低氧/厌氧产品应用案例——眼病研究

文章题目：Hypoxia-Dependent HIF-1 Activation Impacts on Tissue Remodeling in Graves' Ophthalmopathy-Implications for Smoking
低氧依赖性 HIF-1 的激活对吸烟者 Graves 眼病组织重塑的影响

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使用气体浓度:低氧（3% O_2、5%CO_2、92%N_2）,常氧（含 5%CO_2 的空气）

主要内容：在 Graves 的眼病（GO）中，炎症和组织扩张（如骨性眼眶和吸烟）可能导致组织缺氧。缺氧通过激活 OFs（眼眶成纤维细胞）中的 HIF-1 依赖途径以刺激血管和脂肪生成对 GO 中的组织重塑产生影响。研究结果为持续吸烟的有害影响提供了分子机制，并解释了为什么减压可以改善患者的预后。药物靶向抑制 HIF-1/VEGF 可为控制 GO 中的组织扩张提供一种治疗方案。

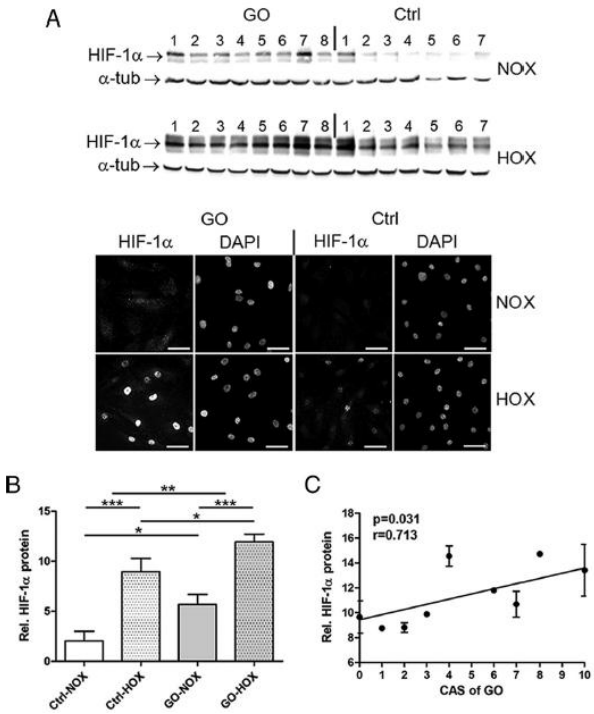

Figure 1

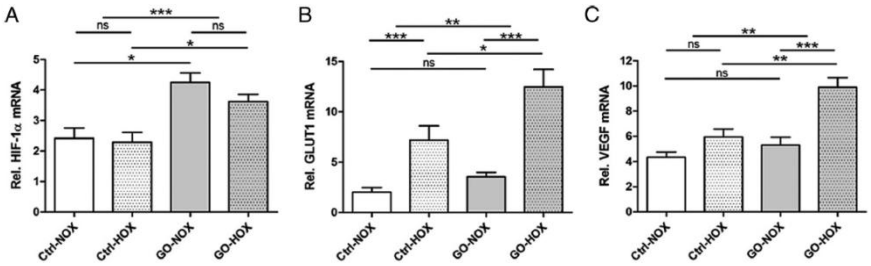

Figure 2

Figure 1. GO-derived OFs express more HIF-1 under normoxia and hypoxia than Ctrl-OF.

OFs were subjected to normoxic (NOX) or hypoxic (HOX) conditions for 24 hours. A, Whole-cell lysates were obtained and subjected to Western-blot analysis for detection of HIF-1α and α-tubulin (α-tub) as a loading Ctrl. Representative Western blots are shown. In addition, OFs were grown on coverslips, and HIF-1α was detected by immunofluorescence microscopy. Cell nuclei were counterstained with DAPI. Images were captured at 200× magnification and shown in gray level. Bars represent 100 μm. Representative images are shown. B, Western blots shown in panel A are representative for at least three separate experiments. Western-blot signals of 15 GO-OF and seven Ctrl-OF were quantified by densitometry of immunoblots. The HIF-1α signal was normalized to the α-tubulin signal and expressed as relative HIF-1α protein. C, Relationship between CAS (1–10) of GO patients and hypoxia-induced HIF-1α.

Figure 2. Expressions of HIF-1 gene and HIF-1 target genes were changed in GO-derived OFs. OFs from six GO patients and six healthy Ctrl persons were incubated under normoxia (NOX) or hypoxia (HOX) for 24 hours. Total mRNA was extracted and reversed transcribed. Real-time PCR was performed for HIF-1 cDNA (A), GLUT1 cDNA (B), and VEGF cDNA (C). The quantified cDNAs were normalized to the cDNA of -actin and expressed as relative levels of HIF-1, GLUT1, or VEGF mRNA. All data represent the mean SEM of experiments done in triplicate.

与 Ctrl-OF 相比，GO 患者的 OFs 在常氧条件下表现出较高的 HIF-1α水平，在缺氧（3% O_2）条件下表现出较强的 HIF-1α蛋白诱导作用；低氧培养时 HIF-1α转移到细胞核，表明其处于激活状态；缺氧诱导的 HIF-1α水平与各 GO 患者的眼眶炎症程度呈正相关，表明 HIF-1α信号可能参与了 GO 患者的炎症发病机制。

在常氧条件下，HIF-1 靶基因的表达与对照相比无显著差异，而缺氧（3% O_2）下诱导的 VEGF 和 GLUT1（糖转运蛋白 1）则明显高于对照组，表明在 GO-OF 中缺氧诱导的基因表达受到了很大的影响，这可能会对代谢和血管生成产生影响。