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LMP1 羧基端活化区 3 对鼻咽癌干细胞 SP18 迁移与侵袭的影响 *

肖 娟[2] 张志伟[1, 3]** 伍石华[1, 4] 刘重元[1] 唐 薇[1]
赵 强[3, 5] 雷明生[6] 杨代水[6]

([1] 南华大学医学院肿瘤研究所，肿瘤细胞与分子病理学湖南省高校重点实验室，衡阳 421001；
[2] 南华大学附属第二医院耳鼻喉科，衡阳 421001；[3] 湖南省胃癌研究中心，衡阳 421001；
[4] 邵阳医学高等专科学校附属医院病理科，邵阳 422000；[5] 南华大学附属第一医院病理科，衡阳 421001；
[6] 南华大学医学院临床医学卓越医师班，衡阳 421001)

摘要 为了观察潜伏性膜蛋白 1(LMP1)羧基端活性区 3($CTAR_3$)对鼻咽癌干细胞 SP18 迁移与侵袭的影响，本研究通过建立稳定表达 LMP1 及 $CTAR_3$ 突变型 LMP1($LMP1^{\Delta 252\text{-}351}$)的 SP18 细胞系(即 SP18-LMP1 和 SP18-$LMP1^{\Delta 252\text{-}351}$)，观察 LMP1-$CTAR_3$ 缺失突变后对 SP18 细胞增殖、迁移与侵袭的影响．采用基因芯片分析 SP18-LMP1 和 SP18-$LMP1^{\Delta 252\text{-}351}$ 间的差异表达基因，并验证基因的表达，用生物信息学分析差异表达基因间的相互关系．结果显示：a. SP-$LMP1^{\Delta 252\text{-}351}$ 细胞生长速度较 SP-LMP1 细胞明显变缓，克隆形成和迁移与侵袭能力降低(n=3，P < 0.05)；b. 鉴定出 LMP1 羧基端 $CTAR_3$ 影响 SP18 细胞迁移与侵袭的 18 个基因(其中表达上调基因 13 个，下调基因 5 个)，经荧光定量 PCR 验证与基因芯片检测结果基本一致．c. 13 个差异基因间相互联系，网络节点联系最多的基因是 FN1、MMP14、THBS1、ITGA2、IL1B 和 IL6 基因．结果提示，LMP1 羧基端 $CTAR_3$ 可能通过调节 FN1、MMP14、THBS1、ITGA2、IL1B 和 IL6 基因的表达，发挥其促鼻咽癌干细胞 SP18 细胞迁移与侵袭的功能．

关键词 鼻咽癌干细胞 SP18，LMP1，羧基端活性区 3，基因芯片，迁移与侵袭
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EB 病毒(Epstein-Barr virus，EBV)与鼻咽癌的发生与发展密切相关[1]，其编码的潜伏性膜蛋白 1 (latent membrane protein，LMP1)是公认的病毒基因组编码，具有促细胞癌变和转移作用的瘤蛋白[2]，但其致病机理仍有待进一步研究．LMP1 羧基端有两个活性区域(carboxyl terminal activating region，CTAR)，即 $CTAR_1$、$CTAR_2$ 和 $CTAR_3$，分别经 NF-κB、AP-1 和 JAK3 信号传导通路参与诱导细胞的恶性转化[3]．肿瘤组织中数量极少的肿瘤干细胞具有顽强的生存能力，决定肿瘤发生、发展和转移，被认为是肿瘤发生和复发的根源[4-5]．目前，LMP1 与鼻咽癌干细胞的相互联系及其在鼻咽癌(nasopharyngeal carcinoma，NPC)发生、发展及转移中的作用作用尚不清楚．

1 材料与方法

1.1 材料

1.1.1 质粒

pLNSX-LMP1(含全长 1.95 kb 野生型 LMP1)和

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** 通讯联系人.
Tel: 0734-8281510, E-mail: nhdxzzw@qq.com
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pLNSX-LMP1$^{\Delta 232\text{-}351}$(第三个活性区域缺失，含1.59 kb的LMP1)逆病毒质粒由中南大学肿瘤研究所贺智敏教授惠赠[6-7].

1.1.2 细胞

鼻咽癌干细胞SP18细胞株[8]，由中山大学肿瘤防治中心惠赠，用含5%小牛血清(购自杭州四季青公司)的DMEM(Gibco BRL公司)培养基培养，传代消化所用胰酶和EDTA均系Gibcol BRL产品.

1.1.3 试剂及基因芯片

Transwell小室(3428型)为Corning公司产品，Matrigel基质胶(5 g/L)为BD公司产品. AMV Reverse Transcription试剂盒和PCR系列均购自Promega公司. G418和Liperfect2000脂质体购自Invitrogen公司，单克隆抗体(一抗和二抗)购自Zymed Ltd，其他化学和生化试剂均为Sigma产品. 基因芯片为Agilent Microarray Scanner(G2505B)扫描芯片，购自上海伯豪生物公司.

1.1.4 引物

本研究所用引用如表1所示.

Table 1　Primer sequences used in fluorescent Real-time quantitative RT-PCR

Gene	Sequence(5′→3′)	Product size/bp
FN1	S 5′ cagtgggagacctcgagaag 3′	169
	AS 5′ gtccctcggaacatcagaaa 3′	
MMP14	S 5′ cagagaaggcacacaaacga 3′	172
	AS 5′ cactggtgagacaggcttga 3′	
ITGA2	S 5′ gtgcctttggacaagtggtt 3′	170
	AS 5′ ggccacttgattgttttgct 3′	
THBS1	S 5′ aaaggataattgccccaacc 3′	177
	AS 5′ cggtctcccacatcatctct 3′	
β-Actin	S 5′ catcgtgatggactctggtg 3′	213
(Interior control)	AS 5′ agggcaacatagcacagctt 3′	

S: Sense; AS: Anti-sense.

1.2 方法

1.2.1 逆转录病毒制备和SP18细胞感染

参考文献[6-7]，建立稳定产逆病毒的PA317细胞，浓缩收集逆病毒液. 将SP18细胞种入6孔板培养，分别用RV-LMP1和RV-LMP1$^{\Delta 232\text{-}351}$逆病毒和8 mg/L聚凝胺37℃孵育(感染)SP18细胞2次(3～4 h/次，间隔8～12 h/次)，400 mg/L G418筛选2～3周，汇合克隆扩大培养，建成稳定传代的转染细胞系(SP18-LMP1和SP18-LMP1$^{\Delta 232\text{-}351}$). 上述细胞用免疫荧光检测LMP1的表达.

1.2.2 免疫荧光试验

制备细胞爬片，用甲醇与丙酮(1∶1)固定、洗片、干燥后用抗LMP1一抗(1∶500)标记1 h(37℃)，洗片后用FITC标记的羊抗鼠二抗标计1 h(37℃)，洗涤后甘油封片，于荧光显微镜下观察，拍照.

1.2.3 绘制生长曲线

将SP18-LMP1和SP18-LMP1$^{\Delta 232\text{-}351}$细胞(5×10^3)接种于96孔板中，每组设3个平行孔，隔天用MTT法对细胞数进行检测，每次重复测量3次，取均值代表测量值，用校正值(每次测量值与第1天的测量值之商)代表细胞生长曲线的测量值，总共检测6天，将校正值绘制在坐标纸上，即得出细胞的生长曲线，本实验独立进行了3次.

1.2.4 平板克隆形成试验

取对数生长期的细胞，制成细胞悬液，按500个细胞/孔接种于6孔板中，静置培养2周. 取出培养皿，用PBS洗2次，甲醇固定15 min后，0.4%结晶紫染色. 用肉眼直接计数克隆数，或在显微镜下计数大于50个细胞的克隆. 然后，按公式计算克隆形成率：克隆形成率=(克隆数/接种细胞数)×100%，本实验亦独立进行了3次.

1.2.5 软琼脂集落形成试验

用DMEM培养基、0.6%琼脂糖(终浓度)配制底层琼脂，取1.5 ml均匀铺于6孔板内，4℃放置10 min. 另外用转染的SP18细胞(密度为1×10^4/孔)、DMEM培养基、0.3%琼脂糖(终浓度)配制顶层琼脂，待底层琼脂凝固后将顶层琼脂铺于底层琼脂上，37℃ 5% CO_2温箱内连续培养2周后，计数集落数. 每组3个平行孔，集落形成率计数：于倒置显微镜下观察集落(≥50个细胞为1个集落)的数目和大小，计数每组每孔集落数的平均数，计算出细胞集落形成率(集落形成率=集落数/接种细胞数×100%)，本实验亦独立进行了3次.

1.2.6 划痕试验

将对数生长期细胞用胰酶消化后，制备成单个细胞悬液，计数并以每孔1×10^6个细胞接种于6孔细胞培养板中，常规培养至孔内细胞长到80%～90%的状态，用PBS缓冲液轻洗细胞3次，加入新鲜的无血清DMEM. 用装10 μl TP头的枪比着直尺在细胞板上划痕，用PBS缓冲液轻洗细胞3次，去掉划下的细胞，加入无血清DMEM，放入37℃、5% CO_2的培养箱内培养. 按0与24 h测量与拍照，计算平均值并进行分析，本实验亦独立进

行了 3 次.

1.2.7　Transwell 迁移和 Transwell 侵袭实验

实验采用滤膜直径 6.5 mm，滤膜孔径 8.0 μm 的 Transwell 培养板．Transwell 侵袭实验：用无血清 DMEM 以 1∶5 稀释基质胶，加入 Transwell 上室中，37℃、5% CO_2 培养箱置 2 h，以形成均匀薄层凝胶．用无血清 DMEM 制备浓度为 1×10^5/ml 单细胞悬液，入 200 μl 于 Transwell 上室中，下室中加入 500 μl 5%小牛血清的 DMEM，置 37℃、5% CO_2 培养箱 24 h．取出 Transwell 小室，用棉签擦净上室面基质胶，下室用 4%多聚甲醛固定 15 min, 将小室倒置风干，结晶紫染色、晾干、观察和拍照，选取上下左右中 5 个视野计数细胞并拍照．Transwell 迁移与 Transwell 侵袭实验基本步骤一致，实验时不需加入基质胶.

