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(54) 发明名称

低氧标志分子 CHL1 及其应用

(57) 摘要

本发明公开了属于生物医学材料技术领域的一种低氧标志分子 CHL1 及其应用。该标志分子为细胞粘附分子 CHL1, 其蛋白序列如 SEQ ID No. 1 或 SEQ ID No. 2 所示。本发明的 CHL1 可作为一种低氧标志分子, 应用免疫学方法, 利用该标志物分子制备的抗体和酶标二抗, 利用酶联免疫学检测方法, 可检测动物及人是否处于低氧状态, 检测灵敏可靠。

1. 一种低氧标志分子,其特征在于,该标志分子为 CHL1,其蛋白序列如 SEQ ID No. 1 或 SEQ ID No. 2 所示。
2. 权利要求 1 所述低氧标志分子在制备动物及人低氧检测试剂盒中的应用。
3. 根据权利要求 2 所述低氧标志分子在制备动物及人低氧检测试剂盒中的应用,其特征在于,所述动物为鼠。
4. 一种动物及人低氧诊断试剂盒,其特征在于,所述试剂盒包括酶标板、CHL1 抗体,酶标二抗,以及酶联免疫反应常用的试剂。
5. 根据权利要求 4 所述一种动物及人低氧诊断试剂盒,其特征在于,所述酶标二抗中的酶为辣根过氧化物酶。

低氧标志分子 CHL1 及其应用

技术领域

[0001] 本发明属于生物医学材料技术领域,具体涉及一种低氧标志分子 CHL1 及其应用。

背景技术

[0002] 环境低氧损伤一直以来是高原医学、航天医学、运动医学等学科领域面临的共性问题,也是特殊环境生理学研究的重要领域^[1,2]。低氧可引起神经、呼吸和循环主要系统功能障碍,严重时可导致呼吸衰竭,危及生命^[3]。低氧也是许多疾病如心肌梗死、脑梗死、动脉粥样硬化等心脑血管疾病共有的病理生理过程,此外,低氧也是实体瘤微环境的重要特征之一,是临床上实体瘤对放疗、化疗产生耐受和预后效果差的重要原因^[4]。因此,低氧是危害人体健康的重要病理生理因素。

[0003] 细胞粘附分子(cell adhesion molecules, CAMs)是体内细胞生存的微环境,可促进细胞与细胞之间,细胞与细胞外基质之间粘附和识别,在维持细胞结构完整和细胞信号转导中起重要作用,是细胞生长和神经系统发育过程的重要调控因子。CAMs 主要分为四类:整合素家族、免疫球蛋白超家族、选择素家族和钙粘蛋白家族^[5]。CHL1(close homologue of L1, CHL1),又称 CALL、L1CAM2,是 1996 年 Holm 等在小鼠基因组中克隆得到,与神经粘附分子 L1 高度同源的基因,属于粘附分子免疫球蛋白超家族的成员。CHL1 作为一种跨膜蛋白,包含 N 端信号序列、6 个免疫球蛋白(Ig)样结构域、5 个纤粘连蛋白 III(FnIII)重复序列、一个跨膜结构域和含有骨架蛋白锚蛋白(anykrin)识别序列(FIGAY)的保守胞内区。与 L1 不同的是,在中枢神经系统中 CHL1 不仅表达于神经元中,在胶质细胞中同样存在^[6]。目前国内外对 CHL1 的研究主要集中在神经系统中,如 CHL1 是一种促神经元存活因子^[7];在中枢神经系统发育过程中,CHL1 通过外功能区的脱落和释放以可溶性底物结合形式促进轴突的形成^[8];通过与细胞外基质蛋白相结合,CHL1 介导整合蛋白依赖的细胞迁移^[9];中枢神经系统损伤可引起 CHL1 在具有再生轴突功能的神经元中高表达^[10];压力应激作用可导致小鼠海马区域 CHL1 表达下调^[11]。同时,粘附分子 CHL1 基因突变是人类精神分裂症的主要病因^[12]。

[0004] 随着 CHL1 研究的逐步深入,相关工具小鼠也应运而生。2002 年, M. Montag-Sallaz 等首次报道:通过基因打靶和同源重组技术获得 CHL1 基因敲除小鼠,并用于实验研究。CHL1 基因缺失小鼠可以正常的存活和繁殖,但在神经突起的发育和成年后的学习和记忆方面存在一定的缺陷^[13]。有研究显示:CHL1 基因缺失后,皮层神经元的突起倒置增多,小鼠的学习和认知行为学受到了影响^[14];近年来粘附分子在损伤修复中的报道也引起了关注,2007 年 Jakovcevski 等研究发现脊髓损伤后 CHL1 基因缺失的小鼠,可通过抑制胶质细胞所致的疤痕形成,而促进脊髓损伤后的功能恢复^[15];发明人的研究发现:不同低氧条件下 CHL1 在不同脑区、心、肺、肾中的表达显著下调^[16]。提示,细胞粘附分子 CHL1 可能作为低氧损伤的标志分子,用于临床诊断。

发明内容

[0005] 本发明的目的在于提供一种低氧标志分子 CHL1 及其在制备低氧诊断试剂盒方面的应用。

[0006] 一种低氧标志分子,该标志分子为 CHL1,其蛋白序列如 SEQ ID No. 1 或 SEQ ID No. 2 所示。

[0007] 所述低氧标志分子在制备动物及人低氧检测试剂盒中的应用。

[0008] 所述动物为鼠。

[0009] 所述试剂盒包括酶标板、CHL1 抗体,酶标二抗,以及酶联免疫反应常用的试剂。

[0010] 所述酶标二抗中的酶为辣根过氧化物酶。

[0011] 本发明的有益效果:本发明的细胞粘附分子 CHL1 可作为一种低氧标志分子,应用免疫学方法,利用该标志物分子制备的抗体和酶标二抗,利用酶联免疫学检测方法,可检测动物及人是否处于低氧状态,检测灵敏可靠。

附图说明

[0012] 图 1 为 ELISA 检测急性低氧处理 24h 后小鼠血浆中 CHL1 含量的结果。

[0013] 图 2 为 ELISA 检测慢性低氧 14d、28d 后小鼠血浆中 CHL1 含量的结果。

[0014] 图 3 为 ELISA 检测海拔 3000m、4800m 米高原低氧下人血浆中 CHL1 含量的结果。

具体实施方式

[0015] 下面结合附图和具体实施例对本发明做进一步说明。

[0016] 以下实施例所用材料蛋白 CHL1,其蛋白序列如 SEQ ID No. 1 或 SEQ ID No. 2 所示。

[0017] 实施例 1 小鼠低氧实验

[0018] (1) 急性低氧

[0019] 将 40 只平均体重 22 ~ 24g 的 C57 小鼠(由军事医学科学院动物中心提供)分为 2 组,每组 20 只,分别是对照组、急性低氧组。实验动物分别在常氧、低氧舱中(给予 5000 米低压低氧)处理 24h。低氧舱以 20 米/秒的速度匀速升至 5000 米,实验结束后以 20 米/秒速度匀速降至常氧。低氧处理结束后立即摘眼球取血,用于 CHL1 的检测。

[0020] (2) 慢性低氧

[0021] 将 60 只平均体重 22 ~ 24g 的 C57 小鼠(由军事医学科学院动物中心提供)分为 3 组,每组 20 只,分别是对照组、慢性低氧 14 天组、慢性低氧 28 天组。实验组动物分别在常氧、低氧舱中给予 10% O₂ 低氧处理 14 天、28 天。低氧舱提前将氧浓度降至 10%,实验当日将小鼠放入低氧舱,分别在 14 天、28 天后取出,立即摘眼球取血,用于 CHL1 的检测。

[0022] (3) 血浆的提取

[0023] 将采取的血液置含有抗凝剂(乙二胺四乙酸二钾)的试管中,混合后,以 3000rpm 离心 10min,使之与血细胞分离,分取上清液即为血浆。血浆保存在 -80 度备用。

