低氧/厌氧产品案例——间充质干细胞

文章题目：The Regulation of Mesenchymal Stem Cell Therapy Through Magnetic Resonance Imaging Agents-Based Cellular Condition and Oxygen Environment

磁共振成像（MRI）示踪低氧预处理骨髓间充质干细胞修复关节软骨损伤的研究

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工作站使用情况：Ruskinn 工作站 Invivo2 300 ;

使用气体 浓度：低氧（1% O_2 , 5% CO_2 ,94 N_2）

主要内容：软骨是由细胞外基质和单一软骨细胞组成的一种乏血管、乏神经的结缔组织，其获取营养的唯一方式是通过周围组织的弥散。基于这样的解剖及生理基础，软骨一旦损伤，其自我修复的能力非常有限。而且，因为它缺乏血管，软骨的含氧量在健康人体的浅表区域为 7%到 10%，相比之下，这个数值在关节腔内低至 1%。目前，间充质干细胞具有良好的分化潜能，被认为是一种很有前途的软骨再生生物学方法。而氧浓度是一个重要的外部因素，它对骨髓间充质干细胞的表型、周期、凋亡、迁移、分化能力都具有一定的影响。在本研究中，使用 MRI 造影剂-超顺磁氧化铁纳米晶体 SPION 与低氧协同作用，研究其对细胞的生物行为的影响。研究发现 SPION 标记的低氧 MSCs 比 SPION 标记的常氧 MSCs 更有效地促进软骨再生。低氧预处理与 SPIONs 协同作用可以促进细胞迁移，促进软骨形成分化。

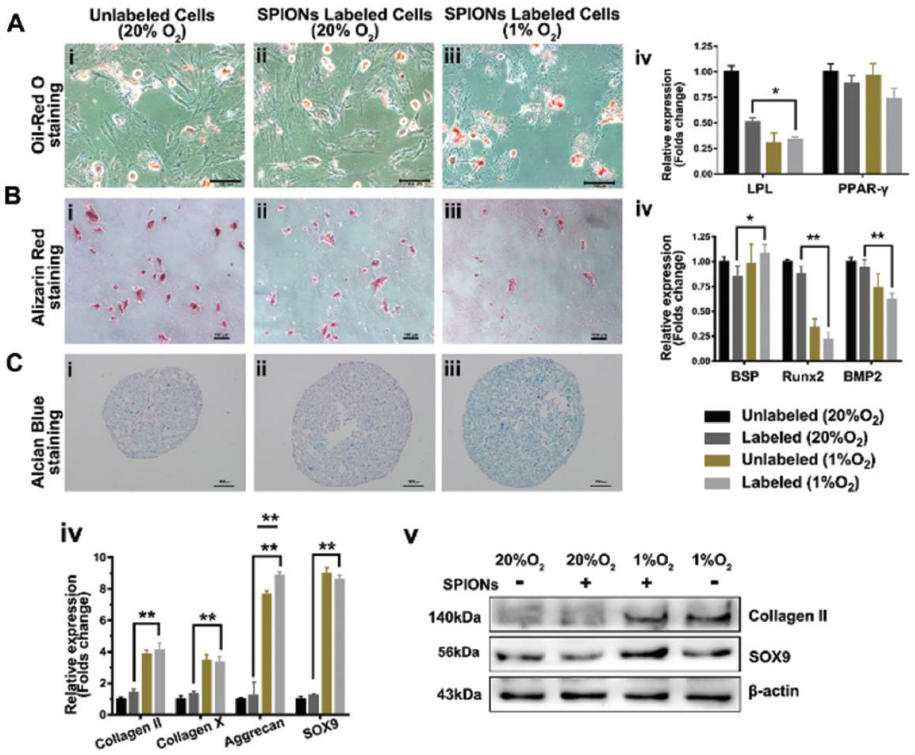

Figure 6. SPION labeling and culture condition impact on cell pluripotency. (A) Oil red O staining for the adipogenic differentiation of BM-MSCs (i–iii) and real-time PCR analysis of LPL and PPAR- mRNA expression (iv). (B) Alizarin red staining for osteogenic differentiation of BM-MSCs (i–iii) and real-time PCR analysis of BSP, Runx2 and BMP-2 mRNA expression (iv). (C) Alcian blue staining for osteogenic differentiation of BM-MSCs (i–iii) and real-time PCR analysis of collagen II, collagen X,aggrecan and SOX-9 mRNA expression (iv). Herein, Western blot assays were used to determine the protein production of CollagenII, SOX-9 and HIF1α (v); α -actin was used as an internal reference. (n = 3, *P <0.05, **P <0.01).