1.2.8　基因芯片检测与分析

取对数生长期的 SP18-LMP1 和 SP18-LMP1$^{\Delta232\text{-}351}$ 细胞，长至 80%融合时，去除培养基，PBS 洗涤 2 次，加入 1 ml TRIzol 于培养瓶中，混匀后收集细胞，分别抽提 SP18-LMP1 和 SP18-LMP1$^{\Delta232\text{-}351}$ 细胞总 RNA，送上海伯豪生物技术有限公司进行基因芯片检测，比较 SP18-LMP1 和 SP18-LMP1$^{\Delta232\text{-}351}$ 细胞的差异表达基因．采用 Agilent Microarray Scanner (G2505B) 扫描芯片，将 Agilent Feature Extraction 软件读出的荧光值导入 Agilent Genepix GX 软件中进行数据分析．数据经过中位数标准化后得出实验组与对照组标记的信号比值，即为该基因组在实验组与对照组中变化情况．筛选出 fold change ≥2 的基因为表达显著上调基因，fold change≤0.5 为表达显著下调基因．将基因芯片结果采用 DAVID 在线软件分析，对差异表达基因进行 Gene Ontology 分类.

1.2.9　实时荧光定量 RT-PCR 检测基因的差异表达

a．使用 SYBR Green Ⅰ荧光染料在密闭的毛细硅管(德国 Roche 公司)中进行定量 PCR 反应．取模板 2 μl，上下游引物各 0.4 μl，超纯水补足体积 20 μl，混匀，再与 10 μl 混合染料混合后注入毛细硅管中，离心后放入 Lightcycler PCR 热循环仪(德国 Roche 公司)中进行反应，(设置条件：95℃ 10 s, 1 个循环；95℃ 4 s，62℃～65℃ 20 s，72℃ 15 s, 40～50 个循环；60℃ 10 s，1 个循环)，计算出 Threshold cycle(Ct)．每一次反应均以 ddH_2O 代替模板做为阴性对照，实验重复 3 次．b．相对定量公式及表达量计算：目的基因的量=$2^{-\Delta\Delta Ct}$(表示实验组目的基因的表达相对于对照组的变化倍数)，$\Delta\Delta Ct=(Ct_{\text{目的基因}}-Ct_{\text{管家基因}})_{\text{实验组}}-(Ct_{\text{目的基因}}-Ct_{\text{管家基因}})_{\text{对照组}}$．c．PCR 扩增产物送 Invitrogen 公司测序分析，确定实时荧光 RT-PCR 扩增产物的特异性.

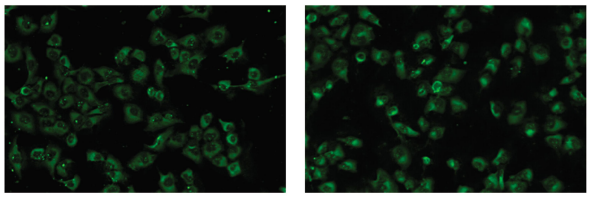
1.2.10　统计学分析

应用 SPSS13.0 统计软件包进行 t 检验和 χ^2 检验．数据以 $\bar{x}\pm s$ 表示，以 $P<0.05$ 表示有统计学意义.

2　结　　果

2.1　SP18 细胞 LMP1 蛋白的表达定位与检测

逆病毒感染 SP18 细胞后，G418 筛选汇合克隆，免疫荧光检测 LMP1 的表达，结果显示 LMP1 和 LMP1$^{\Delta252\text{-}351}$ 在 SP18 细胞浆和胞膜表达，建立了稳定表达 LMP1 及 LMP1$^{\Delta252\text{-}351}$ 的 SP18 细胞系，即 SP18-LMP1 细胞和 SP18-LMP1$^{\Delta232\text{-}351}$ 细胞(图 1).



SP18-LMP1　　SP18-LMP1$^{\Delta232\text{-}351}$

Fig. 1　Expression of LMP1 in SP18-LMP1 and SP18-LMP1$^{\Delta232\text{-}351}$ cells detected with immunofluorescence

2.2　LMP1$^{\Delta232\text{-}351}$ 对 SP18 细胞生长的影响

将上述 2 种细胞以相同的数量接种于 96 孔板，每组设 3 个平行孔，用 MTT 法每隔 1 天测量，连续检测 6 天，绘制出生长曲线．经绘制生长曲线和统计学分析，结果显示 SP18-LMP1$^{\Delta232\text{-}351}$ 细胞生长速度明显慢于 SP18-LMP1 细胞(n=3，$P<0.05$，图 2).

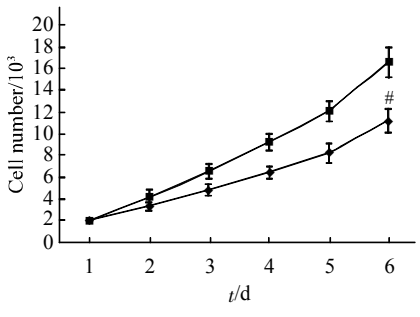


Fig. 2　Growth curve of SP18-LMP1 and SP18-LMP1$^{\Delta232\text{-}351}$ cell

SP18-LMP1 versus SP18-LMP1$^{\Delta232\text{-}351}$, $^{\#}P<0.05$. ◆—◆: SP18-LMP1$^{\Delta232\text{-}351}$; ■—■: SP18-LMP1.

2.3　LMP1$^{\Delta 232\text{-}351}$ 对 SP18 细胞锚定与非停泊依赖性生长能力的影响

SP18-LMP1 和 SP18-LMP1$^{\Delta 232\text{-}351}$ 细胞的平皿克隆与软琼脂集落形成结果(表 2)显示，SP18-LMP1$^{\Delta 232\text{-}351}$ 组较 SP18-LMP1 组的平皿克隆与软琼脂集落形成数少(n=3，P < 0.05)，说明 SP18-LMP1$^{\Delta 232\text{-}351}$ 细胞锚定与非停泊依赖性生长能力较 SP18-LMP1 弱，提示 LMP1 可促进 SP 细胞的增殖，其中 LMP1-CTAR$_3$ 其促进细胞增殖的重要活动区域.

Table 2　Cell culture transformation analysis of SP18-LMP1 and SP18-LMP1$^{\Delta 232\text{-}351}$

Cells	Colony-forming number	Foci-forming number
SP18-LMP1	246±45	1069±178
SP18-LMP1$^{\Delta 232\text{-}351}$	186±34$^{\#}$	874±126$^{\#}$

SP18-LMP1 versus SP18-LMP1$^{\Delta 232\text{-}351}$, $^{\#}P$ < 0.05.

2.4　LMP1$^{\Delta 232\text{-}351}$ 对 SP18 细胞迁移与侵袭的影响

SP18-LMP1 和 SP18-LMP1$^{\Delta 232\text{-}351}$ 细胞划痕(图 3，表 3)与 Transwell 迁移(图 4，表 4)实验结果显示：SP18-LMP1$^{\Delta 232\text{-}351}$ 组的迁移率、迁移与侵袭细胞数较 SP18-LMP1 组少(n=3，P < 0.05)，说明 SP18-LMP1$^{\Delta 232\text{-}351}$ 组的迁移与侵袭能力较 SP18-LMP1 组低，提示 LMP1 可促进 SP 细胞的迁移与侵袭，CTAR$_3$ 是 LMP1 促进细胞迁移与侵袭的重要活动区域.

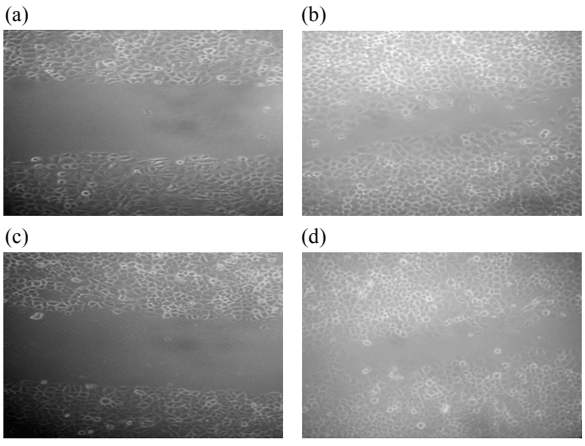


Fig. 3　The scuffing migration of SP18-LMP1 and SP18-LMP1$^{\Delta 232\text{-}351}$ cells

(a) The scuffing of SP18-LMP1 cells in 0 h. (b) The scuffing of SP18-LMP1 cells in 24 h. (c) The scuffing of SP18-LMP1$^{\Delta 232\text{-}351}$ cells in 0 h. (d) The scuffing of SP18-LMP1$^{\Delta 232\text{-}351}$ cells in 24 h.

Table 3　The scuffing migration of SP18-LMP1 and SP18-LMP1$^{\Delta 232\text{-}351}$ cells

Cells	Migration length/mm		Migration rate/%
	0 h	24 h	
SP-LMP1	188.83±1.17	45.50±8.41	75.90±4.32
SP18-LMP1$^{\Delta 232\text{-}351}$	189.33±3.72	57.67±5.01$^{\#}$	69.54±2.75$^{\#}$

SP18-LMP1 versus SP18-LMP1$^{\Delta 232\text{-}351}$. $^{\#}P$ < 0.05.

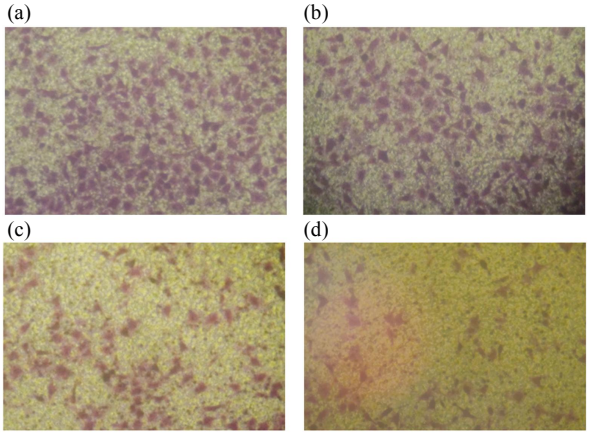


Fig. 4　The transwell migration and invasion of SP18-LMP1 and SP18-LMP1$^{\Delta 232\text{-}351}$ cells

(a) The transwell migration of SP18-LMP1cells. (b) The transwell migration of SP18-LMP1$^{\Delta 232\text{-}351}$ cells. (c) The transwell invasion of SP18-LMP1 cells. (d) The transwell invasion of SP18-LMP1$^{\Delta 232\text{-}351}$ cells.