[0024] (4) 酶联免疫检测所提取的血浆中 CHL1 含量

[0025] 试剂:

[0026] 1、碳酸盐包被液:3.03g Na₂CO₃,6.0g NaHCO₃,溶解于 900ml 双蒸水,调整 pH 至 9.6,定容至 1L;

[0027] 2、PBS:1.16g Na₂HPO₄,0.1g KCl,0.1g K₃PO₄,4.0g NaCl,溶于 500mL 蒸馏水,调整

pH 至 7.4 ;

[0028] 3、封闭液 :溶于 PBS 的 1% BSA,5%脱脂牛奶 ;

[0029] 4、洗涤液 :TBST(Tris-HCl, pH7.4+0.05%吐温 20) ;

[0030] 5、抗体或抗原稀释液 :1× 封闭液 ;

[0031] 6、终止液 :2N H_2SO_4 。

[0032] 操作步骤 :

[0033] a、包被抗体 :将碳酸盐包被液稀释的 CHL1 抗体加入 96 孔酶标板中, CHL1 抗体浓度为 $1 \mu g/ml$, 每孔 $100 \mu l$, 盖上膜板包被 4 度过夜。

[0034] b、弃去包被液用洗涤液洗涤 2 次, 轻拍孔板使洗涤液甩干。

[0035] c、封闭 :每孔中加入 $200 \mu l$ 封闭液 (1% BSA 或 5%脱脂牛奶等) 室温封闭 1 小时。

[0036] d、每孔加入 $100 \mu l$ 稀释好的样品 ($2 \mu l$ 血浆 + $98 \mu l$ 稀释液), 37 度孵育 60 ~ 90 分钟。

[0037] e、甩去孔板里面的溶液, 洗涤液洗涤 3 次, 每次 10 分钟。

[0038] f、每孔加入 $100 \mu l$ 的检测抗体 (1 : 500 稀释), 室温孵育 2 小时。

[0039] g、孵育后洗涤液洗涤 4 次, 每次 10 分钟。

[0040] h、每孔加入 $100 \mu l$ 的辣根过氧化物酶标记的二抗 (1 : 500), 继续室温孵育 1-2 小时。

[0041] i、孵育后洗涤液洗涤四次。

[0042] j、每孔加入 $100 \mu l$ 的 TMB 底物溶液, 待显色充分后加入 $100 \mu l$ 的终止液并在酶标仪上测定 450nm 吸光度值。

[0043] 检测结果如图 1 和图 2 所示, 急性低氧小鼠的 450nm 吸光度值为 0.625, 正常小鼠的为 0.278, 两者的差异达到了极显著的区别, 慢性低氧 14 天和 18 天的吸光度值分别为 0.398 和 0.425, 达到了显著水平, 说明 CHL1 可作为低氧标志分子, 并且可以根据此实验制备相应的低氧检测试剂盒。

[0044] 实施例 2 人低氧实验

[0045] (1) 模拟高原低氧 :随机选取 10 名志愿者进入低氧舱, 分别在常氧、模拟海拔 3600m、海拔 4800m 低氧环境下静脉取血, 用于 CHL1 的检测。

[0046] (2) 血浆的提取

[0047] 将采取的血液置含有抗凝剂 (乙二胺四乙酸二钾) 的试管中, 混合后, 以 3000rpm 离心 10min, 使之与血细胞分离, 分取上清液即为血浆。血浆保存在 -80 度备用。

[0048] (3) 酶联免疫检测所提取的血浆中 CH1 含量

[0049] 试剂 :

[0050] 1、碳酸盐包被液 :3.03g Na_2CO_3 , 6.0g $NaHCO_3$, 溶解于 900ml 双蒸水, 调整 pH 至 9.6, 定容至 1L ;

[0051] 2、PBS :1.16g Na_2HPO_4 , 0.1g KCl, 0.1g K_3PO_4 , 4.0g NaCl, 溶于 500mL 蒸馏水, 调整 pH 至 7.4 ;

[0052] 4、封闭液 :溶于 PBS 的 1% BSA,5%脱脂牛奶 ;

[0053] 4、洗涤液 :TBST(Tris-HCl, pH7.4+0.05%吐温 20) ;

[0054] 5、抗体或抗原稀释液:1× 封闭液;

[0055] 6、终止液:2N H_2SO_4 。

[0056] 操作步骤:

[0057] a、包被抗体:将碳酸盐包被液稀释的 CHL1 抗体加入 96 孔酶标板中, CHL1 抗体浓度为 1 $\mu\text{g}/\text{ml}$, 每孔 100 μl , 盖上膜板包被 4 度过夜。

[0058] b、弃去包被液用洗涤液洗涤 2 次, 轻拍孔板使洗涤液甩干。

[0059] c、封闭:每孔中加入 200 μl 封闭液(1% BSA 或 5% 脱脂牛奶等) 室温封闭 1 小时。

[0060] d、每孔加入 100 μl 稀释好的样品(2 μl 血浆+98 μl 稀释液), 37 度孵育 60 ~ 90 分钟。

[0061] e、甩去孔板里面的溶液, 洗涤液洗涤 3 次, 每次 10 分钟。

[0062] f、每孔加入 100 μl 的检测抗体(1 : 500 稀释), 室温孵育 2 小时。

[0063] g、孵育后洗涤液洗涤 4 次, 每次 10 分钟。

[0064] h、每孔加入 100 μl 的辣根过氧化物酶标记的二抗(1 : 500), 继续室温孵育 1-2 小时。

[0065] i、孵育后洗涤液洗涤四次。

[0066] j、每孔加入 100 μl 的 TMB 底物溶液, 待显色充分后加入 100 μl 的终止液并在酶标仪上测定 450nm 吸光度值。

[0067] 检测结果如图 3 所示, 正常人 450nm 吸光度值为 0. 255, 模拟海拔 3600m 低氧处理的人的吸光度值为 0. 314, 模拟海拔 4800m 低氧处理的人的吸光度值为 0. 356, 说明 CHL1 可作为低氧标志分子, 并且可以根据此实验制备相应的低氧检测试剂盒。

[0068] 参考文献

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[0001]

SEQUENCE LISTING

<110> 中国人民解放军军事医学科学院基础医学研究所

<120> 低氧标志分子 CHL1 及其应用

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<160> 2

<170> PatentIn version 3.5

<210> 1

<211> 1209

<212> PRT

<213> Mus musculus

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Gln Val Pro Thr Ile Val Lys Gln Ser Tyr Val Gln Val Ala Phe Pro
           35           40           45
Phe Asp Glu Tyr Phe Gln Ile Glu Cys Glu Ala Lys Gly Asn Pro Glu
           50           55           60
Pro Ile Phe Ser Trp Thr Lys Asp Asp Lys Pro Phe Asp Leu Ser Asp
65           70           75           80
Pro Arg Ile Ile Ala Ala Asn Asn Ser Gly Thr Phe Lys Ile Pro Asn
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Gly Val Pro Lys Phe Pro Lys Glu Lys Ile Glu Pro Ile Asp Val Glu
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Glu Gly Asp Ser Ile Val Leu Pro Cys Asn Pro Pro Lys Gly Leu Pro
145          150          155          160
Pro Leu His Ile Tyr Trp Met Asn Ile Glu Leu Glu His Ile Glu Gln
           165          170          175
Asp Glu Arg Val Tyr Met Ser Gln Arg Gly Asp Leu Tyr Phe Ala Asn
           180          185          190

Val Glu Glu Asn Asp Ser Arg Asn Asp Tyr Cys Cys Phe Ala Ala Phe
           195          200          205
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[0002]

