32 pg/ml) 显著高于稳定组的样本。

2：ROC曲线显示使用Milliplex多因子进行血清中MIG，IP-10和I-TAC的联合检测能够提供非侵入性且高效的方法用于肾移植后T细胞介导的急性排斥的早期预测。

• 神经性疾病研究

神经降压素在自闭症儿童血清中表达

Neurotensin is increased in serum of young children with autistic disorder.

Neurotensin is increased in serum of young children with autistic disorder. Angelidou A, Francis K, Vasiadi M, et al. Journal of Neuroinflammation, 2010, 7 (2):48.

研究背景：

孤独症谱系障碍 (Autism spectrum disorders, ASD)是儿童早期出现的一种神经发育失调。与"core symptoms"相关，包括在社交技能，语言和非语言交流存在障碍等。目前还没有明确的发病机制和诊断检测。许多自闭症儿童也有"过敏样"症状。然而，实验显示肥大细胞的激活与非过敏性诱发剂无关。

实验设计：

用Milliplex多因子技术平台检测19例自闭症儿童 (男16和女3;平均年龄3.0±0.4岁)和16例健康对照(男13和女3; 平均年龄3±1.2岁)血清中3种刺激肥大细胞的神经肽(neurotensin, b-endorphin 和 substance P)表达水平的差异。

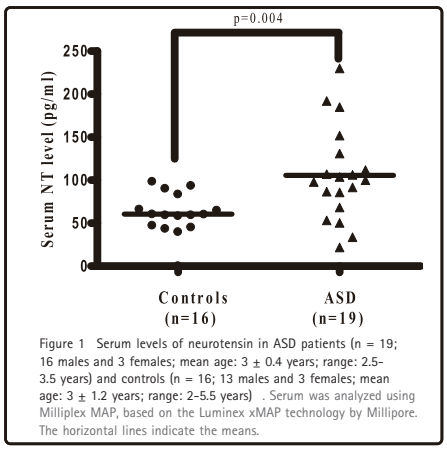


Figure 1 Serum levels of neurotensin in ASD patients (n = 19; 16 males and 3 females; mean age: 3 ± 0.4 years; range: 2.5-3.5 years) and controls (n = 16; 13 males and 3 females; mean age: 3 ± 1.2 years; range: 2-5.5 years) . Serum was analyzed using Milliplex MAP, based on the Luminex xMAP technology by Millipore. The horizontal lines indicate the means.

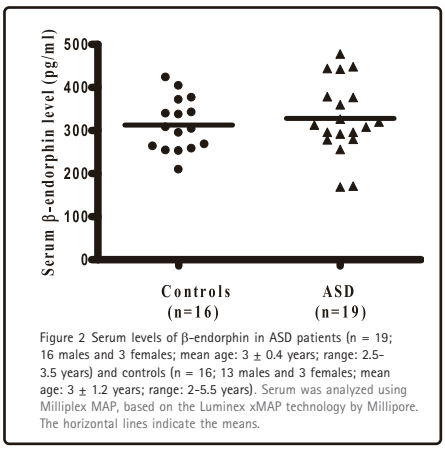


Figure 2 Serum levels of β-endorphin in ASD patients (n = 19; 16 males and 3 females; mean age: 3 ± 0.4 years; range: 2.5-3.5 years) and controls (n = 16; 13 males and 3 females; mean age: 3 ± 1.2 years; range: 2-5.5 years). Serum was analyzed using Milliplex MAP, based on the Luminex xMAP technology by Millipore. The horizontal lines indicate the means.

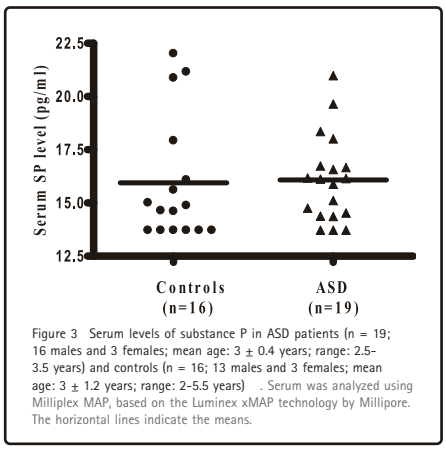


Figure 3 Serum levels of substance P in ASD patients (n = 19; 16 males and 3 females; mean age: 3 ± 0.4 years; range: 2.5-3.5 years) and controls (n = 16; 13 males and 3 females; mean age: 3 ± 1.2 years; range: 2-5.5 years) . Serum was analyzed using Milliplex MAP, based on the Luminex xMAP technology by Millipore. The horizontal lines indicate the means.

ASD病人的 neurotensin，b-endorphin 和 substance P 血清水平 (n = 19; 16 males and 3 females);

结果与意义：

3种神经肽中只有neurotensin (NT)和对照相比显著升高(60.5 ± 6.0 pg/ml - 105.6 ± 12.4 pg/ml)。b-endorphin 和 substance P (SP)水平无显著变化。

由此可以推断，NT能刺激免疫细胞，尤其肥大细胞，可能对脑部炎症反应和自闭症产生具有直接影响。

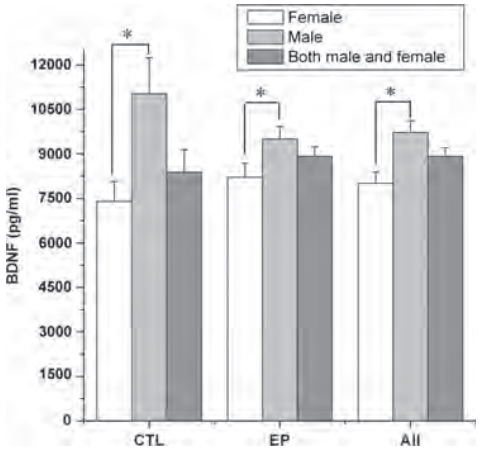
神经系统疾病检测—癫痫(血清脑源性神经营养因子作为癫痫潜在诊断标志物)

Serum brain-derived neurotrophic factor (BDNF) levels in epilepsy

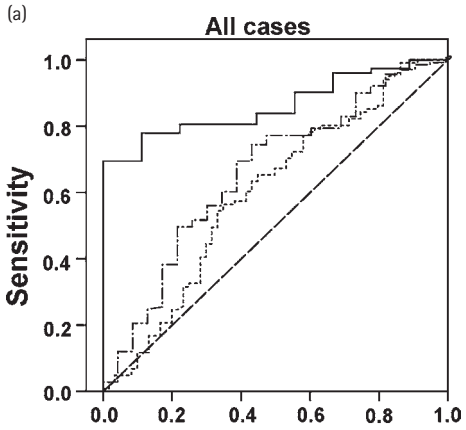
Hong, Z., et al. (2014). "Serum brain-derived neurotrophic factor levels in epilepsy." Eur J Neurol 21(1): 57-64.

实验设计:

Milliplex技术检测135例癫痫患者和34例健康血清样本的脑源性神经营养因子(BDNF)表达水平。



不同性别样本中血清 BDNF水平



A使用ROC(receiver operating characteristic)曲线评价
血清BDNF作为癫痫患者严重性的标志物

Table 3 Summary of receiver operating characteristic curve results for serum BDNF [a]

	All people with epilepsy					Males with epilepsy					Females with epilepsy				
	AUC	P value	Cut-off value (pg/ml)	Sens (%)	Spec (%)	AUC	P value	Cut-off value (ng/ml)	Sens (%)	Spec (%)	AUC	P value	Cut-off value (ng/ml)	Sens (%)	Spec (%)
Monthly versus less frequent	0.60	0.037	6515	80	40	0.63	0.039	7050	80	36	0.54	0.615	4835	90	27
Weekly versus less frequent	0.66	0.014	6330	80	53	0.71	0.035	6335	85	60	0.58	0.345	4835	85	24
Daily versus less frequent	0.86	<0.001	6260	80	90	0.88	0.012	6040	88	75	0.85	0.009	4835	87	60

血清BDNF的ROC曲线结果

结果与意义:

1:不同性别和对照样本血清BDNF水平具体显著区别。BDNF诊断阈值(cut-off values)临界值6260 pg/ml,对于从偶发癫痫(fewer seizures)中区别日常和频繁发作(daily or more frequent seizures)灵敏度80% 和特异性90%。

2:血清 BDNF浓度与癫痫疾病严重性相关,能够作为癫痫严重性评估的辅助标志物.

神经退行性疾病-阿尔茨海默病(唾液样本)

唾液tau作为阿尔茨海默病(Alzheimer disease，AD)潜在标志物

Salivary tau species are potential biomarkers of Alzheimer disease

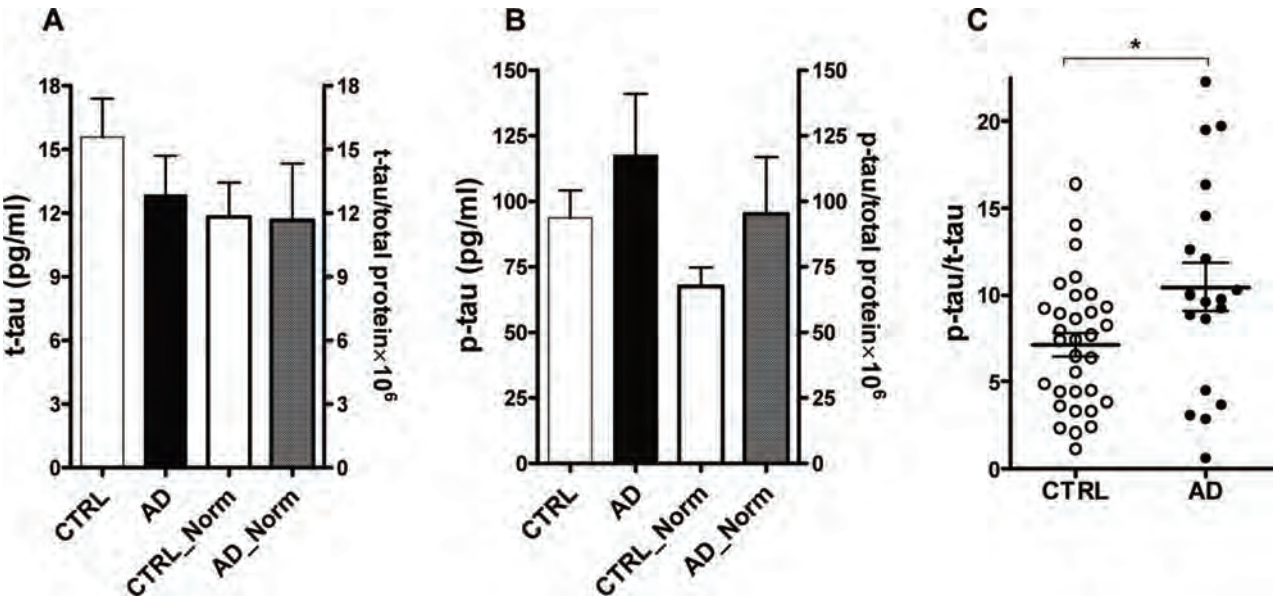
Min Shi, Yu-Ting Sui, Elaine R. Salivary tau species are potential biomarkers of Alzheimer disease[J]. Journal of Alzheimers Disease, 2011, 27(2).

研究背景：

tau 蛋白磷酸化在阿尔茨海默病(Alzheimer disease，AD)致病机理中具有重要作用. 脑脊液(CSF)中磷酸化Tau和总Tau的升高，结合Aβ42的降低已经作为灵敏性的AD诊断标志物. 但是CSF的获取相对较为困难且是有创.因此CSF对于AD的早期诊断和筛选并不是非常理想的样本来源.

实验设计：

Milliplex技术定量检测21例AD患者，38例健康对照样本的唾液总tau蛋白(t-tau)，磷酸化tau(p-tau)和 Aβ42浓度。



AD病人和健康对照(CTRL)样本唾液t-tau和p-tau蛋白水平。
(A) AD病人组t-tau蛋白表达水平低于对照组，但是在唾液t-tau蛋白水平标准化(normalizing)后区别减弱。
(B) AD病人组p-tau蛋白表达水平高于对照组，无论是否标准化(normalized)唾液t-tau水平。
(C) AD病人的p-tau/t-tau 比率显著升高。

结果与意义：

1：AD患者 phosphorylated tau/ total tau 比率显著高于健康对照。

2：显示唾液 tau蛋白能作为AD诊断的理想标志物，特别在疾病早期阶段，甚至在无症状(asymptomatic)样本筛选中，为AD患者提供更大的治疗窗口(therapeutic window)。

HIV相关的认知损伤—脑脊液和血浆样本

Amyloid Beta-42 (Aβ-42), neprilysin and cytokine levels. A pilot study in patients with HIV related cognitive impairments

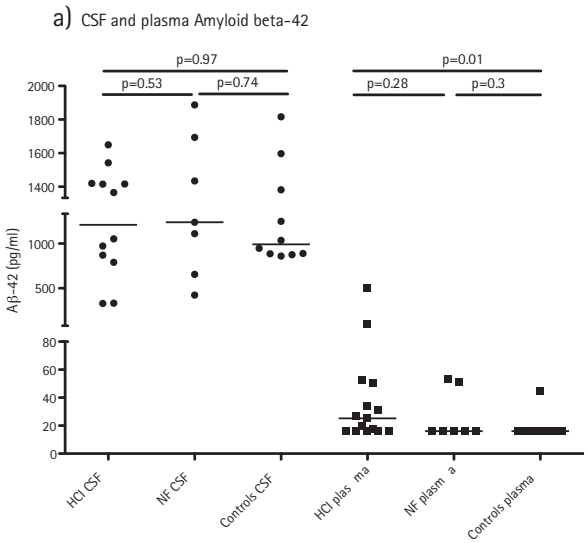
Mothapo K M, Stelma F, Janssen M, et al. Amyloid Beta-42 (Aβ-42), neprilysin and cytokine levels. A pilot study in patients with HIV related cognitive impairments[J]. Journal of Neuroimmunology, 2015, 282:73-79.