Table 4　The transwell migration and invasion of SP18-LMP1 and SP18-LMP1$^{\Delta 232\text{-}351}$ cells

Cells	Cell number of migration	Cell number of invasion
SP18-LMP1	113.47±9.79	69.13±5.10
SP18-LMP1$^{\Delta 232\text{-}351}$	90.87±5.41$^{\#}$	92.87±4.64$^{\#}$

SP18-LMP1 versus SP18-LMP1$^{\Delta 232\text{-}351}$. $^{\#}P$ < 0.05.

2.5　SP18-LMP1 和 SP18-LMP1$^{\Delta 232\text{-}351}$ 细胞差异基因的筛选

采用 Agilent 基因芯片分析，筛选获得 SP18-LMP1 和 SP18- LMP1$^{\Delta 232\text{-}351}$ 细胞间差异表达基因 314 个，在 SP18- LMP1$^{\Delta 232\text{-}351}$ 细胞中上调基因 180 个，下调基因 134 个(见附件表 S1).

2.6　LMP1$^{\Delta 232\text{-}351}$ 影响 SP18 迁移与侵袭相关基因的筛选

采用 DAVID 在线软件分析，对差异表达基因进行 Gene Ontology 分类后，共筛选出 18 个迁移与侵袭相关的差异表达基因，其中表达上调基因 13

个，下调基因 5 个(表 5). 另外，通过 STRING 在线软件对 18 个迁移与侵袭相关基因进行相互作用分析(Confidence Score 为 400)，其中 13 个基因在 STRING 网络中呈现节点，两两间联系，其中联系最多的是 FN1、MMP14、ITGA2、THBS1、IL1B 和 IL6 基因，5 个基因孤立存在，在网络中无节点(图 5).

Table 5　The relation genes of migration and invasion in SP18-LMP1 and SP18-LMP1$^{\Delta 232\text{-}351}$ cells

Cells	Genes
Up-regulation in SP18-LMP1 cells	ACVRL1，NEXN，DCLK1，FN1，MMP14
Up-regulation in SP18-LMP1$^{\Delta 232\text{-}351}$ cells	ALOX15B，BDKRB1，EFNB1，F2R，FOXJ1，HBEGF，IL1B，IL6，IRS1，ITGA2，LAMA3，S1PR1，THBS1

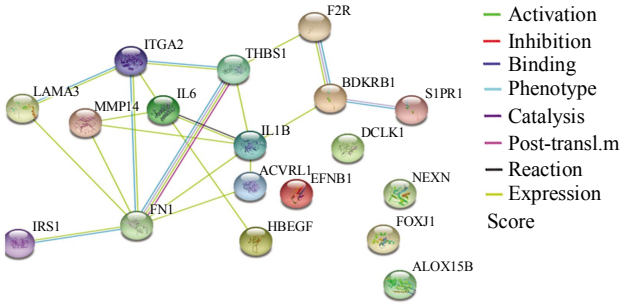


Fig. 5　The cross-talk network of migration and invasion genes

2.7　实时荧光定量 RT-PCR 检测迁移与侵袭相关基因的表达

采用实时荧光定量 RT-PCR 检测部分迁移与侵袭相关基因在 SP18-LMP1 和 SP18-LMP1$^{\Delta 232\text{-}351}$ 细胞中的表达水平(表 6). 结果显示均为特异的 PCR 产物，与基因芯片检测结果基本一致.

Table 6　The relative expression of migration and invasion genes

Genes	SP18-LMP1 *vs*. SP18-LMP1$^{\Delta 232\text{-}351}$ cells
FN1	mean 8.46±0.28 folds increased in SP18-LMP1
MMP14	mean 7.52±0.42 folds increased in SP18-LMP1
ITGA2	mean 6.38±0.29 folds decreased in SP18-LMP1
THBS1	mean 8.45±0.34 folds decreased in SP18-LMP1

3　讨　　论

侵袭与转移是恶性肿瘤的重要生物学特征之一. LMP1 是 EBV 编码的几个被确认与肿瘤细胞侵袭与转移相关的致瘤蛋白. 有研究发现[9]，LMP1 通过降低 RECK 的表达，增加 MMP-9 表达，以及通过 STAT3 诱导 VEGF 表达等，促进鼻咽癌细胞的侵袭与转移[10]. $CTAR_3$ 是 LMP1 发挥生物学作用的主要区域，其可以激活 JAK3/STAT 信号通路，促进鼻咽上皮细胞的增殖[11]，也可通过与 UBC9 之间相互作用，促进 LMP1 介导的细胞迁移[12]，提示 $CTAR_3$ 在 LMP1 介导的肿瘤细胞侵袭与转移中可能发挥重要作用.

本研究结果显示，LMP1 能促进鼻咽癌干细胞 SP18 的增殖、迁移及侵袭，$CTAR_3$ 缺失后 LMP1 促进增殖、迁移及侵袭能力明显降低，提示 $CTAR_3$ 是 LMP1 促进鼻咽癌 SP18 细胞增殖、迁移及侵袭的重要活性区域. 为了解该活性区域影响 SP18 细胞增殖、迁移及侵袭的机制，我们采用基因芯片筛选 SP18-LMP1 和 SP18-LMP1$^{\Delta 232\text{-}351}$ 细胞间差异表达相关基因，通过 DAVID 软件进行 GO 分类和 Pathway 分析，获得 18 个 $CTAR_3$ 在 SP18 细胞中调节的迁移及侵袭相关基因，其中 13 个基因在 STRING 网络中呈现节点，两两间联系，其中联系最多的是 FN1、MMP14、ITGA2、THBS1、IL1B 和 IL6 基因. 我们选取与迁移及侵袭相关且基因间联系密切者进行介绍，为后续的研究提供方向和依据.

THBS1 (thrombospondin-1，THBS1) 基因定位于人类第 15 条染色体 q15，其编码的凝血栓蛋白 1 是一种黏着糖蛋白，可以介导细胞与细胞，细胞与基质之间的黏附作用[13]. THBS1 能与纤维蛋白原、纤维连接蛋白、层粘连蛋白、胶原蛋白 V 和整合素 α-V/β-1 等结合，在血小板聚集，抗血管生成和肿瘤发生过程中发挥重要作用. 有研究发现[14]，在胃癌、乳腺癌、结直肠腺癌、子宫内膜癌等多种恶性肿瘤中 THBS1 表达下调，其在肿瘤发生、发展过程中起到抑制作用. 我们的结果显示，SP18-LMP1$^{\Delta 232\text{-}351}$ 细胞中 THBS1 表达较 SP18-LMP1 细胞高，说明 LMP1-$CTAR_3$ 可能通过抑制 THBS1 的表达，降低其对血管生成的抑制作用，促进肿瘤细胞的迁移与侵袭.

FN1(fibronectin 1，FN1)基因编码纤维连接蛋白 1 是一种糖蛋白，在血浆中以可溶性二聚体形式

存在，在细胞表面和细胞外基质中以二聚体或多聚体形式存在．FN1 可与胶原蛋白、纤维蛋白、肝素和肌动蛋白等结合，参与细胞黏附、细胞运动、调理作用、促进伤口愈合、并维持细胞形状等生物学过程[15]．有文献报道[16]，FN1 的表达与鼻咽癌、结肠癌、人纤维肉瘤的转移呈正相关．FN1 表达与肺癌、恶性周围神经鞘瘤的转移有关[17]．推测 FN1 可促使肿瘤细胞在远处黏附、聚集，促进肿瘤的迁移与侵袭．我们的结果显示，FN1 在 SP18-LMP1 细胞表达较 SP18-LMP1$^{\Delta 232\text{-}351}$ 细胞高，提示 $CTAR_3$ 可促进 SP18 细胞中 FN1 的表达，$CTAR_3$ 在鼻咽癌的转移中发挥正向调节作用．

MMP14 (matrix metalloproteinase 14，MMP14) 基因位于人类第 14 条染色体 q11，是锌依赖性基质金属蛋白酶 MMPs 家族的一员．MMP14 可激活 MMP2 间接降解细胞外基质，也可通过降解胶原蛋白、纤连蛋白、层黏连蛋白、纤维蛋白、玻璃黏连蛋白等直接降解细胞外基质及基底膜，从而在细胞增殖、迁移和血管生成过程中发挥重要作用[18]．研究发现[19]，MMP14 在乳腺癌、前列腺癌、肝癌、胃癌等恶性肿瘤中高表达，与肿瘤的恶性程度、迁移与侵袭呈正相关．另有研究证实[20]，在胃癌中，MMP14 可以激活非经典 Wnt 通路中 Wnt5a 的表达，使肿瘤细胞向上皮间质转化，促进肿瘤的迁移侵袭．降解细胞外基质突破基底膜是肿瘤细胞迁移侵袭的重要环节，MMP14 可能通过降解细胞外基质及基底膜，诱导肿瘤血管形成，促进肿瘤细胞的迁移侵袭．依据我们的结果推测，LMP1-$CTAR_3$ 在 SP18 细胞通过上调 MMP14 的表达，增强肿瘤细胞的迁移与侵袭能力，发挥 LMP1 促进鼻咽癌的迁移与侵袭的作用．

总之，本研究证实 $CTAR_3$ 是 LMP1 发挥促进细胞增殖、迁移及侵袭作用的重要活性区域，鉴定了 18 个该区域调节与迁移及侵袭相关的基因，至于 LMP1-$CTAR_3$ 活性区域如何调控这些基因的表达，以及这些基因如何发挥促进鼻咽癌细胞的增殖、迁移及侵袭等作用还需要进行深入研究．

附件 表 S1 见本文网络版附录(http://www.pibb.ac.cn).