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	275	280	285
Glu Val His Glu Lys Thr Leu Lys Ile Glu Asn Ile Ser Tyr Gln Asp			
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Arg Gly Asn Tyr Arg Cys Thr Ala Asn Asn Leu Leu Gly Lys Ala Ser			
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Pro Gln Ser Ala Val Tyr Ser Thr Gly Ser Ser Gly Ile Leu Leu Cys			
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Leu Pro Ile Glu Lys His Pro Phe Pro Gly Asp Phe Met Phe Pro Arg			
	370	375	380
Glu Ile Ser Phe Thr Asn Leu Leu Pro Asn His Thr Gly Val Tyr Gln			
385	390	395	400
Cys Glu Ala Ser Asn Ile His Gly Thr Ile Leu Ala Asn Ala Asn Ile			
	405	410	415
Asp Val Ile Asp Val Ile Pro Leu Ile Lys Thr Lys Asn Glu Glu Asn			
	420	425	430
Tyr Ala Thr Val Val Gly Tyr Ser Ala Phe Leu His Cys Glu Tyr Phe			
	435	440	445
Ala Ser Pro Lys Ala Thr Val Val Trp Glu Val Ala Asp Glu Thr His			
	450	455	460
Pro Leu Glu Gly Asp Arg Tyr His Thr His Glu Asn Gly Thr Leu Glu			
465	470	475	480
Ile Tyr Arg Thr Thr Glu Glu Asp Ala Gly Ser Tyr Ser Cys Trp Val			
	485	490	495
Asp Asn Ala Met Gly Lys Ala Val Ile Thr Ala Asn Leu Asp Ile Arg			
	500	505	510
Asn Ala Thr Lys Leu Arg Val Ser Pro Lys Asn Pro Arg Ile Pro Lys			
	515	520	525
Ser His Val Leu Glu Leu Tyr Cys Glu Ser Gln Cys Asp Ser His Leu			
	530	535	540
Lys His Ser Leu Lys Leu Ser Trp Ser Lys Asp Gly Glu Ala Phe Glu			
545	550	555	560
Met Asn Gly Thr Glu Asp Gly Arg Ile Val Ile Asp Gly Ala Tyr Leu			
	565	570	575
Thr Ile Ser Asn Ile Thr Ala Glu Asp Gln Gly Val Tyr Ser Cys Ser			

[0003]

580	585	590	
Ala Gln Thr Ser Leu Asp Ser Thr Ser Glu Lys Thr Gln Val Thr Val			
595	600	605	
Leu Gly Val Pro Asp Pro Pro Gly Asn Leu His Leu Ser Glu Arg Gln			
610	615	620	
Asn Arg Ser Val Arg Leu Ser Trp Glu Ala Gly Asp Asp His Asn Ser			
625	630	635	640
Lys Ile Ser Glu Tyr Ile Val Glu Phe Glu Gly Asn Arg Glu Glu Pro			
645	650	655	
Gly Lys Trp Glu Glu Leu Thr Arg Val Gln Gly Glu Glu Thr Asp Val			
660	665	670	
Val Leu Ser Leu Ala Pro Tyr Val Arg Tyr Gln Phe Arg Val Thr Ala			
675	680	685	
Val Asn Glu Val Gly Arg Ser His Ala Ser Leu Pro Ser Asp His His			
690	695	700	
Glu Thr Pro Pro Ala Ala Pro Asp Lys Asn Pro Gln Asn Ile Arg Val			
705	710	715	720
Gln Ala Ser Gln Pro Lys Glu Met Ile Ile Lys Trp Glu Pro Leu Lys			
725	730	735	
Ser Met Glu Gln Asn Gly Pro Gly Leu Glu Tyr Lys Val Ser Trp Lys			
740	745	750	
Pro Gln Gly Ala Pro Glu Glu Trp Glu Glu Glu Ile Val Thr Asn His			
755	760	765	
Thr Leu Arg Val Met Thr Pro Thr Val Tyr Ala Pro Tyr Asp Val Lys			
770	775	780	
Val Gln Ala Ile Asn Gln Leu Gly Ser Ser Pro Asp Pro Gln Pro Val			
785	790	795	800
Thr Leu Tyr Ser Gly Glu Asp Tyr Pro Ser Thr Ala Pro Val Ile Gln			
805	810	815	
Arg Val Asp Val Met Asn Ser Thr Leu Val Lys Val Thr Trp Ser Ser			
820	825	830	
Ile Pro Lys Glu Thr Val His Gly Leu Leu Arg Gly Tyr Gln Ile Asn			
835	840	845	
Trp Trp Lys Thr Lys Ser Leu Leu Asp Gly Arg Thr His Pro Lys Glu			
850	855	860	
Val Asn Ile Leu Arg Phe Ser Gly Gln Arg Asn Ser Gly Met Val Pro			
865	870	875	880
Ser Leu Asp Pro Phe Ser Glu Phe His Leu Thr Val Leu Ala Tyr Asn			
885	890	895	
Ser Lys Gly Ala Gly Pro Glu Ser Glu Pro Tyr Ile Phe Gln Thr Pro			
900	905	910	
Glu Gly Val Pro Glu Gln Pro Ser Phe Leu Lys Val Ile Lys Val Asp			
915	920	925	
Lys Asp Thr Ala Thr Leu Ser Trp Gly Leu Pro Lys Lys Leu Asn Gly			

[0004]

930	935	940	
Asn Leu Thr Gly Tyr Leu Leu Gln Tyr Gln Ile Ile Asn Asp Thr Tyr			
945	950	955	960
Glu Leu Gly Glu Leu Asn Glu Ile Asn Val Thr Thr Pro Ser Lys Ser			
	965	970	975
Ser Trp His Leu Ser Asn Leu Asn Ser Thr Thr Lys Tyr Lys Phe Tyr			
	980	985	990
Leu Arg Ala Cys Thr Ser Arg Gly	Cys Gly Lys Pro Ile	Ser Glu Glu	
995	1000	1005	
Gly Ala Thr Leu Gly Glu Gly	Ser Lys Gly Ile Arg	Lys Ile Thr	
1010	1015	1020	
Glu Gly Val Asn Val Thr Gln	Lys Ile His Pro Val	Glu Val Leu	
1025	1030	1035	
Val Pro Gly Ala Glu His Ile	Val His Leu Met Thr	Lys Asn Trp	
1040	1045	1050	
Gly Asp Asn Asp Ser Ile Phe	Gln Asp Val Ile Glu	Thr Arg Gly	
1055	1060	1065	
Arg Glu Tyr Ala Gly Leu Tyr	Asp Asp Ile Ser Thr	Gln Gly Trp	
1070	1075	1080	
Phe Ile Gly Leu Met Cys Ala	Ile Ala Leu Leu Thr	Leu Ile Leu	
1085	1090	1095	
Leu Thr Ile Cys Phe Val Lys	Arg Asn Arg Gly Gly	Lys Tyr Ser	
1100	1105	1110	
Val Lys Glu Lys Glu Asp Leu	His Pro Asp Pro Glu	Val Gln Ser	
1115	1120	1125	
Ala Lys Asp Glu Thr Phe Gly	Glu Tyr Ser Asp Ser	Asp Glu Lys	
1130	1135	1140	
Pro Leu Lys Gly Ser Leu Arg	Ser Leu Asn Arg Asn	Met Gln Pro	
1145	1150	1155	
Thr Glu Ser Ala Asp Ser Leu	Val Glu Tyr Gly Glu	Gly Asp Gln	
1160	1165	1170	
Ser Ile Phe Asn Glu Asp Gly	Ser Phe Ile Gly Ala	Tyr Thr Gly	
1175	1180	1185	
Ala Lys Glu Lys Gly Ser Val	Glu Ser Asn Gly Ser	Ser Thr Ala	
1190	1195	1200	
Thr Phe Pro Leu Arg Ala			
1205			

<210> 2

<211> 1224

<212> PRT

<213> Homo sapiens

<400> 2

[0005]