研究背景：

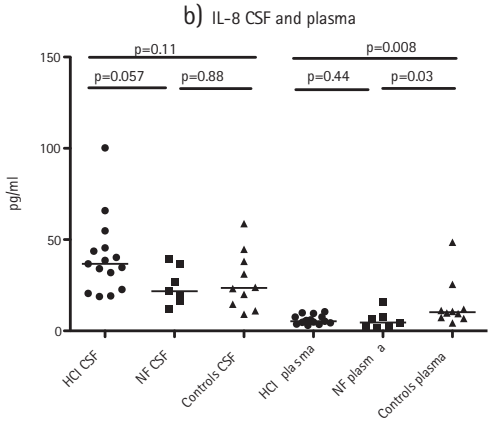
HIV相关痴呆(HAD)与 淀粉样蛋白(amyloid-beta，Aβ)沉积有关。

实验设计：

Milliplex技术检测32例HIV相关的认知损伤(HIV-related cognitive impairments，HCI)，22例HIV认知功能正常(normal cognitive functioning，NF)和10例非HIV对照样本脑脊液和血浆amyloid beta-42 (Aβ-42), neprilysin (NEP) 和细胞因子表达水平。



HCI, NF 和对照组CSF和血浆 Aβ-42 浓度和NEP活性



HCI, NF 和对照组CSF和血浆细胞因子浓度

结果与意义：

1:Aβ-42 在HCI (67%)中表达水平相对在 NF (29%) 和 controls (10%)升高。
显示在CSF中 IL-8水平在HCI相对NF升高(无显著区别)。

2:初步研究显示脑脊液中IL-8和血浆Aβ-42可能作为HCI 潜在标志物。

• 信号通路研究

IL5激活的嗜酸细胞细胞中Siglec-8介导的细胞死亡机制:ROS 增强的MEK/ERK激活

Mechanism of Siglec-8–mediated cell death in IL-5–activated eosinophils: Role for reactive oxygen species–enhanced MEK/ERK activation.

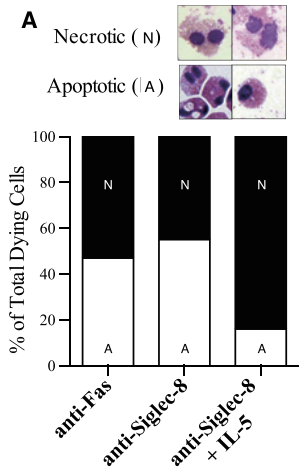
Gen K, Maha A, Bochner B S, et al. Mechanism of Siglec-8–mediated cell death in IL-5–activated eosinophils: Role for reactive oxygen species–enhanced MEK/ERK activation[J]. Journal of Allergy & Clinical Immunology, 2013, 132(2):437–445.

研究背景:

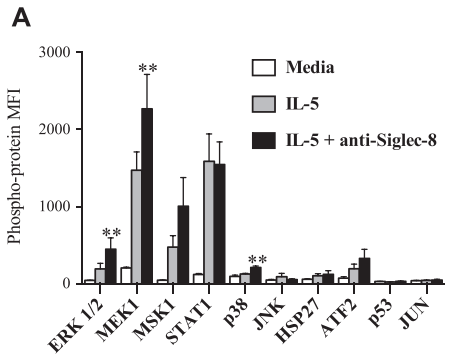
阐明 Siglec(唾液酸结合的Ig样凝集素)8 介导激活的嗜酸细胞死亡的机制。

实验设计:

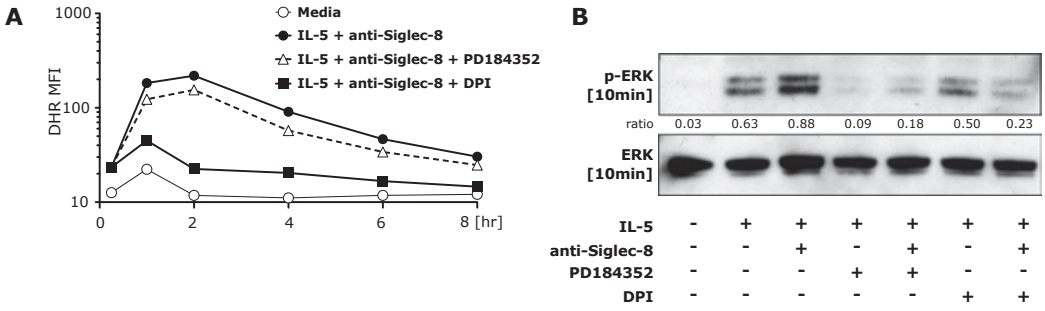
竞争性的 anti–Siglec-8抗体和 IL-5处理外周血嗜酸细胞. Milliplex技术(10 phosphoproteins related to human MAPK Kit),流式细胞,Western Blot(化学发光HRP检测试剂盒和MEK1 inhibitors U0126来自默克公司)检测MAPK的磷酸化作用和细胞功能、荧光检测ROS累积。



不同刺激导致凋亡或坏死的死细胞的形态学和百分率图示



Milliplex phospho-MAPK bead 检测嗜酸细胞(n =4 donors)裂解物(anti–Siglec-8/IL-5共刺激后MEK/ERK 通路表达上调)



anti–Siglec-8/IL-5共刺激的MEK/ERK 上调位于ROS产物的下游。A, 二氢罗丹明123(DHR)进行细胞染色, 流式细胞分析ROS 水平. B, 刺激10min后,收集细胞裂解物进行Western blotting分析

结果与意义:

Anti Siglec-8抗体和IL-5共刺激显著提高细胞死亡(坏死,而非凋亡)率。共刺激情况下,细胞外ERK1/2和MEK1磷酸化被显著提高;MEK1抑制剂阻碍共刺激诱导的死亡。ROS抑制剂能够防止共刺激诱导的 ERK磷酸化和细胞死亡的增加。进一步显示ROS是细胞共刺激ERK激活的上游调节子。

细胞治疗

Milliplex 在CAR-T细胞治疗中应用

Efficacy and toxicity management of 19-28z CAR T cell therapy in B cell acute lymphoblastic leukemia

Davila M L, Isabelle R, Xiuyan W, et al. Efficacy and toxicity management of 19-28z CAR T cell therapy in B cell acute lymphoblastic leukemia.[J]. Science Translational Medicine, 2014, 6(224):224ra25-224ra25.

研究背景：

在肿瘤的治疗中，CAR T细胞治疗是当前最有效的方法之一，但是在CAR T细胞治疗过程中也存在着一些副作用，细胞因子释放综合症（Cytokine release syndrome，CRS）是CAR-T细胞治疗中最常见也是最危险，最严重且可能致死的并发症，患者在输注 CAR-T 细胞后，T 细胞、B 细胞、NK细胞等释放大量的炎性介质（ 如细胞因子和趋化因子），触发急性炎症反应诱导上皮及组织损伤，导致微血管渗漏、心衰甚至死亡。因此对CAR T治疗患者细胞因子的监测非常重要。

实验设计：

研究中使用Milliplex多因子检测平台检测16例B细胞急性淋巴细胞白血病（B cell acute lymphoblastic leukemia，B-ALL））血清中39种细胞因子的水平，进行细胞因子释放综合症（CRS）评价。

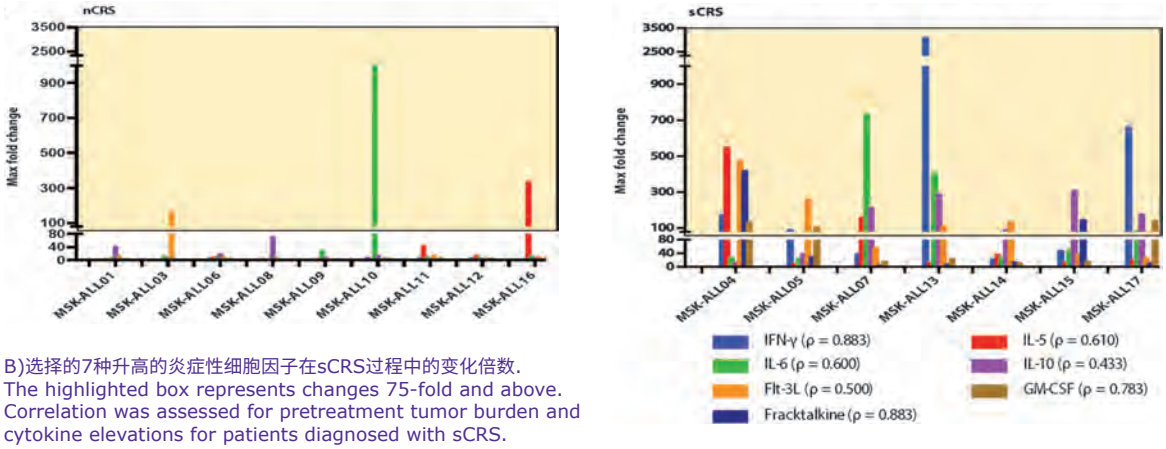
Table 3. Diagnostic criteria for sCRS secondary to CAR T cells.

Criteria for sCRS
Fevers for at least three consecutive days
Two cytokine max fold changes of at least 75 or one cytokine max fold change of at least 250
At least one clinical sign of toxicity such as hypotension (requiring at least one intravenous vasoactive pressor) or,
Hypoxia (PO_2 < 90%) or,
Neurologic disorders (including mental status changes, obtundation, and seizures)

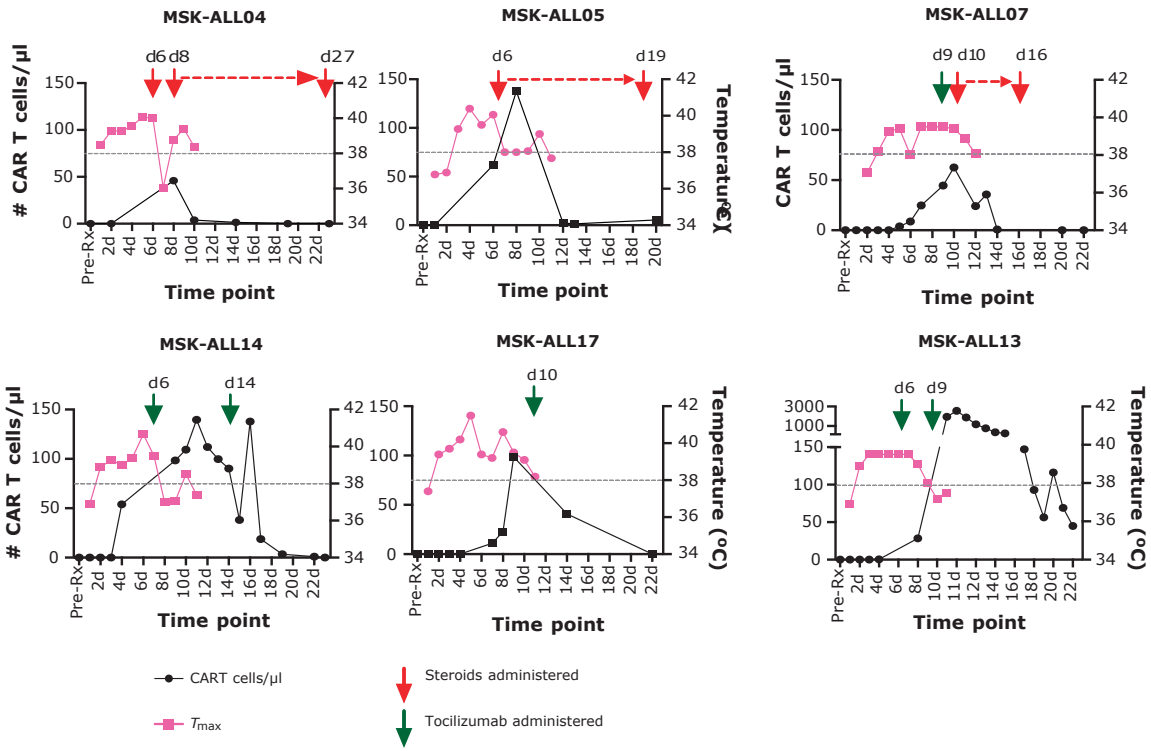
建立CRS 诊断标准包括：(i)发热至少持续3天，(ii)两种细胞因子浓度最高值至少升高75倍或一种细胞因子浓度最高值至少升高250倍，(iii)至少出现一种毒性临床症状如低血压（至少一项静脉血管压力），或缺氧（血氧浓度< 90%），或神经系统症状（包括神志改变，迟钝和癫痫发作）。