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The Effect of Migration and Invasion by Carboxy Terminal Activating Region 3 of LMP1 in Nasopharyngeal Carcinoma Stem Cell*

XIAO Juan[2)], ZHANG Zhi-Wei[1,2)**], WU Shi-Hua[1,4)], LIU Zhong-Yuan[1)], TANG Wei[1)], ZHAO Qiang[3,5)], LEI Ming-Sheng[6)], YANG Dai-Shui[6)]

([1)] *Cancer Research Institute, University of Southern China, University Key Laboratory of Cancer Cellular and Molecular Pathology in Hunan Province, Hengyang* 421001, China;
[2)] *Department of Otorhinolaryngology, the Second Affiliated Hospital of University of South China, Hengyang* 421001, China;
[3)] *Center for Gastric Cancer Research of Hunan Province, Hengyang* 421001, China;
[4)] *Department of Pathology, Shaoyang Medical School, Shaoyang* 422000, China;
[5)] *Department of Pathology, the First Affiliated Hospital of University of South China, Hengyang* 421001, China;
[6)] *Clinical Medicine excellent Undergraduate of Medical College, University of Southern China, Hengyang* 421001, China)

Abstract To investigate mechanism of migration and invasion effected by carboxyl terminal activating region 3 ($CTAR_3$) of Epstein-Barr virus encoded latent membrane protein 1(LMP1) in nasopharyngeal carcinoma stem cell SP18 cells, the SP18 cell of stable expressed LMP1 and deletion mutant type LMP1 ($LMP1^{\Delta 232\text{-}351}$) were established (SP18-LMP1 and SP18-$LMP1^{\Delta 252\text{-}351}$). The effect of LMP1-$CTAR_3$ deletion mutant for cellular proliferation, migration and invasion were observed in SP18 cells. The differential expression genes between SP18-LMP1 and SP18-$LMP1^{\Delta 252\text{-}351}$ cells were analyzed by cDNA chips, and the expression levels of partial identified genes were verified by fluorescent Real-time quantitative RT-PCR. The relation of differential expression genes were analyzed by bioinformatics. The results showed: (1) The ability of $LMP1^{\Delta 232\text{-}351}$ promoting SP18 cell proliferation, migration and invasion was obviously decreased to compare with wild type LMP1(n=3, $P < 0.05$). (2) 18 genes, 13 up- and 5 down-regulated ones, of LMP1-$CTAR_3$ mediated regulation with migration and invasion were identified from in SP18 cell lines. The differential expression of partial identified genes was similar with cDNA chips separated ones and confirmed by fluorescent Real-time quantitative RT-PCR. (3) 13 differential expression genes can be

cross-talk, and among FN1, MMP14, ITGA2, THBS1, IL1B and IL6 genes were frequently correlation. These results suggested that LMP1-CTAR$_3$ probably regulates the expression of FN1, MMP14, ITGA2, THBS1, IL1B and IL6 genes to induce and promote migration and invasion of nasopharyngeal carcinoma stem cell SP18 cell.

Key words nasopharyngeal carcinoma stem cell SP18, LMP1, carboxyl terminal activating region 3, cDNA chips, migration and invasion

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**Corresponding author.
Tel: 86-734-8281510, E-mail: nhdxzzw@qq.com

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附　录

Table S1　Identified differentially expressed genes of SP18-LMP1$^{\Delta 232\text{-}351}$ and SP18-LMP1 cells

Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
1	↑ 8.34	LYPD4	Ly6/PLAUR domain-containing protein 4 Precursor	BC034629	LY6/PLAUR domain containing 4
2	↑ 7.27	CFI	Homo sapiens complement factor I (CFI)	NM_000204	complement factor I
3	↑ 6.88	CTSK	Homo sapiens cathepsin K (CTSK)	NM_000396	cathepsin K
4	↑ 5.58	IL1A	Homo sapiens interleukin 1, alpha (IL1A)	NM_000575	interleukin 1, alpha
5	↑ 5.33	LOC100293208	PREDICTED: Homo sapiens hypothetical protein LOC100293208 (LOC100293208)	XM_002346086	hypothetical protein LOC100293208
6	↑ 4.66	FOXJ1	Homo sapiens forkhead box J1 (FOXJ1)	NM_001454	forkhead box J1
7	↑ 4.58	EGR2	Homo sapiens early growth response 2 (EGR2)	NM_000399	early growth response 2
8	↑ 4.39	CXCL2	Homo sapiens chemokine (C-X-C motif) ligand 2 (CXCL2)	NM_002089	chemokine (C-X-C motif) ligand 2
9	↑ 4.02	CCL20	Homo sapiens chemokine (C-C motif) ligand 20 (CCL20)	NM_004591	chemokine (C-C motif) ligand 20
10	↑ 3.99	ETV7	Homo sapiens ets variant 7 (ETV7)	NM_016135	ets variant 7
11	↑ 3.91	FOSB	Homo sapiens FBJ murine osteosarcoma viral oncogene homolog B (FOSB)	NM_006732	FBJ murine osteosarcoma viral oncogene homolog B
12	↑ 3.82	RTP4	Homo sapiens receptor (chemosensory) transporter protein 4 (RTP4)	NM_022147	receptor (chemosensory) transporter protein 4
13	↑ 3.61	CENPL	Homo sapiens cDNA FLJ31786 fis, clone NT2RI2008526.	AK056348	centromere protein L
14	↑ 3.58	SERPINB3	Homo sapiens serpin peptidase inhibitor, clade B (ovalbumin), member 3 (SERPINB3)	NM_006919	serpin peptidase inhibitor, clade B (ovalbumin), member 3
15	↑ 3.52	KLK8	Homo sapiens kallikrein-related peptidase 8 (KLK8)	NM_144505	kallikrein-related peptidase 8
16	↑ 3.50	NGFR	Homo sapiens nerve growth factor receptor (TNFR superfamily, member 16) (NGFR)	NM_002507	nerve growth factor receptor (TNFR superfamily, member 16)
17	↑ 3.46	ANKRD22	Homo sapiens ankyrin repeat domain 22 (ANKRD22)	NM_144590	ankyrin repeat domain 22
18	↑ 3.45	IL1B	Homo sapiens interleukin 1, beta (IL1B)	NM_000576	interleukin 1, beta
19	↑ 3.44	KRT6C	Homo sapiens keratin 6C (KRT6C)	NM_173086	keratin 6C
20	↑ 3.42	CFH	Homo sapiens complement factor H (CFH)	NM_000186	complement factor H
21	↑ 3.39	ZBED2	Homo sapiens zinc finger, BED-type containing 2 (ZBED2)	NM_024508	zinc finger, BED-type containing 2
22	↑ 3.34	DUSP6	Homo sapiens dual specificity phosphatase 6 (DUSP6)	NM_001946	dual specificity phosphatase 6
23	↑ 3.34	INPP5D	Homo sapiens inositol polyphosphate-5-phosphatase, 145kDa (INPP5D)	NM_001017915	inositol polyphosphate-5-phosphatase, 145kDa
24	↑ 3.34	EML2	Homo sapiens echinoderm microtubule associated protein like 2 (EML2)	NM_012155	echinoderm microtubule associated protein like 2
25	↑ 3.33	SPANXA1	Homo sapiens sperm protein associated with the nucleus, X-linked, family member A1 (SPANXA1)	NM_013453	sperm protein associated with the nucleus, X-linked, family member A1
26	↑ 3.33	ETS2	Homo sapiens v-ets erythroblastosis virus E26 oncogene homolog 2 (avian) (ETS2)	NM_005239	v-ets erythroblastosis virus E26 oncogene homolog 2 (avian)
27	↑ 3.27	CALB2	Homo sapiens calbindin 2 (CALB2)	NM_001740	calbindin 2
28	↑ 3.26	CLCA2	Homo sapiens chloride channel accessory 2 (CLCA2)	NM_006536	chloride channel accessory 2
29	↑ 3.15	STK19	Homo sapiens serine/threonine kinase 19 (STK19)	NM_032454	serine/threonine kinase 19

Continued

Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
30	↑ 3.14	WDR33	WD repeat-containing protein 33 (WD repeat-containing protein WDC146)	NM_018383	WD repeat domain 33
31	↑ 3.10	SERPINB4	Homo sapiens serpin peptidase inhibitor, clade B (ovalbumin), member 4 (SERPINB4)	NM_002974	serpin peptidase inhibitor, clade B (ovalbumin), member 4
32	↑ 3.08	CYP3A5	Homo sapiens cytochrome P450, family 3, subfamily A, polypeptide 5 (CYP3A5)	NM_000777	cytochrome P450, family 3, subfamily A, polypeptide 5
33	↑ 3.07	AIM2	Homo sapiens absent in melanoma 2 (AIM2)	NM_004833	absent in melanoma 2
34	↑ 3.05	MCL1	Homo sapiens myeloid cell leukemia sequence 1 (BCL2-related) (MCL1)	NM_021960	myeloid cell leukemia sequence 1 (BCL2-related)
35	↑ 3.02	KRT6A	Homo sapiens keratin 6A (KRT6A)	NM_005554	keratin 6A
36	↑ 2.90	CFHR3	Homo sapiens complement factor H-related 3 (CFHR3)	NM_021023	complement factor H-related 3
37	↑ 2.90	TNFRSF6B	Homo sapiens tumor necrosis factor receptor superfamily, member 6b, decoy (TNFRSF6B)	NM_032945	tumor necrosis factor receptor superfamily, member 6b, decoy
38	↑ 2.89	ASB8	Homo sapiens ankyrin repeat and SOCS box-containing 8 (ASB8)	NM_024095	ankyrin repeat and SOCS box-containing 8
39	↑ 2.85	APOBEC3G	Homo sapiens apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G (APOBEC3G)	NM_021822	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G
40	↑ 2.84	TXNIP	Homo sapiens thioredoxin interacting protein (TXNIP)	NM_006472	thioredoxin interacting protein
41	↑ 2.83	EVI2B	Homo sapiens ecotropic viral integration site 2B (EVI2B)	NM_006495	ecotropic viral integration site 2B
42	↑ 2.81	DSG3	Homo sapiens desmoglein 3 (pemphigus vulgaris antigen) (DSG3)	NM_001944	desmoglein 3 (pemphigus vulgaris antigen)
43	↑ 2.80	CASP10	Homo sapiens caspase 10, apoptosis-related cysteine peptidase (CASP10)	NM_032977	caspase 10, apoptosis-related cysteine peptidase
44	↑ 2.74	TAF5L	Homo sapiens TAF5-like RNA polymerase II, p300/CBP-associated factor (PCAF)-associated factor, 65kDa (TAF5L)	NM_014409	TAF5-like RNA polymerase II, p300/CBP-associated factor (PCAF)-associated factor, 65kDa
45	↑ 2.73	SYT8	Homo sapiens synaptotagmin VIII (SYT8)	NM_138567	synaptotagmin VIII
46	↑ 2.72	CSRNP1	Homo sapiens cysteine-serine-rich nuclear protein 1 (CSRNP1)	NM_033027	cysteine-serine-rich nuclear protein 1
47	↑ 2.69	ABCA1	Homo sapiens ATP-binding cassette, sub-family A (ABC1), member 1 (ABCA1)	NM_005502	ATP-binding cassette, sub-family A (ABC1), member 1
48	↑ 2.68	C13orf15	Homo sapiens chromosome 13 open reading frame 15 (C13orf15)	NM_014059	chromosome 13 open reading frame 15
49	↑ 2.68	FUT2	Homo sapiens fucosyltransferase 2 (secretor status included) (FUT2), transcript variant 1, mRNA [NM_000511]	NM_000511	fucosyltransferase 2 (secretor status included)
50	↑ 2.68	DAPP1	Homo sapiens dual adaptor of phosphotyrosine and 3-phosphoinositides(DAPP1), mRNA [NM_014395]	NM_014395	dual adaptor of phosphotyrosine and 3-phosphoinositides
51	↑ 2.67	SOCS3	Homo sapiens suppressor of cytokine signaling 3 (SOCS3), mRNA [NM_003955]	NM_003955	suppressor of cytokine signaling 3
52	↑ 2.66	PTHLH	Homo sapiens parathyroid hormone-like hormone (PTHLH)	NM_198965	parathyroid hormone-like hormone
53	↑ 2.65	TNC	Homo sapiens tenascin C (TNC)	NM_002160	tenascin C
54	↑ 2.62	JUN	Homo sapiens jun oncogene (JUN)	NM_002228	jun oncogene
55	↑ 2.61	SLC2A9	Homo sapiens solute carrier family 2 (facilitated glucose transporter), member 9 (SLC2A9)	NM_001001290	solute carrier family 2 (facilitated glucose transporter), member 9