Met Glu Pro Leu Leu Leu Gly Arg Gly Leu Ile Val Tyr Leu Met Phe	
1 5 10 15	
Leu Leu Leu Lys Phe Ser Lys Ala Ile Glu Ile Pro Ser Ser Val Gln	
20 25 30	
Gln Val Pro Thr Ile Ile Lys Gln Ser Lys Val Gln Val Ala Phe Pro	
35 40 45	
Phe Asp Glu Tyr Phe Gln Ile Glu Cys Glu Ala Lys Gly Asn Pro Glu	
50 55 60	
Pro Thr Phe Ser Trp Thr Lys Asp Gly Asn Pro Phe Tyr Phe Thr Asp	
65 70 75 80	
His Arg Ile Ile Pro Ser Asn Asn Ser Gly Thr Phe Arg Ile Pro Asn	
85 90 95	
Glu Gly His Ile Ser His Phe Gln Gly Lys Tyr Arg Cys Phe Ala Ser	
100 105 110	
Asn Lys Leu Gly Ile Ala Met Ser Glu Glu Ile Glu Phe Ile Val Pro	
115 120 125	
Ser Val Pro Lys Phe Pro Lys Glu Lys Ile Asp Pro Leu Glu Val Glu	
130 135 140	
Glu Gly Asp Pro Ile Val Leu Pro Cys Asn Pro Pro Lys Gly Leu Pro	
145 150 155 160	
Pro Leu His Ile Tyr Trp Met Asn Ile Glu Leu Glu His Ile Glu Gln	
165 170 175	
Asp Glu Arg Val Tyr Met Ser Gln Lys Gly Asp Leu Tyr Phe Ala Asn	
180 185 190	
Val Glu Glu Lys Asp Ser Arg Asn Asp Tyr Cys Cys Phe Ala Ala Phe	
195 200 205	
Pro Arg Leu Arg Thr Ile Val Gln Lys Met Pro Met Lys Leu Thr Val	
210 215 220	
Asn Ser Leu Lys His Ala Asn Asp Ser Ser Ser Thr Glu Ile Gly	
225 230 235 240	
Ser Lys Ala Asn Ser Ile Lys Gln Arg Lys Pro Lys Leu Leu Leu Pro	
245 250 255	
Pro Thr Glu Ser Gly Ser Glu Ser Ser Ile Thr Ile Leu Lys Gly Glu	
260 265 270	
Ile Leu Leu Leu Glu Cys Phe Ala Glu Gly Leu Pro Thr Pro Gln Val	
275 280 285	
Asp Trp Asn Lys Ile Gly Gly Asp Leu Pro Lys Gly Arg Glu Thr Lys	
290 295 300	
Glu Asn Tyr Gly Lys Thr Leu Lys Ile Glu Asn Val Ser Tyr Gln Asp	
305 310 315 320	
Lys Gly Asn Tyr Arg Cys Thr Ala Ser Asn Phe Leu Gly Thr Ala Thr	
325 330 335	

[0006]

His Asp Phe His Val Ile Val Glu Glu Pro Pro Arg Trp Thr Lys Lys			
340	345	350	
Pro Gln Ser Ala Val Tyr Ser Thr Gly Ser Asn Gly Ile Leu Leu Cys			
355	360	365	
Glu Ala Glu Gly Glu Pro Gln Pro Thr Ile Lys Trp Arg Val Asn Gly			
370	375	380	
Ser Pro Val Asp Asn His Pro Phe Ala Gly Asp Val Val Phe Pro Arg			
385	390	395	400
Glu Ile Ser Phe Thr Asn Leu Gln Pro Asn His Thr Ala Val Tyr Gln			
405	410	415	
Cys Glu Ala Ser Asn Val His Gly Thr Ile Leu Ala Asn Ala Asn Ile			
420	425	430	
Asp Val Val Asp Val Arg Pro Leu Ile Gln Thr Lys Asp Gly Glu Asn			
435	440	445	
Tyr Ala Thr Val Val Gly Tyr Ser Ala Phe Leu His Cys Glu Phe Phe			
450	455	460	
Ala Ser Pro Glu Ala Val Val Ser Trp Gln Lys Val Glu Glu Val Lys			
465	470	475	480
Pro Leu Glu Gly Arg Arg Tyr His Ile Tyr Glu Asn Gly Thr Leu Gln			
485	490	495	
Ile Asn Arg Thr Thr Glu Glu Asp Ala Gly Ser Tyr Ser Cys Trp Val			
500	505	510	
Glu Asn Ala Ile Gly Lys Thr Ala Val Thr Ala Asn Leu Asp Ile Arg			
515	520	525	
Asn Ala Thr Lys Leu Arg Val Ser Pro Lys Asn Pro Arg Ile Pro Lys			
530	535	540	
Leu His Met Leu Glu Leu His Cys Glu Ser Lys Cys Asp Ser His Leu			
545	550	555	560
Lys His Ser Leu Lys Leu Ser Trp Ser Lys Asp Gly Glu Ala Phe Glu			
565	570	575	
Ile Asn Gly Thr Glu Asp Gly Arg Ile Ile Ile Asp Gly Ala Asn Leu			
580	585	590	
Thr Ile Ser Asn Val Thr Leu Glu Asp Gln Gly Ile Tyr Cys Cys Ser			
595	600	605	
Ala His Thr Ala Leu Asp Ser Ala Ala Asp Ile Thr Gln Val Thr Val			
610	615	620	
Leu Asp Val Pro Asp Pro Pro Glu Asn Leu His Leu Ser Glu Arg Gln			
625	630	635	640
Asn Arg Ser Val Arg Leu Thr Trp Glu Ala Gly Ala Asp His Asn Ser			
645	650	655	
Asn Ile Ser Glu Tyr Ile Val Glu Phe Glu Gly Asn Lys Glu Glu Pro			
660	665	670	
Gly Arg Trp Glu Glu Leu Thr Arg Val Gln Gly Lys Lys Thr Thr Val			
675	680	685	

[0007]

Ile Leu Pro Leu Ala Pro Phe Val Arg Tyr Gln Phe Arg Val Ile Ala			
690	695	700	
Val Asn Glu Val Gly Arg Ser Gln Pro Ser Gln Pro Ser Asp His His			
705	710	715	720
Glu Thr Pro Pro Ala Ala Pro Asp Arg Asn Pro Gln Asn Ile Arg Val			
725	730		735
Gln Ala Ser Gln Pro Lys Glu Met Ile Ile Lys Trp Glu Pro Leu Lys			
740	745		750
Ser Met Glu Gln Asn Gly Pro Gly Leu Glu Tyr Arg Val Thr Trp Lys			
755	760		765
Pro Gln Gly Ala Pro Val Glu Trp Glu Glu Glu Thr Val Thr Asn His			
770	775	780	
Thr Leu Arg Val Met Thr Pro Ala Val Tyr Ala Pro Tyr Asp Val Lys			
785	790	795	800
Val Gln Ala Ile Asn Gln Leu Gly Ser Gly Pro Asp Pro Gln Ser Val			
805	810		815
Thr Leu Tyr Ser Gly Glu Asp Tyr Pro Asp Thr Ala Pro Val Ile His			
820	825		830
Gly Val Asp Val Ile Asn Ser Thr Leu Val Lys Val Thr Trp Ser Thr			
835	840		845
Val Pro Lys Asp Arg Val His Gly Arg Leu Lys Gly Tyr Gln Ile Asn			
850	855	860	
Trp Trp Lys Thr Lys Ser Leu Leu Asp Gly Arg Thr His Pro Lys Glu			
865	870	875	880
Val Asn Ile Leu Arg Phe Ser Gly Gln Arg Asn Ser Gly Met Val Pro			
885	890		895
Ser Leu Asp Ala Phe Ser Glu Phe His Leu Thr Val Leu Ala Tyr Asn			
900	905		910
Ser Lys Gly Ala Gly Pro Glu Ser Glu Pro Tyr Ile Phe Gln Thr Pro			
915	920		925
Glu Gly Val Pro Glu Gln Pro Thr Phe Leu Lys Val Ile Lys Val Asp			
930	935	940	
Lys Asp Thr Ala Thr Leu Ser Trp Gly Leu Pro Lys Lys Leu Asn Gly			
945	950	955	960
Asn Leu Thr Gly Tyr Leu Leu Gln Tyr Gln Ile Ile Asn Asp Thr Tyr			
965	970		975
Glu Ile Gly Glu Leu Asn Asp Ile Asn Ile Thr Thr Pro Ser Lys Pro			
980	985		990
Ser Trp His Leu Ser Asn Leu Asn Ala Thr Thr Lys Tyr Lys Phe Tyr			
995	1000		1005
Leu Arg Ala Cys Thr Ser Gln Gly Cys Gly Lys Pro Ile Thr Glu			
1010	1015	1020	
Glu Ser Ser Thr Leu Gly Glu Gly Ser Lys Gly Ile Gly Lys Ile			
1025	1030	1035	