	sCRS							nCRS								
	MSK-ALL04	MSK-ALL05	MSK-ALL07	MSK-ALL13	MSK-ALL14	MSK-ALL15	MSK-ALL17	MSK-ALL01	MSK-ALL03	MSK-ALL06	MSK-ALL08	MSK-ALL09	MSK-ALL10	MSK-ALL11	MSK-ALL12	MSK-ALL16
IFN-γ	540.48	278.09	147.33	2846.75	125.64	90.90	2781.25	3.82	3.20	30.21	23.97	9.62	30.86	12.23	47.75	17.18
IL-5	1747.37	20.27	60.80	29.42	35.19	56.24	58.70	3.20	3.20	8.21	0.47	2.06	1.89	23.39	31.88	74.34
IL-6	638.39	201.99	621.27	8401.33	1336.70	341.78	625.28	13.97	33.29	54.57	59.31	271.39	17.88	16.19	258.15	31.87
IL-10	986.48	328.64	2019.73	3582.93	698.41	1829.88	10871.2	409.45	8.21	71.25	754.39	134.76	177.71	27.38	237.02	76.02
Flt-3L	1921.74	818.76	738.06	347.84	1184.86	657.72	920.67	410.88	507.17	231.71	434.25	50.23	94.90	235.75	56.45	234.41
Fracktalkine	1323.63	1723.25	305.11	227.97	471.73	454.93	437.09	24.01	30.00	429.71	82.12	73.04	173.24	70.78	977.76	128.94
GM-CSF	403.33	98.91	158.57	179.09	112.34	87.10	601.42	8.54	3.20	17.58	26.27	19.77	80.47	26.05	62.96	15.42

39种细胞因子的检测，发现可根据7种细胞因子在病人体内显著升高，这些因子和病人的临床症状一致，能够作为判断CRS的严重程度



B)选择的7种升高的炎症性细胞因子在sCRS过程中的变化倍数.
The highlighted box represents changes 75-fold and above. Correlation was assessed for pretreatment tumor burden and cytokine elevations for patients diagnosed with sCRS.



类固醇(steroids)和/或塔西单抗(tocilizumab)对CAR T细胞治疗过程中出现sCRS的治疗效果
Treated initial three sCRS patients with lymphotoxic high-dose steroids, >100mg daily of prednisone equivalent, rapidly reversed symptoms but concurrently ablated 19-28z CAR T cells . The IL-6R–blocking (mAb) tocilizumab may ameliorate sCRS rapid resolution of sCRS after IL-6R blockade reduced patients'fevers and sCRS symptoms within 1 to 3 days similar to steroid therapy, but not result in dampened expansion of the 19-28z CAR T cells

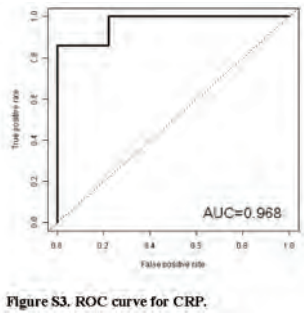


Figure S3. ROC curve for CRP.

CRP的ROC曲线:CRP ≥20 mg/dL列入诊断严重细胞因子释放综合征依据,以替代用细胞因子升高水平为依据的诊断。ROC 的AUC为0.968. 病人CRP≥20 mg/dL具有较高的发生CRS的风险(灵敏度 86%;特异性 100%).

结果与意义:

1:CAR T细胞具有非常好的治疗效果,整体完全缓解率88%。
2:建立CRS诊断标准,发现7种显著升高的细胞因子,可作为判断CRS的严重程度。
3:CRP可作为一个标志物用来判断对病人CRS干预的效果。
4:IL-6受体阻断剂塔西单抗(tocilizumab)可有效抑制CRS,类固醇药物也可抑制CRS,但对CAR-T的疗效也会造成影响,可作为tocilizumab无效的替代方案。
5:CAR-T细胞治疗对急性B淋巴细胞白血病非常有效,细胞因子释放综合症(CRS)为其主要副作用,可通过IL-6受体阻断剂进行辅助治疗。

小M有话说

该论文作者迈克尔·萨德莱恩(Michel Sadelain)是CAR T领域最杰出的科学家之一,也是CAR细胞嵌合抗原受体(chimeric antigen receptor)细胞的命名者。纽约斯隆凯特林癌症纪念中心(Memorial Sloan Kettering Cancer Center)细胞工程与基因转移研究中心(Center for Cell Engineering and Gene Transfer)的主任,朱诺(JUNO)公司联合创始人,针对淋巴细胞白血病CAR T细胞药物JCAR015项目负责人,JCAR015目前已获得FDA突破性疗法认证。

• 疫苗研究

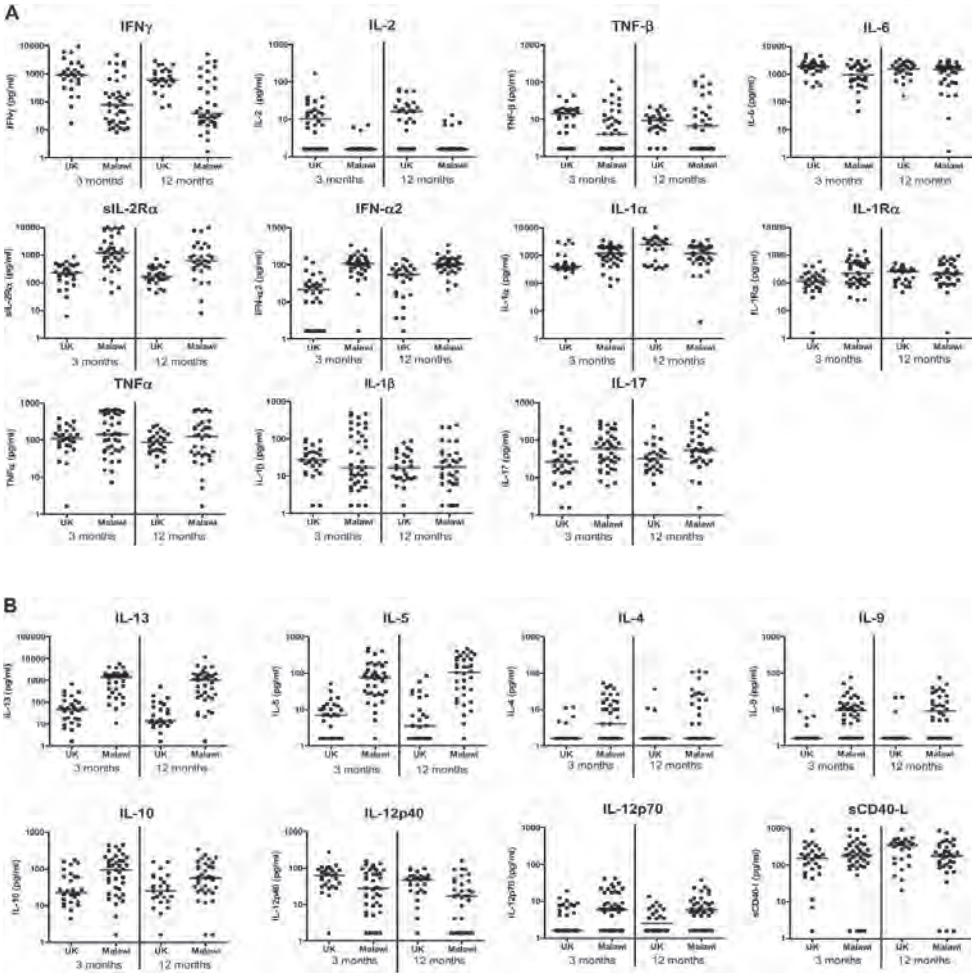
比较英国和马拉维(非洲)两个国家的初生婴儿接种卡介苗后免疫保护的差异

BCG Vaccination Induces Different Cytokine Profiles Following Infant BCG Vaccination in the UK and Malawi

BCG Vaccination Induces Different Cytokine Profiles Following Infant BCG Vaccination in the UK and Malawi. Lalor M K, Sian F, Patricia G S, et al. Journal of Infectious Diseases, 2011, 204(7): 1075–1085.

实验设计:

研究表明非洲马拉维的婴儿接种卡介苗后,免疫效果弱于与英国的初生婴儿。因次,采集两个国家接种卡介苗3个月以及12个月后的婴儿全血样本,通过Milliplex多因子检测平台同时检测血样中的42种细胞因子,对比不同细胞因子表达水平的差异。



血清中42种不同蛋白因子的检测:
A, Proinflammatory cytokines; B, T helper 2, regulatory, and T cell activation cytokines

结果与意义:

1:在两个国家接种婴儿的血清样本中,有27种细胞因子表达不同,其中7种因子在英国接种卡介苗的婴儿表达量较高,主要是Th1细胞相关的;20种因子在马拉维接种婴儿表达量较高,主要涉及不同的细胞因子种类,如促炎症因子、IL17、调节T细胞、Th2、趋化因子、生长因子相关。

2:实验表明,马拉维的婴儿会对卡介苗产生免疫反应,但是细胞因子表达情况与英国婴儿接种后不同。两个地区的婴儿的免疫后有可能存在两种不同的免疫保护途径。

3:Milliplex多因子检测平台可以同时检测多种细胞因子的表达水平,快速鉴定疫苗注射后的效果及免疫反应相关通路。

● 药物研发

药效评估

阿托伐他汀联合吸入性倍氯米松调节吸烟性哮喘的炎性唾液介质

Atorvastatin in combination with inhaled beclometasone modulates inflammatory sputum mediators in smokers with asthma

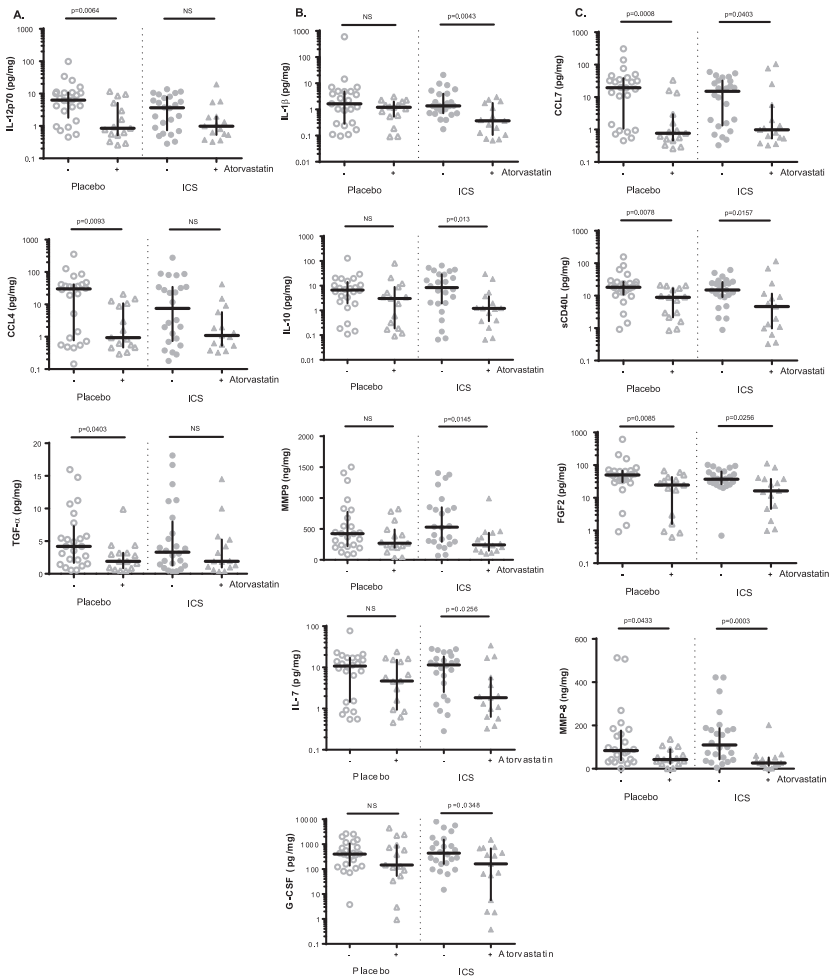
Thomson, N. C., et al. (2015). "Atorvastatin in combination with inhaled beclometasone modulates inflammatory sputum mediators in smokers with asthma." Pulm Pharmacol Ther 31: 1-8.

研究背景：

明确阿托伐他汀单独或联合皮质类固醇在唾液细胞因子，趋化因子和生长因子在哮喘发病机理作用，及与asthma control questionnaire (ACQ)和/或asthma quality of life questionnaire (AQLQ) 评分相关性。

实验设计：

39例患有不同程度哮喘的吸烟唾液样本，比较阿托伐他汀和安慰剂（4周），然后吸入倍氯米松（4周）。
Milliplex对唾液上清液中的35 种因子检测。



阿托伐他汀治疗，安慰剂，阿托伐他汀结合吸入型倍氯米松，或单独倍氯米松治疗后的唾液样本因子浓度.