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Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
56	↑ 2.60	PTX3	Homo sapiens pentraxin-related gene, rapidly induced by IL-1 beta (PTX3)	NM_002852	pentraxin-related gene, rapidly induced by IL-1 beta
57	↑ 2.60	AREG	Homo sapiens amphiregulin (AREG)	NM_001657	amphiregulin
58	↑ 2.60	GJB2	Homo sapiens gap junction protein, beta 2, 26kDa (GJB2)	NM_004004	gap junction protein, beta 2, 26kDa
59	↑ 2.57	CLGN	Homo sapiens calmegin (CLGN), transcript variant 1	NM_004362	calmegin
60	↑ 2.57	ALOX15B	Homo sapiens arachidonate 15-lipoxygenase, type B (ALOX15B)	NM_001141	arachidonate 15-lipoxygenase, type B
61	↑ 2.56	GADD45A	Homo sapiens growth arrest and DNA-damage-inducible, alpha (GADD45A)	NM_001924	growth arrest and DNA-damage-inducible, alpha
62	↑ 2.55	SOCS2	Homo sapiens suppressor of cytokine signaling 2 (SOCS2)	NM_003877	suppressor of cytokine signaling 2
63	↑ 2.55	SFTA1P	Homo sapiens surfactant associated 1 (pseudogene) (SFTA1P)	NR_027082	surfactant associated 1 (pseudogene)
64	↑ 2.55	TMEM33	Homo sapiens transmembrane protein 33 (TMEM33)	NM_018126	transmembrane protein 33
65	↑ 2.54	SQRDL	Homo sapiens sulfide quinone reductase-like (yeast) (SQRDL), nuclear gene encoding mitochondrial protein	NM_021199	sulfide quinone reductase-like (yeast)
66	↑ 2.53	TMEM79	Homo sapiens transmembrane protein 79 (TMEM79)	NM_032323	transmembrane protein 79
67	↑ 2.52	ZBTB32	Homo sapiens zinc finger and BTB domain containing 32 (ZBTB32)	NM_014383	zinc finger and BTB domain containing 32
68	↑ 2.50	LOC151009	Homo sapiens hypothetical LOC151009 (LOC151009), non-coding RNA	NR_027244	hypothetical LOC151009
69	↑ 2.50	PDP1	Homo sapiens pyruvate dehyrogenase phosphatase catalytic subunit 1 (PDP1), nuclear gene encoding mitochondrial protein	NM_018444	pyruvate dehyrogenase phosphatase catalytic subunit 1
70	↑ 2.50	SYTL1	Homo sapiens synaptotagmin-like 1 (SYTL1)	NM_032872	synaptotagmin-like 1
71	↑ 2.50	ALDH3A1	Homo sapiens aldehyde dehydrogenase 3 family, memberA1 (ALDH3A1)	NM_000691	aldehyde dehydrogenase 3 family, memberA1
72	↑ 2.49	PPP1R14C	Homo sapiens protein phosphatase 1, regulatory (inhibitor) subunit 14C (PPP1R14C)	NM_030949	protein phosphatase 1, regulatory (inhibitor) subunit 14C
73	↑ 2.49	FLRT3	Homo sapiens fibronectin leucine rich transmembrane protein 3 (FLRT3)	NM_198391	fibronectin leucine rich transmembrane protein 3
74	↑ 2.48	DDIT3	Homo sapiens DNA-damage-inducible transcript 3 (DDIT3)	NM_004083	DNA-damage-inducible transcript 3
75	↑ 2.47	FST	Homo sapiens follistatin (FST), transcript variant FST344	NM_013409	follistatin
76	↑ 2.46	EGR1	Homo sapiens early growth response 1 (EGR1)	NM_001964	early growth response 1
77	↑ 2.46	SHISA2	Homo sapiens shisa homolog 2 (Xenopus laevis) (SHISA2)	NM_001007538	shisa homolog 2 (Xenopus laevis)
78	↑ 2.45	TNFAIP3	Homo sapiens tumor necrosis factor, alpha-induced protein 3 (TNFAIP3)	NM_006290	tumor necrosis factor, alpha-induced protein 3
79	↑ 2.44	SERPINB1	Homo sapiens serpin peptidase inhibitor, clade B (ovalbumin), member 1 (SERPINB1)	NM_030666	serpin peptidase inhibitor, clade B (ovalbumin), member 1
80	↑ 2.44	THBS1	Homo sapiens thrombospondin 1 (THBS1)	NM_003246	thrombospondin 1
81	↑ 2.43	LEMD1	Homo sapiens LEM domain containing 1 (LEMD1)	NM_001001552	LEM domain containing 1
82	↑ 2.43	EHF	Homo sapiens ets homologous factor (EHF)	NM_012153	ets homologous factor
83	↑ 2.42	IRF1	Homo sapiens interferon regulatory factor 1 (IRF1)	NM_002198	interferon regulatory factor 1
84	↑ 2.42	HES1	Homo sapiens hairy and enhancer of split 1, (Drosophila) (HES1)	NM_005524	hairy and enhancer of split 1, (Drosophila)

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Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
85	↑ 2.42	NFKBIZ	Homo sapiens nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta (NFKBIZ)	NM_031419	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta
86	↑ 2.40	ZSWIM5	Homo sapiens zinc finger, SWIM-type containing 5 (ZSWIM5)	NM_020883	zinc finger, SWIM-type containing 5
87	↑ 2.40	PDZK1IP1	Homo sapiens PDZK1 interacting protein 1 (PDZK1IP1)	NM_005764	PDZK1 interacting protein 1
88	↑ 2.38	SLC25A27	Homo sapiens solute carrier family 25, member 27 (SLC25A27), nuclear gene encoding mitochondrial protein	NM_004277	solute carrier family 25, member 27
89	↑ 2.38	PELI2	Homo sapiens pellino homolog 2 (Drosophila) (PELI2)	NM_021255	pellino homolog 2 (Drosophila)
90	↑ 2.37	GRAMD1C	Homo sapiens GRAM domain containing 1C (GRAMD1C)	NM_017577	GRAM domain containing 1C
91	↑ 2.37	NFE2	Homo sapiens nuclear factor (erythroid-derived 2), 45kDa (NFE2)	NM_006163	nuclear factor (erythroid-derived 2)
92	↑ 2.37	PDE2A	Homo sapiens phosphodiesterase 2A, cGMP-stimulated (PDE2A), transcript variant 1	NM_002599	phosphodiesterase 2A, cGMP-stimulated
93	↑ 2.36	LEPR	Homo sapiens leptin receptor (LEPR)	NM_001003679	leptin receptor
94	↑ 2.36	CCDC64B	Homo sapiens mRNA; cDNA DKFZp666L166 (from clone DKFZp666L166).	AL833749	coiled-coil domain containing 64B
95	↑ 2.34	HAS3	Homo sapiens hyaluronan synthase 3 (HAS3)	NM_005329	hyaluronan synthase 3
96	↑ 2.34	C1orf116	Homo sapiens chromosome 1 open reading frame 116 (C1orf116)	NM_023938	chromosome 1 open reading frame 116
97	↑ 2.34	ARL4D	Homo sapiens ADP-ribosylation factor-like 4D (ARL4D)	NM_001661	ADP-ribosylation factor-like 4D
98	↑ 2.33	ATF3	Homo sapiens activating transcription factor 3 (ATF3), transcript variant 4	NM_001040619	activating transcription factor 3
99	↑ 2.33	TSNARE1	Homo sapiens t-SNARE domain containing 1 (TSNARE1)	NM_145003	t-SNARE domain containing 1
100	↑ 2.33	F2R	Homo sapiens coagulation factor II (thrombin) receptor (F2R)	NM_001992	coagulation factor II (thrombin) receptor
101	↑ 2.32	ANGPTL2	Homo sapiens angiopoietin-like 2 (ANGPTL2)	NM_012098	angiopoietin-like 2
102	↑ 2.31	PPP1R15A	Homo sapiens protein phosphatase 1, regulatory (inhibitor) subunit 15A (PPP1R15A)	NM_014330	protein phosphatase 1, regulatory (inhibitor) subunit 15A
103	↑ 2.31	HBEGF	Homo sapiens heparin-binding EGF-like growth factor (HBEGF)	NM_001945	heparin-binding EGF-like growth factor
104	↑ 2.30	LOC440335	Homo sapiens hypothetical LOC440335 (LOC440335)	NR_029454	hypothetical LOC440335
105	↑ 2.30	FOSL1	Homo sapiens FOS-like antigen 1 (FOSL1)	NM_005438	FOS-like antigen 1
106	↑ 2.30	PHLDA1	Homo sapiens pleckstrin homology-like domain, family A, member 1 (PHLDA1)	NM_007350	pleckstrin homology-like domain, family A, member 1
107	↑ 2.30	ARRDC4	Homo sapiens arrestin domain containing 4 (ARRDC4)	NM_183376	arrestin domain containing 4
108	↑ 2.29	CYP3A7	Homo sapiens cytochrome P450, family 3, subfamily A, polypeptide 7 (CYP3A7)	NM_000765	cytochrome P450, family 3, subfamily A, polypeptide 7
109	↑ 2.28	BDKRB1	Homo sapiens bradykinin receptor B1 (BDKRB1)	NM_000710	bradykinin receptor B1
110	↑ 2.27	FGFBP1	Homo sapiens fibroblast growth factor binding protein 1 (FGFBP1)	NM_005130	fibroblast growth factor binding protein 1