[0008]

Ser Gly	Val Asn Leu Thr Gln	Lys Thr His Pro Ile	Glu Val Phe
1040		1045	1050
Glu Pro	Gly Ala Glu His Ile	Val Arg Leu Met Thr	Lys Asn Trp
1055		1060	1065
Gly Asp	Asn Asp Ser Ile Phe	Gln Asp Val Ile Glu	Thr Arg Gly
1070		1075	1080
Arg Glu	Tyr Ala Gly Leu Tyr	Asp Asp Ile Ser Thr	Gln Gly Trp
1085		1090	1095
Phe Ile	Gly Leu Met Cys Ala	Ile Ala Leu Leu Thr	Leu Leu Leu
1100		1105	1110
Leu Thr	Val Cys Phe Val Lys	Arg Asn Arg Gly Gly	Lys Tyr Ser
1115		1120	1125
Val Lys	Glu Lys Glu Asp Leu	His Pro Asp Pro Glu	Ile Gln Ser
1130		1135	1140
Val Lys	Asp Glu Thr Phe Gly	Glu Tyr Ser Asp Ser	Asp Glu Lys
1145		1150	1155
Pro Leu	Lys Gly Ser Leu Arg	Ser Leu Asn Arg Asp	Met Gln Pro
1160		1165	1170
Thr Glu	Ser Ala Asp Ser Leu	Val Glu Tyr Gly Glu	Gly Asp His
1175		1180	1185
Gly Leu	Phe Ser Glu Asp Gly	Ser Phe Ile Gly Ala	Tyr Ala Gly
1190		1195	1200
Ser Lys	Glu Lys Gly Ser Val	Glu Ser Asn Gly Ser	Ser Thr Ala
1205		1210	1215
Thr Phe	Pro Leu Arg Ala		
1220			

[0009]

seq. txt

SEQUENCE LISTING

<110> 中国人民解放军军事医学科学院基础医学研究所

<120> 低氧标志分子CHL1及其应用

<130> 1111

<160> 2

<170> PatentIn version 3.5

<210> 1

<211> 1209

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<213> Mus musculus

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Phe Leu Leu Leu Lys Leu Ser Ala Ala Glu Ile Pro Leu Ser Val Gln
20 25 30

Gln Val Pro Thr Ile Val Lys Gln Ser Tyr Val Gln Val Ala Phe Pro
35 40 45

Phe Asp Glu Tyr Phe Gln Ile Glu Cys Glu Ala Lys Gly Asn Pro Glu
50 55 60

Pro Ile Phe Ser Trp Thr Lys Asp Asp Lys Pro Phe Asp Leu Ser Asp
65 70 75 80

Pro Arg Ile Ile Ala Ala Asn Asn Ser Gly Thr Phe Lys Ile Pro Asn
85 90 95

Glu Gly His Ile Ser His Phe Gln Gly Lys Tyr Arg Cys Phe Ala Ser
100 105 110

Asn Arg Leu Gly Thr Ala Val Ser Glu Glu Ile Glu Phe Ile Val Pro
115 120 125

Gly Val Pro Lys Phe Pro Lys Glu Lys Ile Glu Pro Ile Asp Val Glu
130 135 140

Glu Gly Asp Ser Ile Val Leu Pro Cys Asn Pro Pro Lys Gly Leu Pro
145 150 155 160

Pro Leu His Ile Tyr Trp Met Asn Ile Glu Leu Glu His Ile Glu Gln
165 170 175

Asp Glu Arg Val Tyr Met Ser Gln Arg Gly Asp Leu Tyr Phe Ala Asn
180 185 190

Val Glu Glu Asn Asp Ser Arg Asn Asp Tyr Cys Cys Phe Ala Ala Phe
195 200 205

Pro Lys Leu Arg Thr Ile Val Gln Lys Met Pro Met Lys Leu Thr Val
210 215 220

[0010]

seq. txt

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Asn Ser Ser Asn Ser Ile Lys Gln Arg Lys Pro Lys Leu Leu Leu Pro
225                               230                               235                               240

Pro Ala Gln Met Gly Ser Leu Ser Ala Lys Thr Val Leu Lys Gly Asp
                               245                               250                               255

Thr Leu Leu Leu Glu Cys Phe Ala Glu Gly Leu Pro Thr Pro His Ile
                               260                               265                               270

Gln Trp Ser Lys Pro Gly Ser Glu Leu Pro Glu Gly Arg Ala Thr Ile
                               275                               280                               285

Glu Val His Glu Lys Thr Leu Lys Ile Glu Asn Ile Ser Tyr Gln Asp
                               290                               295                               300

Arg Gly Asn Tyr Arg Cys Thr Ala Asn Asn Leu Leu Gly Lys Ala Ser
305                               310                               315                               320

His Asp Phe His Val Thr Val Glu Glu Pro Pro Arg Trp Lys Lys Lys
                               325                               330                               335

Pro Gln Ser Ala Val Tyr Ser Thr Gly Ser Ser Gly Ile Leu Leu Cys
                               340                               345                               350

Glu Ala Glu Gly Glu Pro Gln Pro Thr Ile Lys Trp Arg Leu Asn Gly
                               355                               360                               365

Leu Pro Ile Glu Lys His Pro Phe Pro Gly Asp Phe Met Phe Pro Arg
                               370                               375                               380

Glu Ile Ser Phe Thr Asn Leu Leu Pro Asn His Thr Gly Val Tyr Gln
385                               390                               395                               400

Cys Glu Ala Ser Asn Ile His Gly Thr Ile Leu Ala Asn Ala Asn Ile
                               405                               410                               415

Asp Val Ile Asp Val Ile Pro Leu Ile Lys Thr Lys Asn Glu Glu Asn
                               420                               425                               430

Tyr Ala Thr Val Val Gly Tyr Ser Ala Phe Leu His Cys Glu Tyr Phe
                               435                               440                               445

Ala Ser Pro Lys Ala Thr Val Val Trp Glu Val Ala Asp Glu Thr His
                               450                               455                               460

Pro Leu Glu Gly Asp Arg Tyr His Thr His Glu Asn Gly Thr Leu Glu
465                               470                               475                               480

Ile Tyr Arg Thr Thr Glu Glu Asp Ala Gly Ser Tyr Ser Cys Trp Val
                               485                               490                               495

Asp Asn Ala Met Gly Lys Ala Val Ile Thr Ala Asn Leu Asp Ile Arg
                               500                               505                               510

Asn Ala Thr Lys Leu Arg Val Ser Pro Lys Asn Pro Arg Ile Pro Lys
                               515                               520                               525

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[0011]

seq. txt

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Ser His Val Leu Glu Leu Tyr Cys Glu Ser Gln Cys Asp Ser His Leu
 530                      535                      540