结果与意义：

1：单独吸入倍氯米松，唾液因子浓度并不降低.阿托伐他汀和安慰剂相比唾液CCL7，IL-12p70，sCD40L，FGF-2，CCL4，TGF-alpha and MMP-8 浓度显著降低，当结合倍氯米松，和单独ICS相比，唾液MMP-8，IL-1beta，IL-10，MMP-9，sCD40L，FGF-2，IL-7，G-CSF和CCL7 浓度下降. 阿托伐他汀和吸入型皮质类固醇激素（ICS）中ACQ和/或AQLQ评分的升高与G-CSF，IL-7，CCL2和 CXCL8的降低相关.

2：在患有哮喘的吸烟人群中，通过阿托伐他汀单独或联合吸入倍氯米松短期治疗能够降低唾液中对吸入皮质类固醇无反应的部分细胞因子，趋化因子和生长因子的浓度。

药物毒性评估

大环内酯类抗生素抑制慢性阻塞性肺病唾液细胞细胞因子和趋化因子

Macrolide antibiotics broadly and distinctively inhibit cytokine and chemokine production by COPD sputum cells in vitro

Marjanović N, Bosnar M, Michielin F, et al. Macrolide antibiotics broadly and distinctively inhibit cytokine and chemokine production by COPD sputum cells in vitro[J]. Pharmacological Research, 2011, 63(5):389-97.

研究背景：

大环内酯类抗生素具有广泛抗炎活性对慢性阻塞性肺病（COPD）具有很好的治疗效果。明确其免疫调节活性。

实验设计：

从人COPD样本分离的细胞，研究阿奇霉素，克拉霉素，红霉素和罗红霉素刺激炎症因子的产生。比较大环内酯类与其他3种抗炎化合物：皮质类固醇地塞米松，PDE4抑制剂罗氟斯特和p38激酶抑制剂SB203580。

Table 3
Median concentrations with IQR (pg/ml) ofinflammatory mediators spontaneously generated during an overnight incubation of cells isolated from COPD patients (N = 60).

Analyte	Median (IQR)	Analyte	Median (IQR)
IL-1α	80 (56–137)	CCL20	495 (202–1647)
IL-1β	449 (171–814)	CCL22	150 (85–396)
IL-1ra	5305 (3152–7234)	CXCL1	4082 (1554–9210)
IL-6	10899 (4219–23528)	CXCL5	672 (221–2391)
IL-10	193 (77–721)	CXCL8	21199 (14085–54986)
TNF-α	533 (128–1245)	CXCL10	212 (82–551)
CCL2	168 (68–408)	G-CSF	1269 (559–2438)
CCL3	6306 (1846–10576)	GM-CSF	384 (204–943)
CCL5	157 (44–402)	PAI-1	30 (22–47)

COPD病人(N= 60)分离的细胞过夜培养自发产生的炎症介质的浓度 (Median concentrations with IQR, pg/ml)

Table 4
Summary profile ofinhibitory effects (according to LSD test at 5%) of azithromycin (AZM), clarithromycin (CAM), erythromycin (ERM), roxithromycin (RXM) at 50 μM or dexamethasone (DEX), roflumilast (ROF) and SB203580 (SB) at 1 μM on spontaneous production ofinflammatory mediators from COPD sputum cells.

Analyte	AZM	CAM	ERM	RXM	DEX	ROF	SB
IL-1 α	+	+	0	+	+	NT	NT
IL-1 β	++	++	0	++	+	+	+
IL-6	+	++	0	++	++	–	+
IL-10	+	++	0	++	+	NT	NT
TNF- α	+	++	0	++	+	+	+
CCL3	+	++	0	++	+	+	+
CCL5	+	++	0	++	+	+	+
CCL20	+	+	+	+	0	–	+
CCL22	+	+	0	+	0	0	0
CXCL1	+	+	0	+	+	0	+
CXCL5	+	++	0	++	–	–	+
CXCL8	+	+	0	+	+	0	+
G-CSF	+	++	0	++	0	0	0
GM-CSF	+	++	0	0	++	+	++
PAI-1	+	+	0	+	–	NT	NT

++: statistically significant inhibition ≥ 50%; +: statistically significant inhibition <50%; – : statistically significant increase; 0: no statistically significant effect; NT = not tested.

COPD病人唾液细胞中，50μM阿奇霉素(AZM)，克拉霉素(CAM)，红霉素(ERM)，罗红霉素(RXM) 或1μM地塞米松(DEX)，罗氟斯特(ROF)和SB203580 (SB) 对炎症介质自发产生的抑制作用(LSD test at 5%)。

结果与意义：

1：3种大环内酯类药物（阿奇霉素，克拉霉素和罗红霉素）的作用下，IL-1β, IL-6, IL-10, TNF-α, CCL3, CCL5, CCL20, CCL22, CXCL1, CXCL5和G-CSF浓度释放具有显著的降低。轻微抑制IL-1,CXCL8,GM-CSF 和PAI-1的产生。红霉素具有较弱的活性。定性与定量检测显示大环内酯类和其他化合物相比具有更确定的免疫调节效应，特别对趋化因子(CCL3, CCL5, CCL20, CCL22和CXCL5), IL-1, G-CSF 和 PAI-1的释放。

2：免疫调节因子的调节能进一步明确大环内酯类在COPD抗炎活性中的生物标志物。

• 妇产科研究

怀孕与非怀孕妇女子宫颈阴道分泌物免疫调节因子比较

Immunomodulatory factors in cervicovaginal secretions from pregnant and non-pregnant women: a cross-sectional study

Immunomodulatory factors in cervicovaginal secretions from pregnant and non-pregnant women: a cross-sectional study. Walter J, Fraga L, Orin M J, et al. BMC Infectious Diseases, 2011, 11 (4):1-7.

研究背景：

孕妇由于未知原因会增加HIV 感染风险。而黏膜免疫在HIV发病机理中的作用并不清楚。

实验设计：

用Milliplex多因子技术检测21例怀孕女性和24例非怀孕健康女性子宫颈阴道灌洗液(cervicovaginal lavages,CVL) 中 39 种免疫调节因子的浓度。发现怀孕与非怀孕妇女阴道分泌物中免疫调节因子区别，指导后续研究。

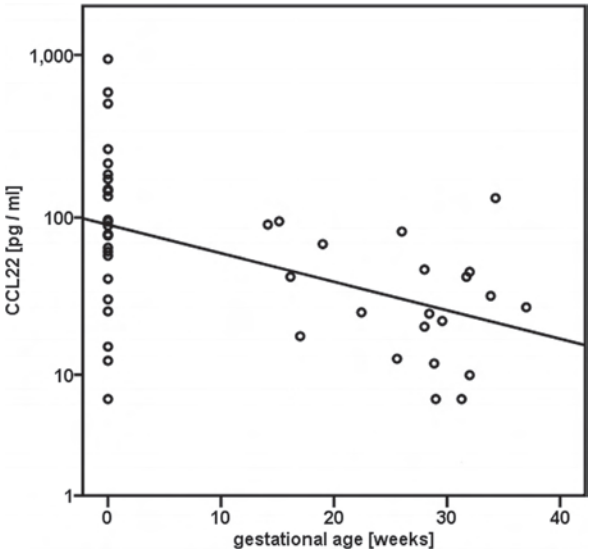


Figure 1 Scatter plot of CCL22 concentration in cervicovaginal lavages with gestational age among 21 pregnant and 24 non-pregnant women . Non-pregnant women were assigned a gestational age of 0 weeks.

21例怀孕和 24例非怀孕女性子宫颈阴道CCL22浓度的散点图.

结果与意义：

1:26种免疫调节因子在至少一半数量的子宫颈阴道灌洗液(CVL)样本中被检测到。孕妇CVL样本中CCL22浓度比非孕妇低3倍 (29.6 pg/ml versus 89.7 pg/ml)。CVL中CCL22的浓度与胎龄负相关，与年龄正相关。

2:怀孕和CCL22浓度降低相关。CCL22在HIV传播中的作用需要进一步实验研究。

3:Milliplex多因子检测平台可以同时检测几十种免疫调节因子，快速发现孕妇和非孕妇免疫调节因子表达水平的差异。指示和HIV传播可能相关的因子。

• 五官科和皮肤科

眼科疾病研究：

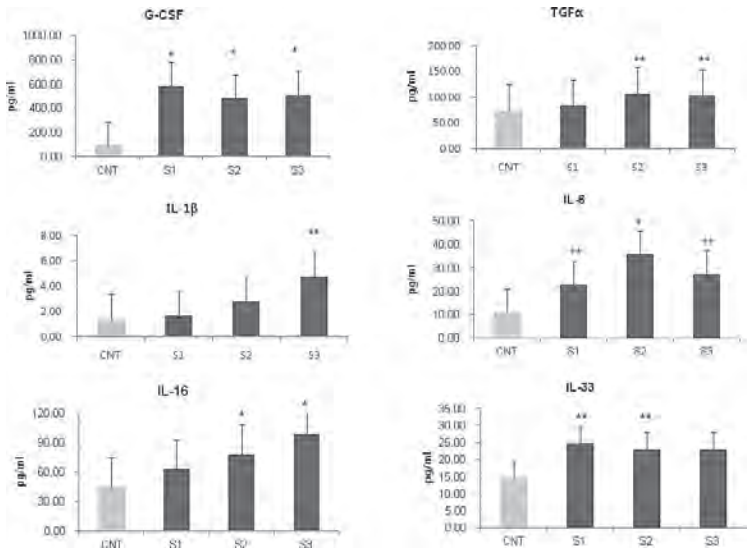
干眼症患者泪液中细胞因子和趋化因子表达高低与临床症状相关性分析

Correlations between tear cytokines, chemokines, and soluble receptors and clinical severity of dry eye disease

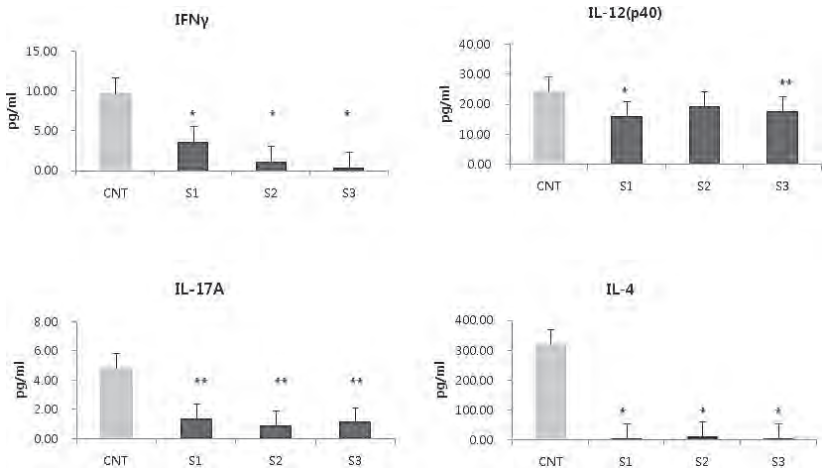
Correlations between tear cytokines, chemokines, and soluble receptors and clinical severity of dry eye disease. Na K S, Mok J W, Kim J Y, et al. [J]. Investigative Ophthalmology & Visual Science, 2012, 53(9):5443-50.

实验设计：

将133例病人和70例健康人群，根据干眼症（dry eye disease）发病程度分为4组，用Milliplex多因子检测平台对泪液中的细胞因子/趋化因子进行检测。



不同程度的干眼病人和对照组泪液细胞因子表达水平。干眼病人的IL-1b, IL-6, Il-16, IL-33, TGFα和 G-CSF表达水平显著升高。



不同程度的干眼病人泪液细胞因子IL-12 (p40), IFN-c, IL-17A和 IL-4的表达水平与对照组相比显著降低。

结果与意义：

1:干眼症人群IL-1b, IL-6, IL-16, IL-33, G-CSF, TGF-a，Fractalkine, MCP-1, MIP-1d, ENA-78, sIL-1RI, sgp 130, sIL-6R, sEGFR, sTNFR2 细胞因子显著升高，与干眼症临床严重性显著相关。

2:干眼症人群泪液中15种细胞因子升高，4种细胞因子降低。

3:IL-6 和 IL-1 b水平的升高是干眼症病人最早期的表现。

4:通过多因子联合检测快速鉴定干眼症，提高了鉴定的及时性和准确性。

皮肤科疾病

高通量分析酒渣鼻患者泪液和血清中炎症因子表达水平

Determination of Tear and Serum Inflammatory Cytokines in Patients with Rosacea Using Multiplex Bead Technology

Correlations between tear cytokines, chemokines, and soluble receptors and clinical severity of dry eye disease. Na K S, Mok J W, Kim J Y, et al. [J]. Investigative Ophthalmology & Visual Science, 2012, 53 (9):5443-50.Determination of Tear and Serum Inflammatory Cytokines in Patients with Rosacea Using Multiplex Bead Technology. Pinar T Y, Nilgun A, Banu B, et al. Ocular Immunology & Inflammation, 2013, 21(5):351-359.