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Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
111	↑ 2.25	LAPTM5	Homo sapiens lysosomal protein transmembrane 5 (LAPTM5)	NM_006762	lysosomal protein transmembrane 5
112	↑ 2.25	DOCK4	Homo sapiens dedicator of cytokinesis 4 (DOCK4)	NM_014705	dedicator of cytokinesis 4
113	↑ 2.25	GJB4	Homo sapiens gap junction protein, beta 4, 30.3kDa (GJB4)	NM_153212	gap junction protein, beta 4, 30.3kDa
114	↑ 2.25	IGFBP7	Homo sapiens insulin-like growth factor binding protein 7 (IGFBP7)	NM_001553	insulin-like growth factor binding protein 7
115	↑ 2.23	TMBIM1	Homo sapiens transmembrane BAX inhibitor motif containing 1 (TMBIM1)	NM_022152	transmembrane BAX inhibitor motif containing 1
116	↑ 2.23	HS3ST1	Homo sapiens heparan sulfate (glucosamine) 3-O-sulfotransferase 1 (HS3ST1)	NM_005114	heparan sulfate (glucosamine) 3-O-sulfotransferase 1
117	↑ 2.23	ABAT	Homo sapiens 4-aminobutyrate aminotransferase (ABAT), nuclear gene encoding mitochondrial protein	NM_000663	4-aminobutyrate aminotransferase
118	↑ 2.21	COL17A1	Homo sapiens collagen, type XVII, alpha 1 (COL17A1)	NM_000494	collagen, type XVII, alpha 1
119	↑ 2.20	IL7R	Homo sapiens interleukin 7 receptor (IL7R)	NM_002185	interleukin 7 receptor
120	↑ 2.20	SNAI2	Homo sapiens snail homolog 2 (Drosophila) (SNAI2)	NM_003068	snail homolog 2 (Drosophila)
121	↑ 2.20	CISH	Homo sapiens cytokine inducible SH2-containing protein (CISH)	NM_145071	cytokine inducible SH2-containing protein
122	↑ 2.19	IL6	Homo sapiens interleukin 6 (interferon, beta 2) (IL6)	NM_000600	interleukin 6 (interferon, beta 2)
123	↑ 2.19	SNPH	Homo sapiens syntaphilin (SNPH)	NM_014723	syntaphilin
124	↑ 2.18	TMEM40	Homo sapiens transmembrane protein 40 (TMEM40)	NM_018306	transmembrane protein 40
125	↑ 2.18	RALGDS	Homo sapiens ral guanine nucleotide dissociation stimulator (RALGDS)	NM_001042368	ral guanine nucleotide dissociation stimulator
126	↑ 2.18	HIST2H2AB	Homo sapiens histone cluster 2, H2ab (HIST2H2AB)	NM_175065	histone cluster 2, H2ab
127	↑ 2.17	UGT8	Homo sapiens UDP glycosyltransferase 8 (UGT8)	NM_003360	UDP glycosyltransferase 8
128	↑ 2.17	TCN1	Homo sapiens transcobalamin I (vitamin B12 binding protein, R binder family) (TCN1)	NM_001062	transcobalamin I (vitamin B12 binding protein, R binder family)
129	↑ 2.16	PMAIP1	Homo sapiens phorbol-12-myristate-13-acetate-induced protein 1 (PMAIP1)	NM_021127	phorbol-12-myristate-13-acetate-induced protein 1
130	↑ 2.16	DDX60	Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 60 (DDX60)	NM_017631	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60
131	↑ 2.14	S1PR1	Homo sapiens sphingosine-1-phosphate receptor 1 (S1PR1)	NM_001400	sphingosine-1-phosphate receptor 1
132	↑ 2.13	ITGA2	Homo sapiens integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor) (ITGA2)	NM_002203	integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)
133	↑ 2.13	TXNL4B	Homo sapiens thioredoxin-like 4B (TXNL4B)	NM_017853	thioredoxin-like 4B
134	↑ 2.13	IRS1	Homo sapiens insulin receptor substrate 1 (IRS1)	NM_005544	insulin receptor substrate 1
135	↑ 2.12	FBXO38	Homo sapiens F-box protein 38 (FBXO38)	NM_030793	F-box protein 38
136	↑ 2.12	PTAFR	Homo sapiens platelet-activating factor receptor (PTAFR)	NM_000952	platelet-activating factor receptor
137	↑ 2.11	GGT5	Homo sapiens gamma-glutamyltransferase 5 (GGT5)	NM_004121	gamma-glutamyltransferase 5
138	↑ 2.11	APOBEC3C	Homo sapiens apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3C (APOBEC3C)	NM_014508	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3C
139	↑ 2.11	WNT7A	Homo sapiens wingless-type MMTV integration site family, member 7A (WNT7A)	NM_004625	wingless-type MMTV integration site family, member 7A
140	↑ 2.10	LOC100134359	PREDICTED: Homo sapiens hypothetical LOC100134359 (LOC100134359)	XM_001726614	hypothetical protein LOC100134359

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Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
141	↑ 2.10	STC1	Homo sapiens stanniocalcin 1 (STC1)	NM_003155	stanniocalcin 1
142	↑ 2.10	CSTA	Homo sapiens cystatin A (stefin A) (CSTA)	NM_005213	cystatin A (stefin A)
143	↑ 2.09	ARL4C	Homo sapiens ADP-ribosylation factor-like 4C(ARL4C)	NM_005737	ADP-ribosylation factor-like 4C
144	↑ 2.09	HHAT	Homo sapiens hedgehog acyltransferase (HHAT), transcript variant 1	NM_018194	hedgehog acyltransferase
145	↑ 2.09	LRGUK	Homo sapiens leucine-rich repeats and guanylate kinase domain containing (LRGUK)	NM_144648	leucine-rich repeats and guanylate kinase domain containing
146	↑ 2.09	SLC47A2	Homo sapiens solute carrier family 47, member 2 (SLC47A2)	NM_152908	solute carrier family 47, member 2
147	↑ 2.08	LAMC2	Homo sapiens laminin, gamma 2 (LAMC2)	NM_018891	laminin, gamma 2
148	↑ 2.08	IFI44L	Homo sapiens interferon-induced protein 44-like (IFI44L)	NM_006820	interferon-induced protein 44-like
149	↑ 2.08	ZNF268	Homo sapiens zinc finger protein 268 (ZNF268)	NM_152943	zinc finger protein 268
150	↑ 2.08	ATP2C2	Homo sapiens ATPase, Ca^{++} transporting, type 2C, member 2 (ATP2C2)	NM_014861	ATPase, Ca^{++} transporting, type 2C, member 2
151	↑ 2.08	NUFIP1	Homo sapiens nuclear fragile X mental retardation protein interacting protein 1 (NUFIP1)	NM_012345	nuclear fragile X mental retardation protein interacting protein 1
152	↑ 2.07	FAM177A1	Homo sapiens family with sequence similarity 177, member A1 (FAM177A1)	NM_001079519	family with sequence similarity 177, member A1
153	↑ 2.07	SLC44A5	Homo sapiens solute carrier family 44, member 5 (SLC44A5)	NM_152697	solute carrier family 44, member 5
154	↑ 2.07	LRRC8B	Homo sapiens leucine rich repeat containing 8 family, member B (LRRC8B)	NM_015350	leucine rich repeat containing 8 family, member B
155	↑ 2.06	MAK	Homo sapiens male germ cell-associated kinase (MAK)	NM_005906	male germ cell-associated kinase
156	↑ 2.06	CARD11	Homo sapiens caspase recruitment domain family, member 11 (CARD11)	NM_032415	caspase recruitment domain family, member 11
157	↑ 2.06	IER2	Homo sapiens immediate early response 2 (IER2)	NM_004907	immediate early response 2
158	↑ 2.06	CARD6	Homo sapiens caspase recruitment domain family, member 6 (CARD6)	NM_032587	caspase recruitment domain family, member 6
159	↑ 2.06	TNPO1	Homo sapiens transportin 1 (TNPO1)	NM_002270	transportin 1
160	↑ 2.06	SEMA7A	Homo sapiens semaphorin 7A, GPI membrane anchor (John Milton Hagen blood group) (SEMA7A)	NM_003612	semaphorin 7A, GPI membrane anchor (John Milton Hagen blood group)
161	↑ 2.05	FGL1	Homo sapiens fibrinogen-like 1 (FGL1)	NM_201553	fibrinogen-like 1
162	↑ 2.05	LAMA3	Homo sapiens laminin, alpha 3 (LAMA3)	NM_000227	laminin, alpha 3
163	↑ 2.05	CCDC68	Homo sapiens coiled-coil domain containing 68 (CCDC68)	NM_025214	coiled-coil domain containing 68
164	↑ 2.05	SOX15	Homo sapiens SRY (sex determining region Y)-box 15 (SOX15)	NM_006942	SRY (sex determining region Y)-box 15
165	↑ 2.05	LHFP	Homo sapiens lipoma HMGIC fusion partner (LHFP)	NM_005780	lipoma HMGIC fusion partner
166	↑ 2.05	SPARCL1	Homo sapiens SPARC-like 1 (hevin) (SPARCL1)	NM_004684	SPARC-like 1 (hevin)
167	↑ 2.04	MATN1	Homo sapiens, clone IMAGE:4901582	BC017506	matrilin 1, cartilage matrix protein
168	↑ 2.04	RALGAPA1	Homo sapiens Ral GTPase activating protein, alpha subunit 1 (catalytic) (RALGAPA1)	NM_194301	Ral GTPase activating protein, alpha subunit 1 (catalytic)
169	↑ 2.03	SDCBP2	Homo sapiens syndecan binding protein (syntenin) 2 (SDCBP2)	NM_080489	syndecan binding protein (syntenin) 2
170	↑ 2.03	FOXQ1	Homo sapiens forkhead box Q1 (FOXQ1)	NM_033260	forkhead box Q1
171	↑ 2.02	ITGA3	Homo sapiens integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor) (ITGA3)	NM_002204	integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor)