Lys His Ser Leu Lys Leu Ser Trp Ser Lys Asp Gly Glu Ala Phe Glu
545                      550                      555                      560

Met Asn Gly Thr Glu Asp Gly Arg Ile Val Ile Asp Gly Ala Tyr Leu
                      565                      570                      575

Thr Ile Ser Asn Ile Thr Ala Glu Asp Gln Gly Val Tyr Ser Cys Ser
                      580                      585                      590

Ala Gln Thr Ser Leu Asp Ser Thr Ser Glu Lys Thr Gln Val Thr Val
                      595                      600                      605

Leu Gly Val Pro Asp Pro Pro Gly Asn Leu His Leu Ser Glu Arg Gln
610                      615                      620

Asn Arg Ser Val Arg Leu Ser Trp Glu Ala Gly Asp Asp His Asn Ser
625                      630                      635                      640

Lys Ile Ser Glu Tyr Ile Val Glu Phe Glu Gly Asn Arg Glu Glu Pro
                      645                      650                      655

Gly Lys Trp Glu Glu Leu Thr Arg Val Gln Gly Glu Glu Thr Asp Val
                      660                      665                      670

Val Leu Ser Leu Ala Pro Tyr Val Arg Tyr Gln Phe Arg Val Thr Ala
675                      680                      685

Val Asn Glu Val Gly Arg Ser His Ala Ser Leu Pro Ser Asp His His
690                      695                      700

Glu Thr Pro Pro Ala Ala Pro Asp Lys Asn Pro Gln Asn Ile Arg Val
705                      710                      715                      720

Gln Ala Ser Gln Pro Lys Glu Met Ile Ile Lys Trp Glu Pro Leu Lys
725                      730                      735

Ser Met Glu Gln Asn Gly Pro Gly Leu Glu Tyr Lys Val Ser Trp Lys
740                      745                      750

Pro Gln Gly Ala Pro Glu Glu Trp Glu Glu Glu Ile Val Thr Asn His
755                      760                      765

Thr Leu Arg Val Met Thr Pro Thr Val Tyr Ala Pro Tyr Asp Val Lys
770                      775                      780

Val Gln Ala Ile Asn Gln Leu Gly Ser Ser Pro Asp Pro Gln Pro Val
785                      790                      795                      800

Thr Leu Tyr Ser Gly Glu Asp Tyr Pro Ser Thr Ala Pro Val Ile Gln
805                      810                      815

Arg Val Asp Val Met Asn Ser Thr Leu Val Lys Val Thr Trp Ser Ser
820                      825                      830

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[0012]

seq. txt

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Ile Pro Lys Glu Thr Val His Gly Leu Leu Arg Gly Tyr Gln Ile Asn
      835                      840                      845

Trp Trp Lys Thr Lys Ser Leu Leu Asp Gly Arg Thr His Pro Lys Glu
      850                      855                      860

Val Asn Ile Leu Arg Phe Ser Gly Gln Arg Asn Ser Gly Met Val Pro
      865                      870                      875                      880

Ser Leu Asp Pro Phe Ser Glu Phe His Leu Thr Val Leu Ala Tyr Asn
      885                      890                      895

Ser Lys Gly Ala Gly Pro Glu Ser Glu Pro Tyr Ile Phe Gln Thr Pro
      900                      905                      910

Glu Gly Val Pro Glu Gln Pro Ser Phe Leu Lys Val Ile Lys Val Asp
      915                      920                      925

Lys Asp Thr Ala Thr Leu Ser Trp Gly Leu Pro Lys Lys Leu Asn Gly
      930                      935                      940

Asn Leu Thr Gly Tyr Leu Leu Gln Tyr Gln Ile Ile Asn Asp Thr Tyr
      945                      950                      955                      960

Glu Leu Gly Glu Leu Asn Glu Ile Asn Val Thr Thr Pro Ser Lys Ser
      965                      970                      975

Ser Trp His Leu Ser Asn Leu Asn Ser Thr Thr Lys Tyr Lys Phe Tyr
      980                      985                      990

Leu Arg Ala Cys Thr Ser Arg Gly Cys Gly Lys Pro Ile Ser Glu Glu
      995                      1000                      1005

Gly Ala Thr Leu Gly Glu Gly Ser Lys Gly Ile Arg Lys Ile Thr
      1010                      1015                      1020

Glu Gly Val Asn Val Thr Gln Lys Ile His Pro Val Glu Val Leu
      1025                      1030                      1035

Val Pro Gly Ala Glu His Ile Val His Leu Met Thr Lys Asn Trp
      1040                      1045                      1050

Gly Asp Asn Asp Ser Ile Phe Gln Asp Val Ile Glu Thr Arg Gly
      1055                      1060                      1065

Arg Glu Tyr Ala Gly Leu Tyr Asp Asp Ile Ser Thr Gln Gly Trp
      1070                      1075                      1080

Phe Ile Gly Leu Met Cys Ala Ile Ala Leu Leu Thr Leu Ile Leu
      1085                      1090                      1095

Leu Thr Ile Cys Phe Val Lys Arg Asn Arg Gly Gly Lys Tyr Ser
      1100                      1105                      1110

Val Lys Glu Lys Glu Asp Leu His Pro Asp Pro Glu Val Gln Ser

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[0013]

seq. txt

1115	1120	1125
Ala Lys Asp Glu Thr Phe Gly	Glu Tyr Ser Asp Ser	Asp Glu Lys
1130	1135	1140
Pro Leu Lys Gly Ser Leu Arg	Ser Leu Asn Arg Asn	Met Gln Pro
1145	1150	1155
Thr Glu Ser Ala Asp Ser Leu	Val Glu Tyr Gly Glu	Gly Asp Gln
1160	1165	1170
Ser Ile Phe Asn Glu Asp Gly	Ser Phe Ile Gly Ala	Tyr Thr Gly
1175	1180	1185
Ala Lys Glu Lys Gly Ser Val	Glu Ser Asn Gly Ser	Ser Thr Ala
1190	1195	1200
Thr Phe Pro Leu Arg Ala		
1205		
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<400> 2		
Met Glu Pro Leu Leu Leu Gly Arg Gly	Leu Ile Val Tyr Leu Met Phe	
1	5	10 15
Leu Leu Leu Lys Phe Ser Lys Ala Ile	Glu Ile Pro Ser Ser Val Gln	
20	25	30
Gln Val Pro Thr Ile Ile Lys Gln	Ser Lys Val Gln Val Ala Phe Pro	
35	40	45
Phe Asp Glu Tyr Phe Gln Ile	Glu Cys Glu Ala Lys Gly Asn Pro Glu	
50	55	60
Pro Thr Phe Ser Trp Thr Lys Asp Gly	Asn Pro Phe Tyr Phe Thr Asp	
65	70	75 80
His Arg Ile Ile Pro Ser Asn Asn Ser	Gly Thr Phe Arg Ile Pro Asn	
85	90	95
Glu Gly His Ile Ser His Phe Gln Gly	Lys Tyr Arg Cys Phe Ala Ser	
100	105	110
Asn Lys Leu Gly Ile Ala Met Ser	Glu Glu Ile Glu Phe Ile Val Pro	
115	120	125
Ser Val Pro Lys Phe Pro Lys	Glu Lys Ile Asp Pro Leu Glu Val Glu	
130	135	140
Glu Gly Asp Pro Ile Val Leu Pro Cys	Asn Pro Pro Lys Gly Leu Pro	
145	150	155 160
Pro Leu His Ile Tyr Trp Met Asn	Ile Glu Leu Glu His Ile Glu Gln	