实验设计：

用Milliplex多因子技术检测12例酒渣鼻未伴发眼病，20例酒渣鼻伴发眼病，22例健康人群中泪液与血清中IL-1a, IL-6, IL-8, IL-10, MCP-1,MIP-1a, EGF和 VEGF的表达水平。

TABLE 2. Comparison of tear cytokine levels in rosacea patients with and without ocular involvement and control subjects.

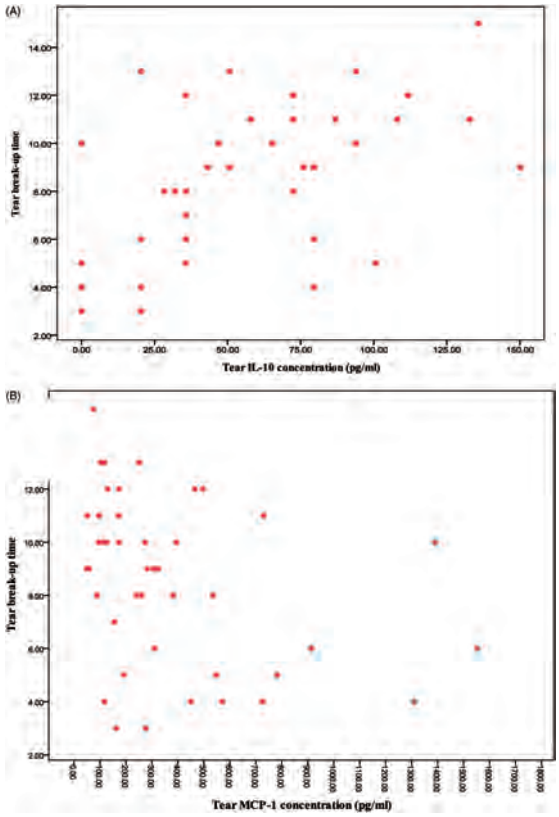
		Rosacea patients without ocular involvement (group 1)	Rosacea patients with ocular involvement (group 2)	Healthy subjects (group 3)	ρ
IL-1 α (pg/mL)	Mean±SD	34.84 ± 94.02	9.88 ± 23.04	66.27 ± 126.02	NS $^{\alpha,\beta,\delta}$
	Median	0	0	0	
	(Range)	(0–327.49)	(0–72.08)	(0–413.11)	
IL-6 (pg/mL)	Mean ± SD	12.72 ± 19.12	13.67 ± 27.36	24.15 ± 25.92	NS $^{\alpha,\beta,\delta}$
	Median	0	0	16.90	
	(Range)	(0–48.29)	(0–105.37)	(0–66.53)	
IL-8 (pg/mL)	Mean ±SD	426.63 ± 508.33	277.80 ± 301.90	275.47 ± 296.21	NS $^{\alpha,\beta,\delta}$
	Median	227.56	211.63	213.12	
	(Range)	(86.07–1872.27)	(43.55–1398.80)	(45.31–1474.98)	
IL-10 (pg/mL)	Mean ± SD	49.51 ± 38.33	38.36 ± 40.94	86.48 ± 36.85	0.008 $^{\alpha}$
	Median	35.78	26.25	75.96	0.001 $^{\beta}$
	(Range)	(0–135.87)	(0–150.55)	(35.78–192.56)	NS $^{\delta}$
MCP-1 (pg/mL)	Mean ± SD	516.83 ± 796.76	431.63 ± 380.60	489.62 ± 670.97	NS $^{\alpha,\beta,\delta}$
	Median	238.11	259.05	262.14	
	(Range)	(49.15–2803.83)	(95.38–1551.40)	(51.40–2427.76)	
MIP-1 α (pg/mL)	Mean ± SD	10.34 ± 24.22	26.69 ± 76.14	61.72 ± 168.19	NS $^{\alpha,\beta,\delta}$
	Median	0	0	0	
	(Range)	(0–66.44)	(0–311.56)	(0–782.57)	
VEGF (pg/mL)	Mean ± SD	466.72 ± 166.65	339.20 ± 94.95	524.88 ± 192.39	0.025 $^{\alpha}$
	Median	427.29	348.32	480.12	0.001 $^{\beta}$
	(Range)	(270.88–785.09)	(180.36–556.59)	(242.50–1069.44)	NS $^{\delta}$
EGF (pg/mL)	Mean ± SD	800.93 ± 385.55	727.12 ± 352.74	814.23 ± 567.15	NS $^{\alpha,\beta,\delta}$
	Median	795.44	706.94	758.05	
	(Range)	(297.53–1382.66)	(159.64–1414.10)	(204.66–2710.83)	

不同酒渣鼻病人（是否伴发眼部病变）和对照组样本的泪液细胞因子表达水平的比较

TABLE 3. Comparison of serum cytokine levels in rosacea patients with and without ocular involvement and control subjects.

		Rosacea patients without ocular involvement (group 1)	Rosacea patients with ocular involvement (group 2)	Control subjects (group 3)	ρ
IL-1 α (pg/mL)	Mean± SD	15.31 ± 14.69	27.12 ± 51.11	21.64 ± 20.92	NS $^{\alpha,\beta,\delta}$
	Median	12.39	9.42	17.49	
	(Range)	(0–49.01)	(0–215.86)	(0–57.53)	
IL-6 (pg/mL)	Mean± SD	6.19 ± 5.73	7.30 ± 14.34	5.92 ± 6.57	NS $^{\alpha,\beta,\delta}$
	Median	5.46	2.81	3.90	
	(Range)	(0–17.35)	(0–51.86)	(0–23.96)	
IL-8 (pg/mL)	Mean± SD	5.20 ± 7.86	2.36 ± 5.55	6.56 ± 10.35	.004 $^{\beta}$
	Median	3.06	0	3.98	NS $^{\alpha,\delta}$
	(Range)	(0–24.81)	(0–19.30)	(0–46.84)	
IL-10 (pg/mL)	Mean± SD	82.53 ± 87.79	54.63 ± 54.04	83.02 ± 59.59	NS $^{\alpha,\beta,\delta}$
	Median	48.20	40.04	97.36	
	(Range)	(2.36–306.80)	(0–207.82)	(8.18–192.52)	
MCP-1 (pg/mL)	Mean± SD	100.95 ± 78.88	64.82 ± 24.14	86.44 ± 60.50	NS $^{\alpha,\beta,\delta}$
	Median	67.17	64.71	65.33	
	(Range)	(27.31–288.03)	(31.76–116.74)	(22.33–230.61)	
MIP-1 α (pg/mL)	Mean± SD	17.71 ± 15.12	13.13 ± 22.21	18.73 ± 14.27	NS $^{\alpha,\beta,\delta}$
	Median	16.89	8.24	15.38	
	(Range)	(0–43.33)	(0–94.43)	(0–42.86)	
VEGF (pg/mL)	Mean± SD	107.55 ± 59.55	64.71 ± 65.51	83.84 ± 65.64	NS $^{\alpha,b,\delta}$
	Median	99.76	42.17	67.4	
	(Range)	(21.13–227.50)	(0–240.19)	(10.66–302.90)	
EGF (pg/mL)	Mean± SD	63.89 ± 66.58	65.77 ± 142.71	35.15 ± 32.91	NS α,β,δ
	Median	37.38	31.49	26.17	
	(Range)	(0–234.85)	(0–629.77)	(0–150.56)	

不同酒渣鼻病人（是否伴发眼部病变）和对照组样本的血清细胞因子表达水平的比较



(A)眼泪IL-10浓度和眼泪分解时间的相关性.
(B)眼泪MCP-1浓度和眼泪分解时间的相关性.

结果与意义：

1：疾病人群的泪液中IL-10 和VEGF水平显著低于健康人群；未伴发眼病的酒渣鼻患者血清中 IL-8 水平显著低于伴发眼病组。

2：眼泪分解时间（Tear breakup time）与IL-10正显著相关，与MCP-1负相关。

3：泪液IL-10（抗炎因子）水平降低导致炎性视角面（ocular surface environment），加剧炎症。后续增加伴发眼病的样本量确定细胞因子的作用。

● 系统医学

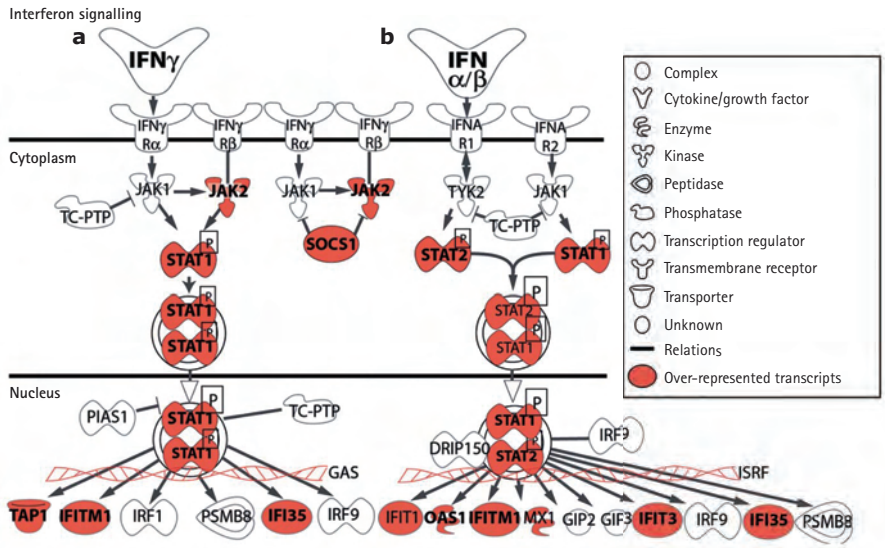
系统生物学方法被用来比较患有活性和休眠结核的患者与健康对照组所表达基因的转录谱。

An interferon-inducible neutrophil-driven blood transcriptional signature in human tuberculosis

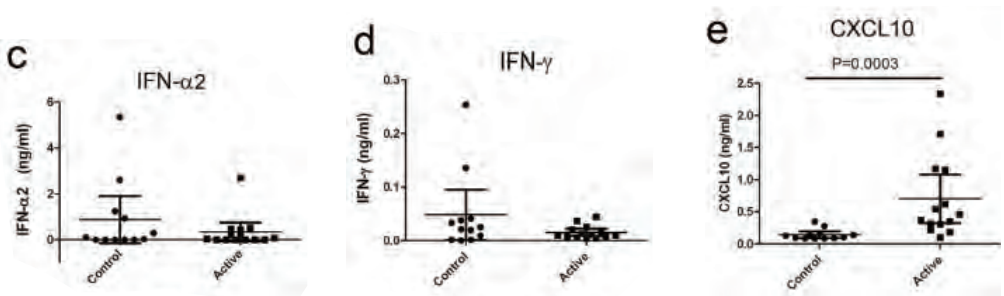
Berry M P R, Graham C M, McNab F W, et al. An interferon-inducible neutrophil-driven blood transcriptional signature in human tuberculosis[J]. Nature, 2010, 466(7309): 973-977.

实验设计：

Milliplex技术检测血清样本的63种细胞因子(cytokines),趋化因子(chemokines),可溶性受体(soluble receptors),生长因子(growth factors),粘附分子(adhesion molecules)和急性期蛋白(acute phase proteins)的表达水平,检测因子包括MMP-9, CRP, serum amyloid A, EGF, eotaxin, FGF-2, Flt-3 ligand, fractalkine, G-CSF, GM-CSF, GRO, IFN-a2, IFN-c, IL-10, IL-12p40, IL-12p70, IL-13, IL-15, IL-17, IL-1a, IL-1b, IL-1Ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, CXCL10 (IP10), MCP-1, MCP-3, MIP-1 a, MIP-1b, PDGF-AA, PDGF-AB/BB, RANTES, soluble CD40 ligand, soluble IL-2RA, TGF-a, TNF-a, VEGF, MIF, soluble Fas, soluble Fas ligand, tPAI-1, soluble ICAM-1, soluble VCAM-1, soluble CD30, soluble gp130, soluble IL-1RII, soluble IL-6R, soluble RAGE, soluble TNF-RI, soluble TNF-RII, IL-16, TGF-b1, TGF-b2 and TGF-b3.



Interferon-inducible gene expression in active TB.



IFN inducible gene expression is dominant in the TB transcriptional signature. c, Milliplex技术检测12 例健康对照和13例active TB病人的interferon-α2, and d, IFN-γ和 e, CXCL10 (IP10)的血清水平.

结果与意义：

1:筛选出血液中393种肺结核病的转录物

2:鉴定出86种肺结核标志物以和其它感染疾病进行区分

Milliplex在健康人群中应用

Milliplex 技术对于健康人群和老年人群血清细胞因子检测

Serum cytokine profiles in healthy young and elderly population assessed using multiplexed bead-based immunoassays

Kim, H. O., et al. (2011). "Serum cytokine profiles in healthy young and elderly population assessed using multiplexed bead-based immunoassays." J Transl Med 9: 113.