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Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
172	↑ 2.02	THBD	Homo sapiens thrombomodulin (THBD), mRNA [NM_000361]	NM_000361	thrombomodulin
173	↑ 2.02	HBA2	Homo sapiens hemoglobin, alpha 2 (HBA2)	NM_000517	hemoglobin, alpha 2
174	↑ 2.02	ZC3HAV1	Homo sapiens zinc finger CCCH-type, antiviral 1 (ZC3HAV1)	NM_024625	zinc finger CCCH-type, antiviral 1
175	↑ 2.02	PLK2	Homo sapiens polo-like kinase 2 (Drosophila) (PLK2)	NM_006622	polo-like kinase 2 (Drosophila)
176	↑ 2.02	LRRC20	Homo sapiens leucine rich repeat containing 20 (LRRC20)	NM_018205	leucine rich repeat containing 20
177	↑ 2.02	DNAJB5	Homo sapiens DnaJ (Hsp40) homolog, subfamily B, member 5 (DNAJB5)	NM_012266	DnaJ (Hsp40) homolog, subfamily B, member 5
178	↑ 2.01	SEC31A	Homo sapiens cDNA FLJ46167	AK128047	SEC31 homolog A (S. cerevisiae)
179	↑ 2.01	PABPC4L	Homo sapiens poly(A) binding protein, cytoplasmic 4-like (PABPC4L)	NM_001114734	poly(A) binding protein, cytoplasmic 4-like
180	↑ 2.00	EFNB1	Homo sapiens ephrin-B1 (EFNB1)	NM_004429	ephrin-B1
181	↓ 0.50	CUL5	602299712F1 NIH_MGC_87 Homo sapiens cDNA clone IMAGE: 4394138 5'	BG031574	cullin 5
182	↓ 0.50	GPR98	Homo sapiens G protein-coupled receptor 98 (GPR98)	NM_032119	G protein-coupled receptor 98
183	↓ 0.50	UNQ565	Homo sapiens mRNA; cDNA DKFZp451E1418 (from clone DKFZp451E1418)	AL832629	IGYY565
184	↓ 0.50	MTUS2	Homo sapiens microtubule associated tumor suppressor candidate 2 (MTUS2)	NM_001033602	microtubule associated tumor suppressor candidate 2
185	↓ 0.49	ASTN2	Homo sapiens astrotactin 2 (ASTN2)	NM_014010	astrotactin 2
186	↓ 0.49	CPS1	Homo sapiens carbamoyl-phosphate synthetase 1, mitochondrial (CPS1), nuclear gene encoding mitochondrial protein	NM_001875	carbamoyl-phosphate synthetase 1, mitochondrial
187	↓ 0.49	AOC3	Homo sapiens amine oxidase, copper containing 3 (vascular adhesion protein 1) (AOC3)	NM_003734	amine oxidase, copper containing 3 (vascular adhesion protein 1)
188	↓ 0.49	FLRT1	Homo sapiens fibronectin leucine rich transmembrane protein 1 (FLRT1)	NM_013280	fibronectin leucine rich transmembrane protein 1
189	↓ 0.49	FGF21	Homo sapiens fibroblast growth factor 21 (FGF21)	NM_019113	fibroblast growth factor 21
190	↓ 0.49	NANOS1	Homo sapiens nanos homolog 1 (Drosophila) (NANOS1)	NM_199461	nanos homolog 1 (Drosophila)
191	↓ 0.49	DCLK1	Homo sapiens doublecortin-like kinase 1 (DCLK1)	NM_004734	doublecortin-like kinase 1
192	↓ 0.49	FGR	Homo sapiens Gardner-Rasheed feline sarcoma viral (v-fgr) oncogene homolog (FGR)	NM_001042747	Gardner-Rasheed feline sarcoma viral (v-fgr) oncogene homolog
193	↓ 0.49	C9orf3	Homo sapiens chromosome 9 open reading frame 3 (C9orf3)	NM_032823	chromosome 9 open reading frame 3
194	↓ 0.49	SLCO2A1	Homo sapiens solute carrier organic anion transporter family, member 2A1 (SLCO2A1)	NM_005630	solute carrier organic anion transporter family, member 2A1
195	↓ 0.48	KBTBD11	Homo sapiens kelch repeat and BTB (POZ) domain containing 11 (KBTBD11)	NM_014867	kelch repeat and BTB (POZ) domain containing 11
196	↓ 0.48	LMO1	Homo sapiens LIM domain only 1 (rhombotin 1) (LMO1)	NM_002315	LIM domain only 1 (rhombotin 1)
197	↓ 0.48	CSGALNACT1	Homo sapiens chondroitin sulfate N-acetylgalactosaminyltransferase 1(CSGALNACT1)	NM_018371	chondroitin sulfate N-acetylgalactosaminyltransferase 1
198	↓ 0.48	ATP8B2	Homo sapiens ATPase, class I, type 8B, member 2 (ATP8B2)	NM_020452	ATPase, class I, type 8B, member 2

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Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
229	↓ 0.45	SARDH	Homo sapiens SARDH mRNA, alternatively spliced	AF095737	sarcosine dehydrogenase
230	↓ 0.45	MAG	Homo sapiens myelin associated glycoprotein (MAG)	NM_080600	myelin associated glycoprotein
231	↓ 0.45	APH1B	Homo sapiens anterior pharynx defective 1 homolog B (C. elegans) (APH1B)	NM_031301	anterior pharynx defective 1 homolog B (C. elegans)
232	↓ 0.45	ALPI	Homo sapiens alkaline phosphatase, intestinal (ALPI)	NM_001631	alkaline phosphatase, intestinal
233	↓ 0.45	SVEP1	Homo sapiens sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1 (SVEP1)	NM_153366	sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1
234	↓ 0.45	FOXO4	Homo sapiens forkhead box O4 (FOXO4)	NM_005938	forkhead box O4
235	↓ 0.45	C9orf24	Homo sapiens chromosome 9 open reading frame 24 (C9orf24)	NM_032596	chromosome 9 open reading frame 24
236	↓ 0.45	HTATIP2	Homo sapiens HIV-1 Tat interactive protein 2, 30kDa (HTATIP2)	NM_001098523	HIV-1 Tat interactive protein 2, 30kDa
237	↓ 0.44	RHO	Homo sapiens rhodopsin (RHO)	NM_000539	rhodopsin
238	↓ 0.44	ZNF207	Zinc finger protein 207	CA435041	zinc finger protein 207
239	↓ 0.44	CLIC3	Homo sapiens chloride intracellular channel 3(CLIC3)	NM_004669	chloride intracellular channel 3
240	↓ 0.43	PPFIBP2	Homo sapiens PTPRF interacting protein, binding protein 2 (liprin beta 2) (PPFIBP2)	NM_003621	PTPRF interacting protein, binding protein 2 (liprin beta 2)
241	↓ 0.43	DMD	Homo sapiens dystrophin (DMD), transcript variant Dp427p2	NM_004010	dystrophin
242	↓ 0.43	C16orf45	Homo sapiens chromosome 16 open reading frame 45 (C16orf45)	NM_033201	chromosome 16 open reading frame 45
243	↓ 0.43	AHRR	Homo sapiens aryl-hydrocarbon receptor repressor (AHRR)	NM_020731	aryl-hydrocarbon receptor repressor
244	↓ 0.43	DNHD1	Homo sapiens dynein heavy chain domain 1 (DNHD1)	NM_144666	dynein heavy chain domain 1
245	↓ 0.43	FXYD4	Homo sapiens FXYD domain containing ion transport regulator 4 (FXYD4)	NM_173160	FXYD domain containing ion transport regulator 4
246	↓ 0.43	DACT2	Homo sapiens dapper, antagonist of beta-catenin, homolog 2 (Xenopus laevis) (DACT2)	NM_214462	dapper, antagonist of beta-catenin, homolog 2 (Xenopus laevis)
247	↓ 0.42	DISP2	Homo sapiens dispatched homolog 2 (Drosophila) (DISP2)	NM_033510	dispatched homolog 2 (Drosophila)
248	↓ 0.42	BMP2	Homo sapiens bone morphogenetic protein 2 (BMP2)	NM_001200	bone morphogenetic protein 2
249	↓ 0.42	GMPR	Homo sapiens guanosine monophosphate reductase (GMPR)	NM_006877	guanosine monophosphate reductase
250	↓ 0.42	FAM101B	Homo sapiens family with sequence similarity 101, member B (FAM101B)	NM_182705	family with sequence similarity 101, member B
251	↓ 0.42	DIO2	Homo sapiens deiodinase, iodothyronine, type II (DIO2)	NM_013989	deiodinase, iodothyronine, type II
252	↓ 0.42	GDPD5	Homo sapiens glycerophosphodiester phosphodiesterase domain containing 5 (GDPD5)	NM_030792	glycerophosphodiester phosphodiesterase domain containing 5
253	↓ 0.42	LOC100288303	PREDICTED: Homo sapiens similar to C21orf105 protein (LOC100288303)	XM_002343753	similar to C21orf105 protein
254	↓ 0.41	C11orf86	Homo sapiens chromosome 11 open reading frame 86 (C11orf86)	NM_001136485	chromosome 11 open reading frame 86
255	↓ 0.41	WNT6	Homo sapiens wingless-type MMTV integration site family, member 6 (WNT6)	NM_006522	wingless-type MMTV integration site family, member 6
256	↓ 0.41	PTPRB	Homo sapiens protein tyrosine phosphatase, receptor type, B (PTPRB)	NM_002837	protein tyrosine phosphatase, receptor type, B