[0014]

										seq.txt									
165										170									
Asp	Glu	Arg	Val	Tyr	Met	Ser	Gln	Lys	Gly	Asp	Leu	Tyr	Phe	Ala	Asn				
					180						185						190		
Val	Glu	Glu	Lys	Asp	Ser	Arg	Asn	Asp	Tyr	Cys	Cys	Phe	Ala	Ala	Phe				
					195						200						205		
Pro	Arg	Leu	Arg	Thr	Ile	Val	Gln	Lys	Met	Pro	Met	Lys	Leu	Thr	Val				
					210						215						220		
Asn	Ser	Leu	Lys	His	Ala	Asn	Asp	Ser	Ser	Ser	Ser	Thr	Glu	Ile	Gly				
					225						230						240		
Ser	Lys	Ala	Asn	Ser	Ile	Lys	Gln	Arg	Lys	Pro	Lys	Leu	Leu	Leu	Pro				
					245						250						255		
Pro	Thr	Glu	Ser	Gly	Ser	Glu	Ser	Ser	Ile	Thr	Ile	Leu	Lys	Gly	Glu				
					260						265						270		
Ile	Leu	Leu	Leu	Glu	Cys	Phe	Ala	Glu	Gly	Leu	Pro	Thr	Pro	Gln	Val				
					275						280						285		
Asp	Trp	Asn	Lys	Ile	Gly	Gly	Asp	Leu	Pro	Lys	Gly	Arg	Glu	Thr	Lys				
					290						295						300		
Glu	Asn	Tyr	Gly	Lys	Thr	Leu	Lys	Ile	Glu	Asn	Val	Ser	Tyr	Gln	Asp				
					305						310						320		
Lys	Gly	Asn	Tyr	Arg	Cys	Thr	Ala	Ser	Asn	Phe	Leu	Gly	Thr	Ala	Thr				
					325						330						335		
His	Asp	Phe	His	Val	Ile	Val	Glu	Glu	Pro	Pro	Arg	Trp	Thr	Lys	Lys				
					340						345						350		
Pro	Gln	Ser	Ala	Val	Tyr	Ser	Thr	Gly	Ser	Asn	Gly	Ile	Leu	Leu	Cys				
					355						360						365		
Glu	Ala	Glu	Gly	Glu	Pro	Gln	Pro	Thr	Ile	Lys	Trp	Arg	Val	Asn	Gly				
					370						375						380		
Ser	Pro	Val	Asp	Asn	His	Pro	Phe	Ala	Gly	Asp	Val	Val	Phe	Pro	Arg				
					385						390						400		
Glu	Ile	Ser	Phe	Thr	Asn	Leu	Gln	Pro	Asn	His	Thr	Ala	Val	Tyr	Gln				
					405						410						415		
Cys	Glu	Ala	Ser	Asn	Val	His	Gly	Thr	Ile	Leu	Ala	Asn	Ala	Asn	Ile				
					420						425						430		
Asp	Val	Val	Asp	Val	Arg	Pro	Leu	Ile	Gln	Thr	Lys	Asp	Gly	Glu	Asn				
					435						440						445		
Tyr	Ala	Thr	Val	Val	Gly	Tyr	Ser	Ala	Phe	Leu	His	Cys	Glu	Phe	Phe				
					450						455						460		

[0015]

seq.txt

Ala Ser Pro Glu Ala Val Val Ser Trp Gln Lys Val Glu Glu Val Lys
465 470 475 480

Pro Leu Glu Gly Arg Arg Tyr His Ile Tyr Glu Asn Gly Thr Leu Gln
485 490 495

Ile Asn Arg Thr Thr Glu Glu Asp Ala Gly Ser Tyr Ser Cys Trp Val
500 505 510

Glu Asn Ala Ile Gly Lys Thr Ala Val Thr Ala Asn Leu Asp Ile Arg
515 520 525

Asn Ala Thr Lys Leu Arg Val Ser Pro Lys Asn Pro Arg Ile Pro Lys
530 535 540

Leu His Met Leu Glu Leu His Cys Glu Ser Lys Cys Asp Ser His Leu
545 550 555 560

Lys His Ser Leu Lys Leu Ser Trp Ser Lys Asp Gly Glu Ala Phe Glu
565 570 575

Ile Asn Gly Thr Glu Asp Gly Arg Ile Ile Ile Asp Gly Ala Asn Leu
580 585 590

Thr Ile Ser Asn Val Thr Leu Glu Asp Gln Gly Ile Tyr Cys Cys Ser
595 600 605

Ala His Thr Ala Leu Asp Ser Ala Ala Asp Ile Thr Gln Val Thr Val
610 615 620

Leu Asp Val Pro Asp Pro Pro Glu Asn Leu His Leu Ser Glu Arg Gln
625 630 635 640

Asn Arg Ser Val Arg Leu Thr Trp Glu Ala Gly Ala Asp His Asn Ser
645 650 655

Asn Ile Ser Glu Tyr Ile Val Glu Phe Glu Gly Asn Lys Glu Glu Pro
660 665 670

Gly Arg Trp Glu Glu Leu Thr Arg Val Gln Gly Lys Lys Thr Thr Val
675 680 685

Ile Leu Pro Leu Ala Pro Phe Val Arg Tyr Gln Phe Arg Val Ile Ala
690 695 700

Val Asn Glu Val Gly Arg Ser Gln Pro Ser Gln Pro Ser Asp His His
705 710 715 720

Glu Thr Pro Pro Ala Ala Pro Asp Arg Asn Pro Gln Asn Ile Arg Val
725 730 735

Gln Ala Ser Gln Pro Lys Glu Met Ile Ile Lys Trp Glu Pro Leu Lys
740 745 750

Ser Met Glu Gln Asn Gly Pro Gly Leu Glu Tyr Arg Val Thr Trp Lys
755 760 765

[0016]

seq. txt

Pro Gln Gly Ala Pro Val Glu Trp Glu Glu Glu Thr Val Thr Asn His
 770 775 780
 Thr Leu Arg Val Met Thr Pro Ala Val Tyr Ala Pro Tyr Asp Val Lys
 785 790 795 800
 Val Gln Ala Ile Asn Gln Leu Gly Ser Gly Pro Asp Pro Gln Ser Val
 805 810 815
 Thr Leu Tyr Ser Gly Glu Asp Tyr Pro Asp Thr Ala Pro Val Ile His
 820 825 830
 Gly Val Asp Val Ile Asn Ser Thr Leu Val Lys Val Thr Trp Ser Thr
 835 840 845
 Val Pro Lys Asp Arg Val His Gly Arg Leu Lys Gly Tyr Gln Ile Asn
 850 855 860
 Trp Trp Lys Thr Lys Ser Leu Leu Asp Gly Arg Thr His Pro Lys Glu
 865 870 875 880
 Val Asn Ile Leu Arg Phe Ser Gly Gln Arg Asn Ser Gly Met Val Pro
 885 890 895
 Ser Leu Asp Ala Phe Ser Glu Phe His Leu Thr Val Leu Ala Tyr Asn
 900 905 910
 Ser Lys Gly Ala Gly Pro Glu Ser Glu Pro Tyr Ile Phe Gln Thr Pro
 915 920 925
 Glu Gly Val Pro Glu Gln Pro Thr Phe Leu Lys Val Ile Lys Val Asp
 930 935 940
 Lys Asp Thr Ala Thr Leu Ser Trp Gly Leu Pro Lys Lys Leu Asn Gly
 945 950 955 960
 Asn Leu Thr Gly Tyr Leu Leu Gln Tyr Gln Ile Ile Asn Asp Thr Tyr
 965 970 975
 Glu Ile Gly Glu Leu Asn Asp Ile Asn Ile Thr Thr Pro Ser Lys Pro
 980 985 990
 Ser Trp His Leu Ser Asn Leu Asn Ala Thr Thr Lys Tyr Lys Phe Tyr
 995 1000 1005
 Leu Arg Ala Cys Thr Ser Gln Gly Cys Gly Lys Pro Ile Thr Glu
 1010 1015 1020
 Glu Ser Ser Thr Leu Gly Glu Gly Ser Lys Gly Ile Gly Lys Ile
 1025 1030 1035
 Ser Gly Val Asn Leu Thr Gln Lys Thr His Pro Ile Glu Val Phe
 1040 1045 1050
 Glu Pro Gly Ala Glu His Ile Val Arg Leu Met Thr Lys Asn Trp
 1055 1060 1065