研究背景：

脂代谢和细胞因子是免疫细胞功能和分化的关键因子，这些因子的失调与多种疾病相关。

实验设计：

Milliplex技术检测55例（age >65）和55例（age <45）健康人群血清中22种细胞因子的表达水平。

Table 1. Correlation between age and serum cytokine concentration.

	Day 0			Day 7		
	ρ	R^2	p value	ρ	R^2	p value
PDGF-BB	**0.05**	4.84E-05	0.934	**-0.08**	5.33E-03	0.385
IL-1b	-0.16	2.10E-02	0.083	-0.21	2.64E-02	0.052
IL-1Rα	0.03	3.81E-04	0.816	0.007	1.03E-04	0.904
IL-2	not applicable			not applicable		
IL-4	0.12	7.92E-03	0.289	0.07	1.64E-03	0.630
IL-5	-0.01	2.33E-03	0.565	-0.008	2.96E-03	0.517
IL-6	-0.07	4.56E-03	0.421	-0.18	1.72E-02	0.117
IL-7	0.006	6.74E-05	0.922	0.01	1.46E-05	0.964
IL-8	0.05	6.78E-05	0.922	0.04	9.16E-03	0.254
IL-9	-0.01	5.04E-03	0.398	-0.13	3.04E-03	0.512
IL-10	-0.06	3.11E-02	0.334	-0.2	2.53E-04	0.850
IL-12p70	0.08	1.45E-05	0.964	0.007	2.58E-03	0.546
IL-13	0.07	2.28E-02	0.071	0.04	2.44E-03	0.557
IL-15	not applicable			not applicable		
IL-17	**0.08**	2.11E-03	0.585	**-0.02**	5.45E-04	0.781
Eotaxin	0.2	4.05E-02	0.0156*	0.17	3.62E-02	0.0224*
FGF-b	-0.23	2.61E-02	0.053	-0.27	3.73E-02	0.070
G-CSF	**0.08**	1.19E-03	0.681	**-0.03**	1.26E-03	0.673
GM-CSF	not applicable			not applicable		
IFN-γ	0.01	7.31E-03	0.308	0.01	9.25E-03	0.252
IP-10	**0.05**	4.96E-04	0.791	**-0.12**	5.02E-03	0.399
MCP-1	-0.17	2.94E-02	0.0399*	-0.25	3.63E-02	0.0223*
MIP-1α	-0.16	2.40E-02	0.064	-0.23	3.63E-02	0.062
MIP-1β	-0.06	1.42E-02	0.155	-0.21	3.51E-02	0.125
RANTES	0.1	2.37E-03	0.562	0.08	7.63E-04	0.742
TNF-α	-0.18	1.92E-02	0.098	-0.3	3.99E-02	0.106
VEGF	**0.05**	1.50E-03	0.645	**-0.03**	9.02E-04	0.721

Pvalue with * are significant (P<0.05)

In bold are highlighted spearman correlation that are different between Day 0 and Day 7

Results shown are ρ, R^2 values and p values calculated from Spearman correlation and linear regression for both Day 0 and Day 7.

doi: 10.1371/journal.pone.0076091.t001

不同年龄样本人群的免疫细胞因子平均基础临床值

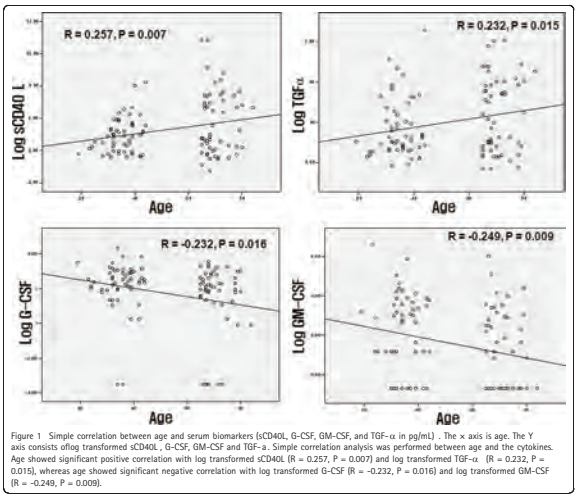


Figure 1 Simple correlation between age and serum biomarkers (sCD40L, G-CSF, GM-CSF, and TGF-α in pg/mL) . The x axis is age. The Y axis consists oflog transformed sCD40L , G-CSF, GM-CSF and TGF-a. Simple correlation analysis was performed between age and the cytokines. Age showed significant positive correlation with log transformed sCD40L (R = 0.257, P = 0.007) and log transformed TGF-α (R = 0.232, P = 0.015), whereas age showed significant negative correlation with log transformed G-CSF (R = -0.232, P = 0.016) and log transformed GM-CSF (R = -0.249, P = 0.009).

年龄和血清标志物 (sCD40L, G-CSF, GM-CSF和TGF-a in pg/mL)的相关性

结果与意义：

1：老年人群sCD40L 和TGF- a 细胞因子水平显著升高，老年人群G-CSF， GM-CSF和MCP-1细胞因子表达水平显著降低。

2：集中检测年龄相关显著变化的细胞因子及其他血清标志物及他们在年龄相关疾病形成中的潜在作用。

小M有话说

使用Milliplex技术不仅能够对不同类型的疾病样本进行检测，同样选择健康人群样本也可以进行分析，本研究针对不同年龄健康人群血清细胞因子表达水平的分析，对于一些疾病的进展具有潜在预测价值，能够作为疾病进展研究的血清标志物。

建立正常人群免疫炎症因子的参考值

Baseline Levels and Temporal Stability of 27 Multiplexed Serum Cytokine Concentrations in Healthy Subjects

Biancotto, A., et al. (2013). "Baseline levels and temporal stability of 27 multiplexed serum cytokine concentrations in healthy subjects." PLoS One 8(12): e76091.

研究背景：

细胞因子是检测免疫系统重要的标志物。

实验设计：

Milliplex技术检测144例健康人群血清样本27种细胞因子表达水平。

Figure 1

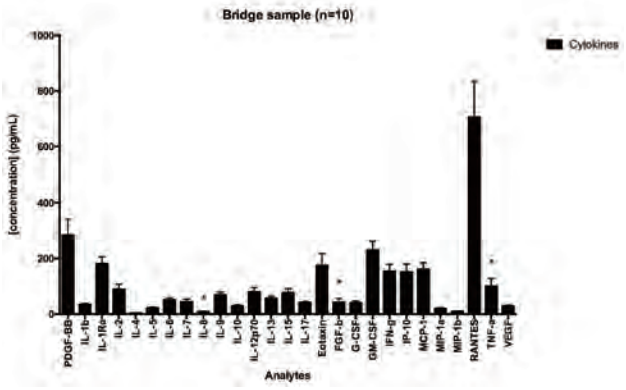


Figure 1. Cytokine concentrations in bridge sample. Results show mean concentrations of analytes for the bridge sample assayed in 10 plates with the bars representing the standard errors of the mean.
doi: 10.1371/journal.pone.0076091.g001

bridge样本细胞因子浓度.

Figure 2

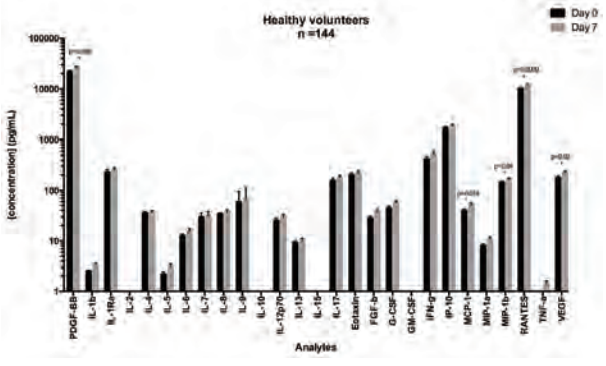


Figure 2. Mean concentrations for cytokines in serum samples at Day 0 and Day 7. Serum cytokine concentrations were measured on matched samples at Day 0 and Day 7. Paired T-tests were performed to measure the significance of the difference of the mean between Day 0 and Day 7. Cytokines for which %CV is higher than 20% are shown with "*".
doi: 10.1371/journal.pone.0076091.g002

第0天和第7天血清样本的平均细胞因子浓度

Figure 3

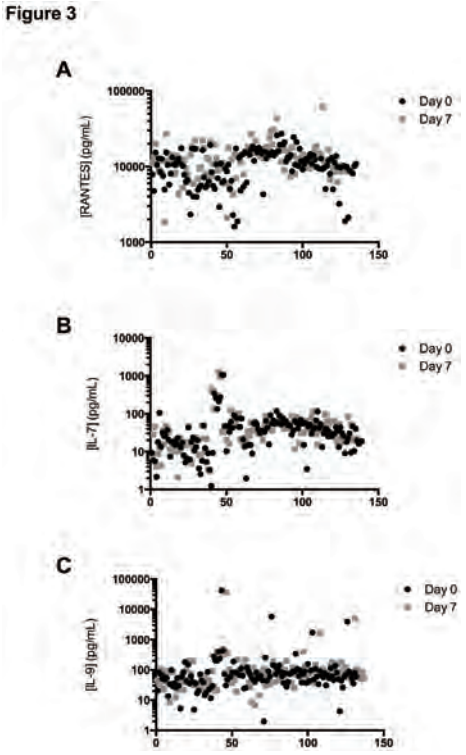


Figure 3. Concentrations for three cytokines in serum specimens measured at Day 0 and Day 7 for all 144 healthy volunteers. Serum cytokine concentrations were measured on samples at day 0 and day 7. Each data point corresponds to a matched measurement at Day 0 (black circle) and Day 7 (black square). These plots demonstrate 3 of the 27 analytes and display RANTES (A), IL-7 (B), IL-9 (C) concentrations.
doi: 10.1371/journal.pone.0076091.g003

144例健康血清样本在第0天和第7天的3种细胞因子浓度

结果与意义：

1：选择两个时间点（第0天和第7天）进行分析，显示3种细胞因子(IL-2，IL-15和GM-CSF) 低于检测下限，5种细胞因子(RANTES, MCP-1, VEGF, MIP-1 β和PDGF-BB) 血清浓度在第0天和第7天具有显著性区别。

2：提供正常人血清样本细胞因子浓度能够作为检测基线或标准。

小M有话说

当前多种疾病，包括自身免疫性，过敏性，肿瘤，心血管疾病，糖尿病，退行性疾病，感染性疾病等均认为和免疫与炎症反应具有密切关系。目前已建立了正常人群的生化和生理指标参考值，能够对于一些疾病进行很好的预测。如果进一步对正常人群进行免疫指标的大量检测建立健康人群免疫蛋白因子参考值也是具有非常重要的意义和价值，能够对当前多种重要疾病尤其是慢性病和老年病具有潜在的预测价值。而Milliplex高通量多蛋白因子分析技术中每例样本仅需微量体积便能获得多达40种免疫指标数值，在建立正常人群免疫指标参考值的方面具有非常明显的优势和应用价值。