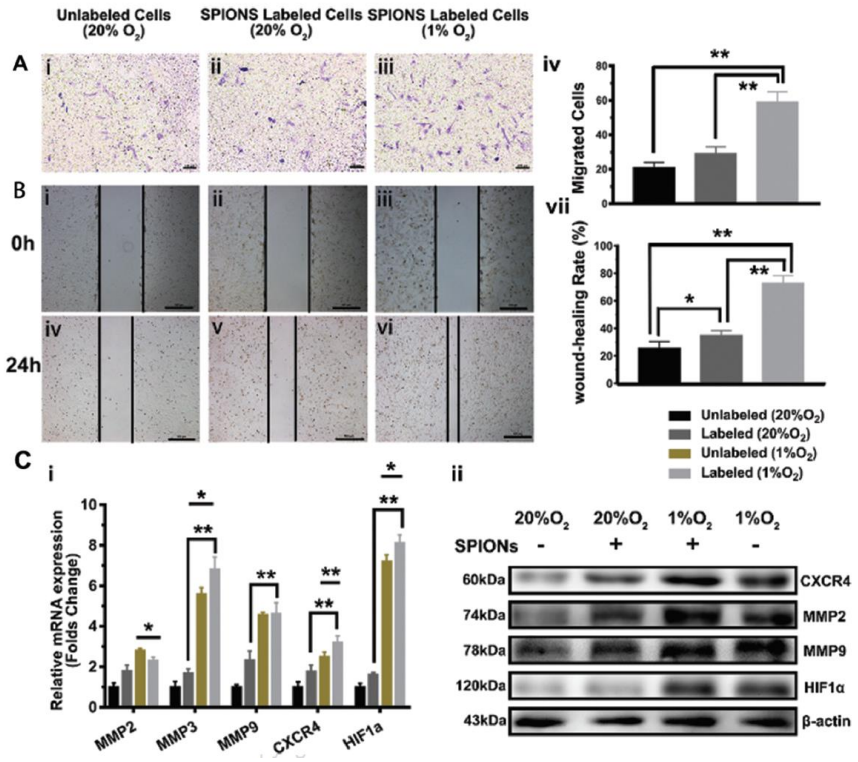

Figure 7. SPION labeling impact on the migration capability of BM-MSCs at different oxygen concentrations. (A) Transwell assaysfor the unlabeled BM-MSCs (i) and the SPION-labeled BM-MSCs (ii, iii). The average migrated cells were calculated from five random fields, and three independent assays were completed (iv). (B) Wound-healing assays and statistical analysis.. (C) Relative mRNA expressions of MMP2, MMP3, MMP9, CXCR4 and HIF1α s. Western blot analyses of MMP2, MMP9, CXCR4and HIF1α protein expressions. Herein, β-actin was used as an internal reference.

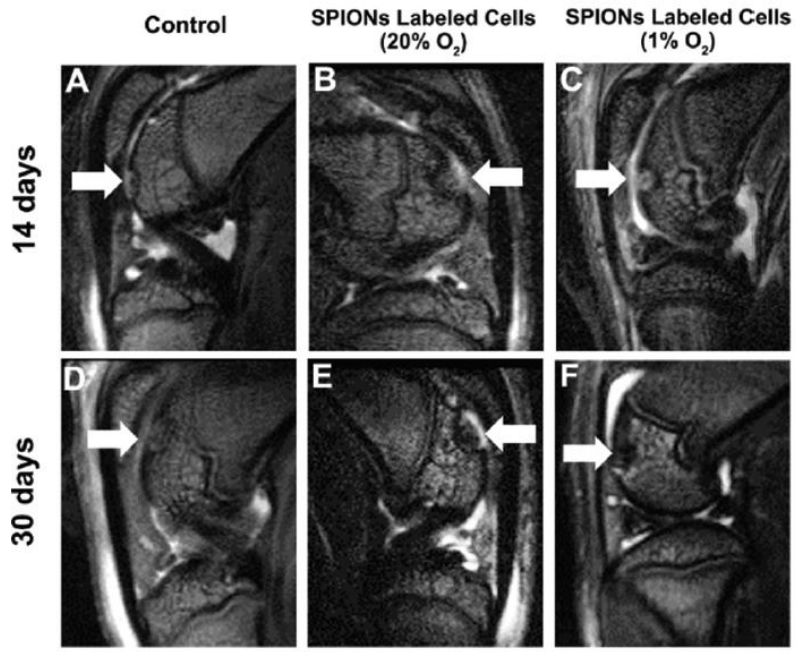

Figure 13. MRI images of a cartilage defect after BM-MSC therapy. (A) and (D) MRI images of the cartilage defect 14 and 30 days after injection of PBS (control group). (B) and (E) MRI images of the cartilage defect 14 and 30 days after injection of the SPION-labeled BM-MSCs under normoxia culture conditions. (C) and (F) MRI images of the cartilage defect 14 and 30 days after injection of the hypoxia-preconditioned SPION-labeled BM-MSCs. The white arrows show the tochlear of the rat's right legs in A, C, D, and F, and the tochlear of the rat's left legs in B and E.

与 SPION 标记的常氧 MSCs 相比，低氧（1% O_2）可抑制 SPION 标记的 MSCs 细胞的成骨分化，促进 MSCs 细胞的软骨分化（图 1）；低氧（1% O_2）可促进 SPION 标记的 MSCs 细胞的迁移能力（图 7）；低氧预处理的 SPION 标记的 MSCs 细胞治疗组在治疗第 30 天软骨缺损处出现大面积、低强度 T2 信号，然而，常氧 SPION 标记的 MSCs 细胞组出现小面积、低强度的信号，并没有覆盖缺陷区域。对照组未见明显的低信号（图 13）。表明低氧协同 SPION 标记 MSCs 细胞修复关节软骨损伤效果更好。