[0017]

seq. txt

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Gly Asp Asn Asp Ser Ile Phe Gln Asp Val Ile Glu Thr Arg Gly
1070      1075      1080

Arg Glu Tyr Ala Gly Leu Tyr Asp Asp Ile Ser Thr Gln Gly Trp
1085      1090      1095

Phe Ile Gly Leu Met Cys Ala Ile Ala Leu Leu Thr Leu Leu Leu
1100      1105      1110

Leu Thr Val Cys Phe Val Lys Arg Asn Arg Gly Gly Lys Tyr Ser
1115      1120      1125

Val Lys Glu Lys Glu Asp Leu His Pro Asp Pro Glu Ile Gln Ser
1130      1135      1140

Val Lys Asp Glu Thr Phe Gly Glu Tyr Ser Asp Ser Asp Glu Lys
1145      1150      1155

Pro Leu Lys Gly Ser Leu Arg Ser Leu Asn Arg Asp Met Gln Pro
1160      1165      1170

Thr Glu Ser Ala Asp Ser Leu Val Glu Tyr Gly Glu Gly Asp His
1175      1180      1185

Gly Leu Phe Ser Glu Asp Gly Ser Phe Ile Gly Ala Tyr Ala Gly
1190      1195      1200

Ser Lys Glu Lys Gly Ser Val Glu Ser Asn Gly Ser Ser Thr Ala
1205      1210      1215

Thr Phe Pro Leu Arg Ala
1220

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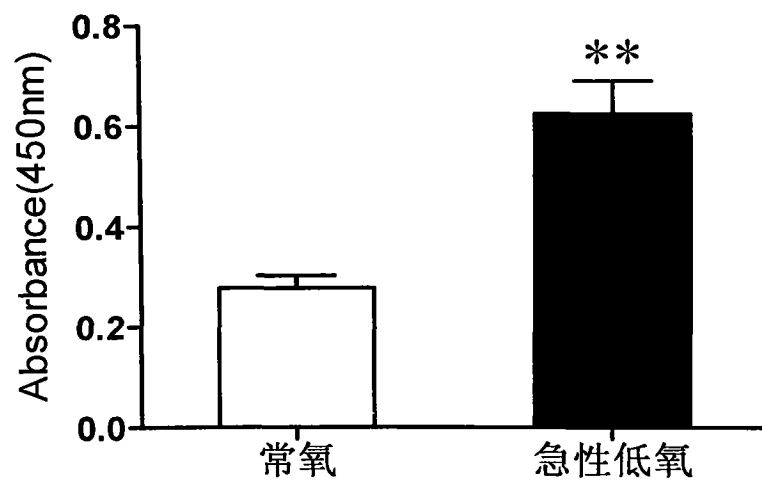


图 1

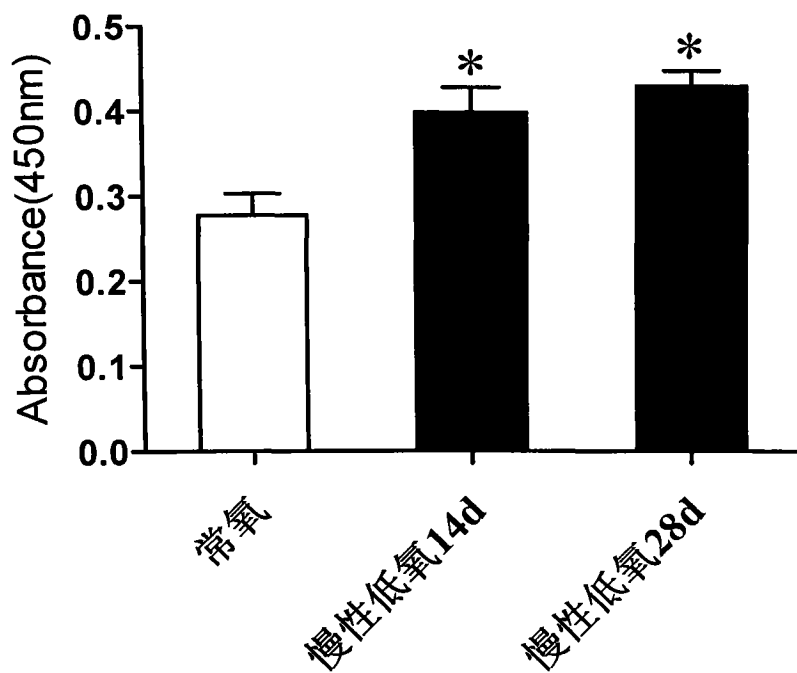


图 2

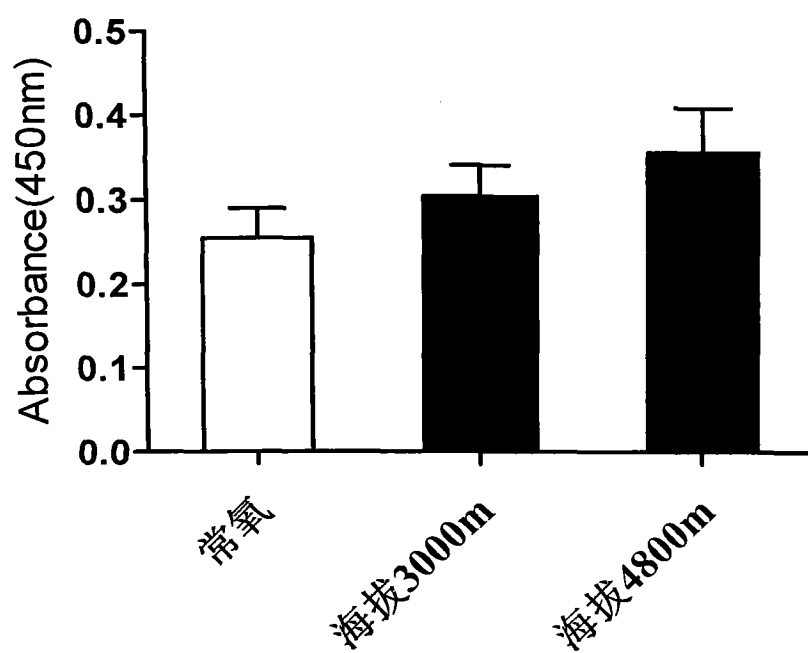


图 3

专利名称(译)	低氧标志分子CHL1及其应用		
公开(公告)号	CN103278624A	公开(公告)日	2013-09-04
申请号	CN201310138817.0	申请日	2013-04-22
[标]申请(专利权)人(译)	中国人民解放军军事医学科学院基础医学研究所		
申请(专利权)人(译)	中国人民解放军军事医学科学院基础医学研究所		
当前申请(专利权)人(译)	中国人民解放军军事医学科学院基础医学研究所		
[标]发明人	黄欣 朱玲玲 范明 吴奎武 赵彤 吴丽颖		
发明人	黄欣 朱玲玲 范明 吴奎武 赵彤 吴丽颖		
IPC分类号	G01N33/535		
其他公开文献	CN103278624B		
外部链接	Espacenet SIPO		

摘要(译)

本发明公开了属于生物医学材料技术领域的一种低氧标志分子CHL1及其应用。该标志分子为细胞粘附分子CHL1，其蛋白序列如SEQ ID No.1或SEQ ID No.2所示。本发明的CHL1可作为一种低氧标志分子，应用免疫学方法，利用该标志物分子制备的抗体和酶标二抗，利用酶联免疫学检测方法，可检测动物及人是否处于低氧状态，检测灵敏可靠。