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Pegu A, Asokan M, Wu L, et al.	Activation and lysis of human CD4 cells latently infected with HIV-1[J].	Nature communications, 2015, 6:8447	11.47	细胞因子试剂盒	病原：SIV，非人灵长类	PRCYTOMAG-41K
Lai R P J, Meintjes G, Wilkinson K A, et al.	HIV-tuberculosis-associated immune reconstitution inflammatory syndrome is characterized by Toll-like receptor and inflammasome signalling[J].	Nature communications, 2015, 6: 8451	11.47	HIV，结核 TLR	病原：病毒/细菌（传染病）	HCYTOMAG-62K
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Kobayashi T, Glatz M, Horiuchi K, et al.	Dysbiosis and Staphyloccus aureus Colonization Drives Inflammation in Atopic Dermatitis[J].	2015.43:998-1010 Immunity, 2015, 42(4):	21.56	过敏性皮肤炎，细胞因子	过敏性疾病：过敏性皮肤炎	MCYTOMAG-73K
Fitzpatrick AM, Higgins M, Holguin F, Brown LA, Teague WG.	The molecular phenotype of severe asthma in children.	756-766. J Allergy Clin Immunol. 2010; 125(4):851-857.e18.	11.476	哮喘	过敏：变态反应科	High Sensitivity Human Cytokine Milliplex
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Hall K D, Bemis T, Brychta R, et al.	Calorie for Calorie, Dietary Fat Restriction Results in More Body Fat Loss than Carbohydrate Restriction in People with Obesity[J].	Cell metabolism, 2015, 22(3): 427-436.	17.565	代谢类试剂盒	肥胖/代谢	HMMHMAG-34K
Dalmas E, Toubal A, Alzaid F, et al.	Irf5 deficiency in macrophages promotes beneficial adipose tissue expansion and insulin sensitivity during obesity[J].	Nature medicine, 2015, 21: 610–618.	27.363	肥胖，小鼠模型	肥胖/代谢	MCYTOMAG-70K
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Ariës IM, Jerchel IS, van den Dungen RE, van den Berk LC, Boer JM, Horstmann MA, Escherich G, Pieters R, den Boer ML.	EMP1, a Novel Poor Prognostic Factor In Pediatric Leukemia Regulates Prednisolone Resistance, Cellular Proliferation, Migration and Adhesion	Blood 2013; 122(21): 616	10.452	小儿白血病，细胞迁移，粘附	信号通路: 肿瘤，小儿白血病	
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Lu W, You R, Yuan X, et al.	The microRNA miR-22 inhibits the histone deacetylase HDAC4 to promote TH17 cell-dependent emphysema[J].	Nature immunology, 2015.16:1185–1194	20.004	肺气肿	消化内科：呼吸科，肺气肿	HCYTOMAG-61K
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Wenzel L, Osann K, Hsieh S, Tucker JA, Monk BJ, Nelson EL.	Psychosocial telephone counseling for survivors of cervical cancer: results of a randomized biobehavioral trial.	J Clin Oncol. 2015; 33(10):1171-9.	18.428	宫颈癌	肿瘤：宫颈癌，妇科	
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Younes A, Romaguera J, Fanale M, et al. P	hase I study of a novel oral Janus kinase 2 inhibitor, SB1518, in patients with relapsed lymphoma: evidence of clinical and biologic activity in multiple lymphoma subtypes[J].	Journal of Clinical Oncology, 2012, 30(33): 4161-4167. J Natl Cancer Inst 105(24):	18.428	肿瘤：淋巴瘤 Lymphoma	肿瘤：淋巴瘤 Lymphoma	
Shiels, M. S., et al.	Circulating inflammation markers and prospective risk for lung cancer.	1871-1880. Gut. 2009; 58(4):520-9.	15.161	肺癌	肿瘤：肺癌，呼吸科	
Chaput N, Louafi S, Bardier A, Charlotte F, Vaillant JC, Ménégaux F, Rosenzwajg M, Lemoine F, Klatzmann D, Taieb J.	Identification of CD8+CD25+Foxp3+ suppressive T cells in colorectal cancer tissue.		14.66	结直肠癌	肿瘤：结直肠癌，消化科	Human Cytokine Panel
Gunter M J, Wang T, Cushman M, et al.	Circulating Adipokines and Inflammatory Markers and Postmenopausal Breast Cancer Risk[J].	Journal of the National Cancer Institute, 2015, 107(9): djv169.	12.583	肿瘤：乳腺癌 Breast cancer	肿瘤：乳腺癌 Breast cancer	
Blanchard C, Stucke E M, Rodriguez-Jimenez B, et al.	A striking local esophageal cytokine expression profile in eosinophilic esophagitis[J].	Journal of Allergy and Clinical Immunology, 2011, 127(1): 208-217. e7.	11.476	肿瘤：食管癌 Esophagus cancer：嗜酸细胞性食管炎	肿瘤：食管癌 Esophagus cancer：嗜酸细胞性食管炎	
Hoffman LM, Foreman NK., et al.	Molecular sub-group-specific immunophenotypic changes are associated with outcome in recurrent posterior fossa ependymoma.	Acta Neuropathol. 2013; 127(5):731-45	10.762	室管膜瘤	肿瘤：室管膜瘤，神经	High Sensitivity Human Cytokine Milliplex
Blonska M, Zhu Y, Chuang H H, et al.	Jun-regulated genes promote interaction of diffuse large B-cell lymphoma with the microenvironment[J].	Blood, 2015, 125(6): 981-991.	10.452	肿瘤：淋巴瘤 Lymphoma	肿瘤：淋巴瘤 Lymphoma	
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Shiels MS, Chaturvedi AK., et al.	Cigarette Smoking and Variations in Systemic Immune and Inflammation Markers	JNCI J Natl Cancer Inst (2014) 106(11): dju294 doi:10.1093/jnci/dju294	15.161	吸烟，细胞因子	公共卫生，吸烟	
Miller W P, Srinivasan S, Panoskaltsis-Mortari A, et al.	GVHD after haploidentical transplantation: a novel, MHC-defined rhesus macaque model identifies CD28− CD8+ T cells as a reservoir of breakthrough T-cell proliferation during costimulation blockade and sirolimus-based immunosuppression[J].	Blood, 2010, 116(24): 5403-5418.	10.452	CD8 T 细胞，移植排斥	移植科	

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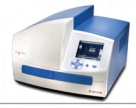
Luminex® platform 	Multiplex detection Flexible platform	Yes	pg	~25 µL	••	▬	Yes
Gyrolab® workstation 	Fully automated High precision	Yes	pg	< 5 µL	••	▭	Yes
Singulex Erenna® system 	Ultrasensitivity High performance	Yes	fg	5 -100 µL	•••	▭	Yes

• Good Performance •• Strong Performance ••• Superior Performance ▭ Not recommended ▬ Recommended

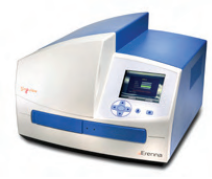
GyroMark™ HT Assays:

高通量，仅需1ul样本量，实现nano级检测。

Kit	Species	Catalog No.
Clusterin	Rat	GYRCLU-37K
Cystatin C	Rat	GYRCYSC-48K
GLP-1 Active	Multi-species	GYGLP1A-35K
GLP-1 Total	Multi-species	GYGLP1T-36K
Glucagon	Multi-species	coming soon!
Insulin	Human	GYHINS-14K
Insulin	Rat/Mouse	GYRMI-13K
KIM-1	Rat	GYRKIM1-20K
NGAL/Lipocalin-2	Rat	GYRNGAL-50K
β-2 Microglobulin	Rat	GYRB2M-49K

Description	Species	Status
IL-6	Human	Custom
TNFα	Human	Custom
IL-6	Mouse	Custom
TNFα	Mouse	Custom

试剂盒定制服务请联系:400-889-1988 或asiatechserv@merckgroup.com



ELISA和RIA:
目标蛋白定量，保证数据准确性和批次一致性。

Neuroscience: Neuropeptide & Neurodegenerative ELISA Kits

Get a complete picture of the complex, interconnected nervous system functions and dysfunctions with reliable quantification of biomarkers. Trust Merck Millipore's neuropeptide and neurodegenerative ELISA kits to precisely quantify soluble biomarkers in sera and lysates.

Neuroscience

Description	Species	Standard Curve Range	Sensitivity	Sample Volume	Cat. No.
α-Synuclein	Human, Mouse, Rat	3–60 ng/mL	3 ng/mL	100 µL	NS400
Amyloid β, 1-40	Human	16–500 pg/mL	4 pg/mL	50 µL	EZHS40
Amyloid β, 1-42	Human	16–500 pg/mL	5 pg/mL	50 µL	EZHS42
Amyloid β, Set	Human	Contains 1 each of EZHS40 and EZHS42			EZHS-SET
Amyloid β(Brain), 1-40	Human	16–500 pg/mL	4 pg/mL	50 µL	EZBRAIN40
Amyloid β(Brain), 1-42	Human	16–500 pg/mL	5 pg/mL	50 µL	EZBRAIN42
Amyloid β(Brain), Set	Human	Contains 1 each of EZBRAIN40 and EZBRAIN42			EZBRAIN-SET
BDNF (Brain-Derived Neurotrophic Factor)	Human, Rat	7.8–500 pg/mL	7.8 pg/mL	50 µL	CYT306
GFAP (Glial Fibrillary Acidic Protein)	Human, Mouse, Rat	1.5-100 ng/mL	1.5 ng/mL	100 µL	NS830
NGF (Nerve Growth Factor)	Mouse, Rat	10–1000 pg/mL	10-15 pg/mL	50 µL	CYT304
NPY (Neuropeptide Y)	Human	5-1000 pg/mL	2 pg/mL	50 µL	EZHNPY-25K
NPY (Neuropeptide Y)	Mouse, Rat	0.01-2 ng/mL	0.004 ng/mL	20 µL	EZRMNPY-27K
PEDF (Pigment Epithelium-Derived Factor)	Human	0.9–62.5 ng/mL	0.9 ng/mL	50 µL	CYT420
Phosphorylated Neurofilament, (pNF-H) Sandwich	Multi-species	0.0293–15 ng/mL	0.0585 ng/mL	1-10 µL	NS170
S100B	Human	2.7-2000 pg/mL	1.3 pg/mL	50 µL	EZHS100B-33K

Metabolic/Endocrine ELISAs

Get a complete picture of metabolism and endocrinology with sensitive, specific and reliable quantitation of circulating biomarkers. Our broad range of ELISA kits can help elucidate therapeutic mechanisms of action, reveal the possibility for early diagnosis of disease, predict toxicity, and more, particularly for studies of metabolic disease.

ELISAs for Circulating Metabolism and Endocrine Biomarkers

Description	Species	Standard Curve Range	Sensitivity	Sample Volume	Cat. No.	Bulk Packaging Cat. No.*
Adiponectin	Human	1.56–200 ng/mL	0.2 ng/mL	10 µL	EZHADP-61K	EZHADP-61BK
Adiponectin	Mouse	1–50 ng/mL	0.2 ng/mL	10 µL	EZMADP-60K	EZMADP-60BK
Adiponectin	Rat	3.125–200 ng/mL	0.4 ng/mL	10 µL	EZRADP-62K	
Amylin (active)	Human	1–100 pM	0.7 pM	50 µL	EZHA-52K	EZHA-52BK
C-Peptide	Human	0.2–20 ng/mL	0.05 ng/mL	10 µL	EZHCP-20K	EZHCP-20BK
C-Peptide	Canine	0.2-10 ng/mL	0.24 ng/mL	25 µL	EZCCP-47K	EZCCP-47BK
C-Peptide 2	Mouse, Rat	25–1600 pM	15.0 pM	20 µL	EZRMCP2-21K	
FGF-21	Human	31.25–2000 pg/mL	10.0 pg/mL	50 µL	EZHFGF21-19K	
FGF-21	Mouse, Rat	49.4–12,000 pg/mL	10.0 pg/mL	10 µL	EZRMFGF21-26K	
FGF-23	Human	9.9–2400 pg/mL	3.5 pg/mL	50 µL	EZHFGF23-32K	EZHFGF23-32BK
FGF-23	Mouse	0.137 - 100 ng/mL	0.69 pg/mL	20 µL	EZMFGF23-43K	
FGF-23	Rat	0.082-20 ng/mL	0.05 ng/mL	50 µL	EZRFGF23-42K	
Ghrelin (active)	Human	25–2000 pg/mL	15.0 pg/mL	20 µL	EZGRA-88K	EZGRA-88BK
Ghrelin (active)	Mouse, Rat	25–2000 pg/mL	8.0 pg/mL	20 µL	EZRGRA-90K	
Ghrelin (total)	Human	100–5000 pg/mL	50.0 pg/mL	20 µL	EZGRT-89K	EZGRT-89BK
Ghrelin (total)	Mouse, Rat	0.1–10 ng/mL	0.04 ng/mL	20 µL	EZRGRT-91K	
GIP (total)	Human	8.2–2000 pg/mL	4.2 pg/mL	20 µL	EZHGIP-54K	EZHGIP-54BK
GIP (total)	Mouse, Rat	8.2–2000 pg/mL	4.2 pg/mL	10 µL	EZRMGIP-55K	EZRMGIP-55BK
GLP-1 (active)	Multi-species	2–100 pM	1.0 pM	100 µL	EGLP-35K •	EGLP-35BK
GLP-1 High Sensitivity (active) Δ	Multi-species	See data sheet	0.14 pM	50 µL	**EZGLPHS-35K** ••	EZGLPHS-35BK
GLP-1 (total)	Multi-species	4.1-1000 pM	1.0 pM	20-50 µL	EZGLP1T-36K	EZGLP1T-36BK
GLP-2	Multi-species	1-64 ng/mL	0.3 ng/mL	50 µL	EZGLP2-37K	

* Bulk packaging now available on select kits – more environmentally friendly and saves space (10 kit equivalent).