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Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
257	↓ 0.41	PBX1	Homo sapiens pre-B-cell leukemia homeobox 1 (PBX1)	NM_002585	pre-B-cell leukemia homeobox 1
258	↓ 0.40	FAM123A	hypothetical protein LOC219287 isoform 2	AL832586	family with sequence similarity 123A
259	↓ 0.40	DPPA2	Homo sapiens developmental pluripotency associated 2 (DPPA2)	NM_138815	developmental pluripotency associated 2
260	↓ 0.40	SLC7A7	Homo sapiens solute carrier family 7 (cationic amino acid transporter, y+ system), member 7 (SLC7A7)	NM_003982	solute carrier family 7(cationic amino acid transporter, y^+ system),member 7
261	↓ 0.40	ACVRL1	Homo sapiens activin A receptor type II-like 1 (ACVRL1)	NM_000020	activin A receptor type II-like 1
262	↓ 0.39	PGC	Homo sapiens progastricsin (pepsinogen C) (PGC)	NM_002630	progastricsin (pepsinogen C)
263	↓ 0.39	COL12A1	Homo sapiens collagen, type XII, alpha 1 (COL12A1)	NM_004370	collagen, type XII, alpha 1
264	↓ 0.39	GHRLOS	Homo sapiens ghrelin opposite strand (non-protein coding) (GHRLOS)	NR_004431	ghrelin opposite strand (non-protein coding)
265	↓ 0.39	SH3BP5	Homo sapiens SH3-domain binding protein 5 (BTK-associated) (SH3BP5)	NM_004844	SH3-domain binding protein 5 (BTK-associated)
266	↓ 0.38	ERN1	Homo sapiens cDNA FLJ30999	AK055561	endoplasmic reticulum to nucleus signaling 1
267	↓ 0.38	VIL1	Villin-1	ENST00000248444	villin 1
268	↓ 0.38	SOX2	Homo sapiens SRY (sex determining region Y)-box 2 (SOX2)	NM_003106	SRY (sex determining region Y) -box 2
269	↓ 0.38	PNPLA7	Homo sapiens cDNA FLJ44279 fis, clone TRACH2001549, moderately similar to Homo sapiens mRNA for neuropathy target esterase.	AK126267	patatin-like phospholipase domain containing 7
270	↓ 0.38	WISP2	Homo sapiens WNT1 inducible signaling pathway protein 2 (WISP2)	NM_003881	WNT1 inducible signaling pathway protein 2
271	↓ 0.37	OLR1	Homo sapiens oxidized low density lipoprotein (lectin-like) receptor 1 (OLR1)	NM_002543	oxidized low density lipoprotein (lectin-like) receptor 1
272	↓ 0.37	NR4A3	Homo sapiens nuclear receptor subfamily 4, group A, member 3 (NR4A3)	NM_173198	nuclear receptor subfamily 4, group A, member 3
273	↓ 0.36	NEXN	Homo sapiens nexilin (F actin binding protein) (NEXN)	NM_144573	nexilin (F actin binding protein)
274	↓ 0.36	tcag7.1307	Homo sapiens hypothetical LOC154822(LOC154822)	NR_024394	hypothetical LOC154822
275	↓ 0.36	WNT11	Homo sapiens wingless-type MMTV integration site family, member 11 (WNT11)	NM_004626	wingless-type MMTV integration site family, member 11
276	↓ 0.36	CSF1R	Homo sapiens colony stimulating factor 1 receptor (CSF1R)	NM_005211	colony stimulating factor 1 receptor
277	↓ 0.35	EFR3B	Homo sapiens EFR3 homolog B (S. cerevisiae) (EFR3B)	NM_014971	EFR3 homolog B (S. cerevisiae)
278	↓ 0.35	QPRT	Homo sapiens quinolinate phosphoribosyltransferase (QPRT)	NM_014298	quinolinate phosphoribosyltransferase
279	↓ 0.35	NNMT	Homo sapiens nicotinamide N-methyltransferase (NNMT)	NM_006169	nicotinamide N-methyltransferase
280	↓ 0.35	RHOBTB3	Homo sapiens Rho-related BTB domain containing 3 (RHOBTB3)	NM_014899	Rho-related BTB domain containing 3
281	↓ 0.35	C10orf90	Homo sapiens chromosome 10 open reading frame 90 (C10orf90)	NM_001004298	chromosome 10 open reading frame 90
282	↓ 0.34	GDF6	Homo sapiens growth differentiation factor 6 (GDF6)	NM_001001557	growth differentiation factor 6
283	↓ 0.34	CLIC5	Homo sapiens chloride intracellular channel 5 (CLIC5)	NM_016929	chloride intracellular channel 5

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Number	Fold change expressed	Abbreviation	Description	Genbank	Gene name
284	↓ 0.34	SAMD11	Homo sapiens sterile alpha motif domain containing 11 (SAMD11)	NM_152486	sterile alpha motif domain containing 11
285	↓ 0.33	TFF1	Homo sapiens trefoil factor 1 (TFF1)	NM_003225	trefoil factor 1
286	↓ 0.33	FN1	Homo sapiens fibronectin 1 (FN1)	NM_212482	fibronectin 1
287	↓ 0.33	PSG6	Homo sapiens pregnancy specific beta-1-glycoprotein 6 (PSG6)	NM_002782	pregnancy specific beta-1-glycoprotein 6
288	↓ 0.32	DLX2	Homo sapiens distal-less homeobox 2 (DLX2)	NM_004405	distal-less homeobox 2
289	↓ 0.32	CA12	Homo sapiens carbonic anhydrase XII (CA12)	NM_001218	carbonic anhydrase XII
290	↓ 0.32	ANXA6	Homo sapiens annexin A6 (ANXA6)	NM_001155	annexin A6
291	↓ 0.32	KCNQ1	Homo sapiens potassium voltage-gated channel, KQT-like subfamily, member 1 (KCNQ1)	NM_000218	potassium voltage-gated channel, KQT-like subfamily, member 1
292	↓ 0.31	SLC16A6	Homo sapiens solute carrier family 16, member 6 (monocarboxylic acid transporter 7) (SLC16A6)	NM_004694	solute carrier family 16, member 6 (monocarboxylic acid transporter 7)
293	↓ 0.31	LOXL1	Homo sapiens lysyl oxidase-like 1 (LOXL1)	NM_005576	lysyl oxidase-like 1
294	↓ 0.31	PYCARD	Homo sapiens PYD and CARD domain containing (PYCARD)	NM_013258	PYD and CARD domain containing
295	↓ 0.30	CCL26	Homo sapiens chemokine (C-C motif) ligand 26 (CCL26)	NM_006072	chemokine (C-C motif) ligand 26
296	↓ 0.30	SPINK4	Homo sapiens serine peptidase inhibitor, Kazal type 4 (SPINK4)	NM_014471	serine peptidase inhibitor, Kazal type 4
297	↓ 0.30	ID3	Homo sapiens inhibitor of DNA binding 3, dominant negative helix-loop-helix protein (ID3)	NM_002167	inhibitor of DNA binding 3, dominant negative helix-loop-helix protein
298	↓ 0.29	PSG8	Homo sapiens pregnancy specific beta-1-glycoprotein 8 (PSG8)	NM_182707	pregnancy specific beta-1-glycoprotein 8
299	↓ 0.29	C15orf59	Homo sapiens chromosome 15 open reading frame 59 (C15orf59)	NM_001039614	chromosome 15 open reading frame 59
300	↓ 0.28	APOC1	Homo sapiens apolipoprotein C-I (APOC1)	NM_001645	apolipoprotein C-I
301	↓ 0.28	RGS11	Homo sapiens regulator of G-protein signaling 11 (RGS11)	NM_003834	regulator of G-protein signaling 11
302	↓ 0.27	EGFLAM	Homo sapiens EGF-like, fibronectin type III and laminin G domains (EGFLAM)	NM_152403	EGF-like, fibronectin type III and laminin G domains
303	↓ 0.26	MMP14	Homo sapiens matrix metallopeptidase 14 (membrane-inserted) (MMP14)	NM_004995	matrix metallopeptidase 14 (membrane-inserted)
304	↓ 0.26	CYP1A1	Homo sapiens cytochrome P450, family 1, subfamily A, polypeptide 1 (CYP1A1)	NM_000499	cytochrome P450, family 1, subfamily A, polypeptide 1
305	↓ 0.26	PON3	Homo sapiens paraoxonase 3 (PON3)	NM_000940	paraoxonase 3
306	↓ 0.25	ZNF469	Homo sapiens zinc finger protein 469 (ZNF469)	NM_001127464	zinc finger protein 469
307	↓ 0.22	MSMB	Homo sapiens microseminoprotein, beta- (MSMB)	NM_002443	microseminoprotein, beta-
308	↓ 0.20	GLP2R	Glucagon-like peptide 2 receptor Precursor (GLP-2 receptor)(GLP-2-R)(GLP-2R)	BC043390	glucagon-like peptide 2 receptor
309	↓ 0.20	NPTX1	Homo sapiens neuronal pentraxin I (NPTX1)	NM_002522	neuronal pentraxin I
310	↓ 0.17	C4BPB	Homo sapiens complement component 4 binding protein, beta (C4BPB)	NM_000716	complement component 4 binding protein, beta
311	↓ 0.16	MFAP5	Homo sapiens microfibrillar associated protein 5 (MFAP5)	NM_003480	microfibrillar associated protein 5
312	↓ 0.16	MCAM	Homo sapiens melanoma cell adhesion molecule (MCAM)	NM_006500	melanoma cell adhesion molecule
313	↓ 0.10	SLC12A3	Homo sapiens solute carrier family 12 (sodium/ chloride transporters), member 3 (SLC12A3)	NM_000339	solute carrier family 12 (sodium/ chloride transporters), member 3
314	↓ 0.10	ID2	Homo sapiens inhibitor of DNA binding 2, dominant negative helix-loop-helix protein (ID2)	NM_002166	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein

↑ exhibited up-regulation in SP18-LMP1$^{\Delta 232\text{-}351}$ to compare with SP18-LMP1; ↓ showed down-regulation in SP18-LMP1$^{\Delta 232\text{-}351}$ to compare with SP18-LMP1.