• Please consider using the GLP-1 High Sensitivity Assay, EZGLPHS-35K

•• Preferred assay for measuring GLP-1 (active)

Δ Chemiluminescent assay

ELISAs for Circulating Metabolism and Endocrine Biomarkers (continued)

Description	Species	Standard Curve Range	Sensitivity	Sample Volume	Cat. No.	Bulk Packaging Cat. No.*
Glucagon Δ	Human, Mouse, Rat	0.02-2 ng/mL	0.003 ng/mL	150-300 µL	EZGLU-30K	EZGLU-30BK
Growth Hormone	Mouse, Rat	0.7–50 ng/mL	0.07 ng/mL	10 µL	EZRMGH-45K	EZRMGH-45BK
Insulin	Human	2–200 µU/mL	1.0 µU/mL	20 µL	EZHI-14K	EZHI-14BK
Insulin	Rat, Mouse	0.2–10 ng/mL	0.1 ng/mL	10 µL	EZRMI-13K	EZRMI-13BK
Insulin (Animal serum free)	Human	2–200 µU/mL	0.85 µU/m	20 µL	EZHIASF-14K	
Leptin	Canine	0.78–50 ng/mL	0.21 ng/mL	20 µL	EZCL-31K	
Leptin	Mouse	0.2–30 ng/mL	0.05 ng/mL	10 µL	EZML-82K	EZML-82BK
Leptin	Rat	0.2–30 ng/mL	0.08 ng/mL	10 µL	EZRL-83K	EZRL-83BK
Leptin "Dual Range"	Human	0.5–100 ng/mL	0.2 ng/mL	25 µL	EZHL-80SK	EZHL-80BK
Omentin-1	Human	2-200 ng.mL	0.23 ng/mL	20 µL	EZHØMNTN1-29K	
Pancreatic Polypeptide	Human	12.6–3000 pg/mL	12.3 pg/mL	50 µL	EZHPP-40K	EZHPP-40BK
Procollagen Type IIA N-Propeptide (PIIANP)	Human	lot dependent	30.0 ng/mL	5 µL	EZPIIANP-53K	
Proinsulin (total)	Human	2–200 pM	0.5 pM	20 µL	EZHPI-15K	EZHPI-15BK
PYY (total)	Human	10–2000 pg/mL	6.5 pg/mL	20 µL	EZHPYYT66K	
RBP4	Human	0.14–100 ng/mL	0.07 ng/mL	10 µL	EZHRBP4-18K	
Resistin	Human	0.16–5 ng/mL	0.02 ng/mL	20 µL	EZHR-95K	EZHR-95BK
SAA-3	Mouse	0.078-5 µg/mL	0.078 µg/mL	10 µL	EZMSAA3-12K	

Cytokine / Chemokine ELISA Kits

Cytokines are soluble proteins and peptides that modulate activities of cells and tissues, under both normal and pathological conditions. Merck Millipore's high-quality, cost-effective cytokine/chemokine ELISAs provide consistent and reliable measurements for your studies of inflammation, immune response, metabolism, neurological disorders and more.

ELISAs for Circulating Cytokines

Description	Species	Cat. No.
CRP	Human	CYT298
CRP	Rat	CYT294
IFN γ	Human	EZHIFNG
IFN γ	Mouse	EZMIFNG
IL-1 β	Human	EZHIL1B
IL-2	Human	EZHIL2
IL-2	Mouse	EZMIL2
IL-4	Human	EZHIL4
IL-4	Mouse	EZMIL4
IL-6	Human	EZHIL6
IL-6	Mouse	EZMIL6

Description	Species	Cat. No.
IL-6	Rat	EZRIL6
IL-8	Human	EZHIL8
IL-10	Human	EZHIL10
IL-10	Mouse	EZMIL10
IL-12(p70)	Human	EZHIL12
IL-13	Human	EZHIL13
IL-15	Human	EZHIL15
IL-17A	Rat	EZRIL17A
IL-17F	Mouse	EZMIL17F
TNF- α	Human	EZHTNFA
TNF- α	Mouse	EZMTNFA
TNF- α	Rat	EZRTNFA

Cell Signaling ELISAs

STAR (Signal Transduction Assay Reaction) ELISA kits are a fast, sensitive method to for measuring relative levels of total and phosphorylated signaling proteins with phospho-specific antibodies. Easily quantitate the phosphorylation states of key signaling proteins, second messengers transmitting intracellular signals and apoptosis pathway proteins using these kits in less than five hours with minimal hands-on time.

STAR ELISAs

Description	Cat. No.
cAMP HTS (5X)	17-518
cAMP HTS	17-418
ERK 1/2	17-463
Phospho-Akt (Ser473)	17-457
Phospho-EGFR (Tyr1173)	17-461
Phospho-ERK1/2 (T183/Y187)	17-464
Phospho-I κ B (Ser32)	17-486

Extracellular Matrix (ECM)

Gain deeper insights into cell adhesion, migration, differentiation, invasion and survival by quantitating circulating ECM proteins using our sensitive, specific and reliable ECM ELISA kits.

ECMs

Description	Species	Cat. No.
Quantimatrix Fibronectin	Human	ECM300
Quantimatrix Laminin	Human	ECM310
E-Selectin	Human	ECM330
ICAM-1	Human	ECM335
VCAM-1	Human	ECM340
SCD26	Human	ECM345
MMP-2	Human	ECM492
MMP-9	Human	ECM494
TIMP-1	Human	ECM496
TIMP-2	Human	ECM498

Radioimmunoassays (RIAs)

RIAs have long been considered a valuable, economical and accurate way to measure protein concentration. However, as many researchers move away from using radioactive material, we would like to recommend that you consider using our ELISA or MILLIPLEX® **MAP** kits for you research needs.

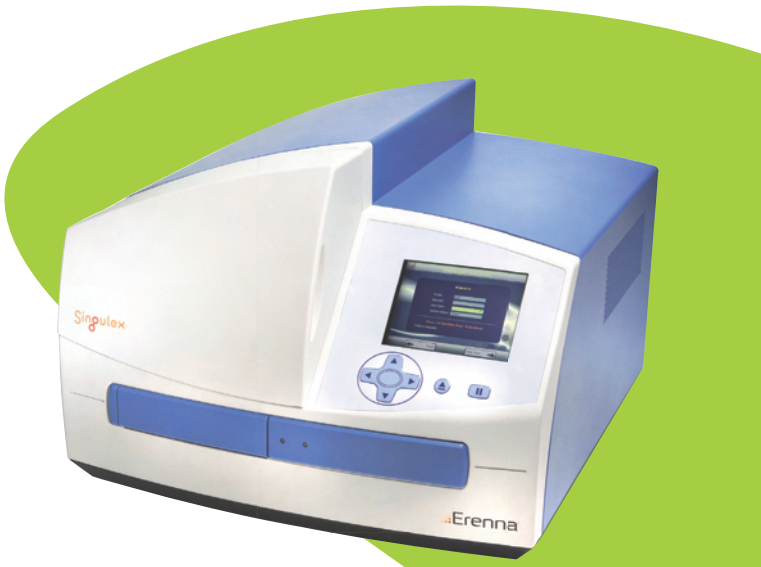
RIAs

Description	Species	Standard Curve Range	Sensitivity	Sample Volume	Cat. No.
Adiponectin	Human	lot dependent	1 ng/mL	5 µL	HADP-61HK
C-Peptide	Canine	0.156–20 ng/mL	0.15 ng/mL	50 µL	CCP-24HK
C-Peptide	Human	0.1–5 ng/mL	0.1 ng/mL	50 µL	HCP-20K
Ghrelin (active)	Human	lot dependent	7.8 pg/mL	50 µL	GHRA-88HK
Ghrelin (total)	Human	lot dependent	93 pg/mL	50 µL	GHRT-89HK
GLP-1 (active)	Multi-species	10–500 pM	3 pM	300 µL	GLP1A-35HK
GLP-1 (total)	Multi-species	10–1000 pM	3 pM	300 µL	GLP1T-36HK
Glucagon	Multi-species	20–400 pg/mL	20 pg/mL	50 µL	GL-32K
Insulin	Porcine	2–200 µU/mL	2 µU/mL	50 µL	PI-12K
Insulin	Rat	0.1–10 ng/mL	0.1 ng/mL	50 µL	RI-13K
Insulin LisPro	Multi-species	2.5–250 µU/mL	2.5 µU/mL	100 µL	LPI-16K
Insulin (sensitive)	Rat	0.02–1 ng/mL	0.02 ng/mL	50 µL	SRI-13K
Insulin Specific	Human	2-200 µU/mL	2 µU/mL	50 µL	HI-14K
Leptin	Human	0.5–100 ng/mL	0.5 ng/mL	50-100 µL	HL-81K
Leptin	Multi-species	1–50 ng/mL	1 ng/mL	50 µL	XL-85K
Leptin (sensitive)	Human	0.05–10 ng/mL	0.05 ng/mL	50 µL	SHL-81K
Proinsulin	Human	2–100 pM	2 pM	100-200 µL	HPI-15K
PYY	Mouse, Rat	lot dependent	15.6 pg/mL (78.1 pg/mL)	100 µL (20 µL)	RMPYY-68HK
PYY (3-36)	Human	lot dependent	20 pg/mL	<100 µL	PYY-67HK
PYY (total)	Human	lot dependent	10 pg/mL	<100 µL	PYYT-66HK

Erenna®单分子免疫检测平台

生物标志物检测突破性技术，灵敏度高达到ELISA的1000倍

Erenna®单分子免疫检测技术是蛋白生物标志物检测领域的突破性新技术。利用激光聚焦于爱里斑中单个荧光标记分子，人类首次实现了在单分子水平对蛋白进行计量，并造就了1000倍于ELISA技术的超高检测灵敏度。Erenna®单分子检测技术具备宽至4个log的大动态检测范围，可根据靶标丰度和成本灵活选择实验方案，便于自行开发检测试剂盒，接近于ELISA的易用性等特征。该技术已被广泛应用于多种疾病生物标志物的检测，包括心血管疾病，炎症，糖尿病，神经疾病，癌症等等，使研究者对生物标志物的应用和认识达到了全新的高度。更重要的是，针对创新性生物标志物的研究，Erenna®免疫检测系统提供工具，帮助研究者便捷地自行开发和优化检测试剂盒，实现全新生物标志物的高效率检测。默克的Erenna®仪器平台、试剂盒以及专家定制化服务为疾病和生物标志物研究提供三位一体的研究工具，必将加速和助力转化医学研究。



Erenna®单分子检测技术的主要特点：

1. 突破性的超高检测灵敏度

Erenna®单分子检测技术与ELISA操作一样简便，但灵敏度可达到ELISA的约1000倍，成功实现浓度在fmol级别蛋白靶标的检测。高能量的激光通过爱里斑聚焦于溶液里的单个荧光素标记二抗分子，产生的荧光闪烁进行数字化计量，从而实现“单分子检测”。灵敏度远高于传统ELISA，Multiplex等技术的全新单分子检测方法使种类远多于已知蛋白的未知蛋白靶标检测成为现实，将带来全新的基础和转化医学新发现。

2. 宽至4个log的大动态检测范围

Erenna®动态检测范围超过4个log，有利于蛋白靶标表达量存在巨大差异的样本进行同时检测。

3. 根据靶标丰度灵活选择实验方案

Erenna®既可使用磁珠又可使用普通96孔板作为抗体包被介质。在灵敏度和成本方面取得了巧妙平衡。

4. 便于自行开发检测试剂盒

开创性的新技术往往会应用于开创性的工作。如果检测的是全新的标志物，默克提供整套的试剂盒开发工具，可在极短时间内开发新检测试剂盒。

Plate-Based Discovery Immunoassay Kits

Analyte	Catalog No.	LLoQ (pg/mL)	Sample Type
Mouse IL-4	03-0136-00	0.49	Serum
Mouse IL-5	03-0132-00	0.24	Serum
Mouse IL-10	03-0134-00	6.2	Serum
Mouse IL-13	03-0133-00	3.91	Serum
Mouse IL-17A	03-0123-00	0.98	Serum
Mouse IL-17F	03-0125-01	0.49	Serum
Mouse IL-21	03-0126-00	4.9	Serum
Mouse IL-22	03-0127-00	100	Serum
Mouse TNF-α	03-0137-00	0.49	Serum

2016年 Milliplex讲座，欢迎预约！

讲座标题	主要内容
蛋白液相芯片检测平台（Milliplex） 在精准/转化医学领域的应用(前沿科学系统讲座)	蛋白多因子检测Milliplex技术在精准/转化医学如：新型细胞治疗CAR-T、癌症、感染与免疫性疾病、神经退行性疾病、代谢疾病等领域，以及疫苗评估，药物筛选等的应用实例分析；为疾病的预防，早期诊断和个体化治疗提供新的策略。
蛋白液相芯片检测（Milliplex）技术如何快速发表文章 —— 适用多学科，多方向和多领域	1. 成功发表文章的核心要素 2. Milliplex发表文章的优势 3. 应用Milliplex技术设计课题，操作实验及分析结果 4. Milliplex技术撰写文章模板大全（经典文献分享）
蛋白液相芯片检测（Milliplex）技术在CAR T细胞治疗中应用的最新进展 —— CAR T细胞治疗细胞因子释放综合症(CRS)必备检测方法	1.CAR T细胞治疗技术的背景、原理和发展 2.CAR T细胞治疗国内外科研和行业最新进展 3.CAR T细胞治疗中CRS的检测，预防和治疗 4.Milliplex技术原理及在CRS检测中的优势
蛋白液相芯片检测（Milliplex）技术在医学中应用 （基础研究和临床研究提供专业性讲座）	基础医学：生化与分子；药理学；免疫学；病原生物学；神经生物学；细胞生物学；药学；流行病学；公共卫生学；运动医学等…… 临床研究科室：血液病科；消化科；心血管科；风湿病科；儿科；神经科；肾脏病科；呼吸科；皮肤科；肿瘤科；感染科；变态反应科；骨科；口腔科；耳鼻喉；眼科；妇产科；移植科；检验科；细胞治疗等……

网络课堂：
如何用Milliplex平台快速发文章

- 文章成功发表的要素？
- 有哪些资源可以利用？
- 有哪些研究方向思路？
- 如何设计课题？
- 如何操作实验？
- 如何分析结果？
- 如何撰写文章？

主讲人：默克生命科学部门应用科学家 张涛博士

讲座时长：20分钟

http://vclub.biomart.cn/webinar/Milliplex

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