低氧/厌氧产品案例——低氧与肝癌研究

文章题目：Silencing of HIF-1α inhibited the expression of lncRNA NEAT1 to suppress development of hepatocellular carcinoma under hypoxia

沉默 HIF-1α可以抑制 lncRNA NEAT1 的表达，从而抑制缺氧条件下肝细胞癌的发展

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工作站使用情况：Ruskinn Hypoxia Work Station

使用气体浓度：低氧（1% O_2）

摘要：本研究旨在探讨缺氧诱导因子-1α (HIF-1α)和 lncRNA 核富集丰富转录本 1 (NEAT1)之间的关系，以及它们在缺氧条件下肝细胞癌(HCC)中的作用。NEAT1 和 HIF-1α在肝细胞癌组织中呈高表达并呈正相关，其中 NEAT1 高表达与肿瘤淋巴结转移（TNM）晚期及远处转移呈正相关； NEAT1 或 HIF-1α上调的 HCC 患者预后较差。 NEAT1 由 HIF-1α诱导，siHIF-1α抑制 NEAT1 表达；NEAT1 的过表达进一步促进了缺氧条件下肝癌的发展，同时促进细胞活力、迁移和侵袭，抑制细胞凋亡，下调 HIF-1α可逆转这种作用。 NEAT1 过表达促进肿瘤生长，下调 HIF-1α可逆转 NEAT1 促进肿瘤生长的发生， 揭示下调 HIF-1α可抑制 NEAT1 的表达，抑制 HCC 的进展，改善预后。

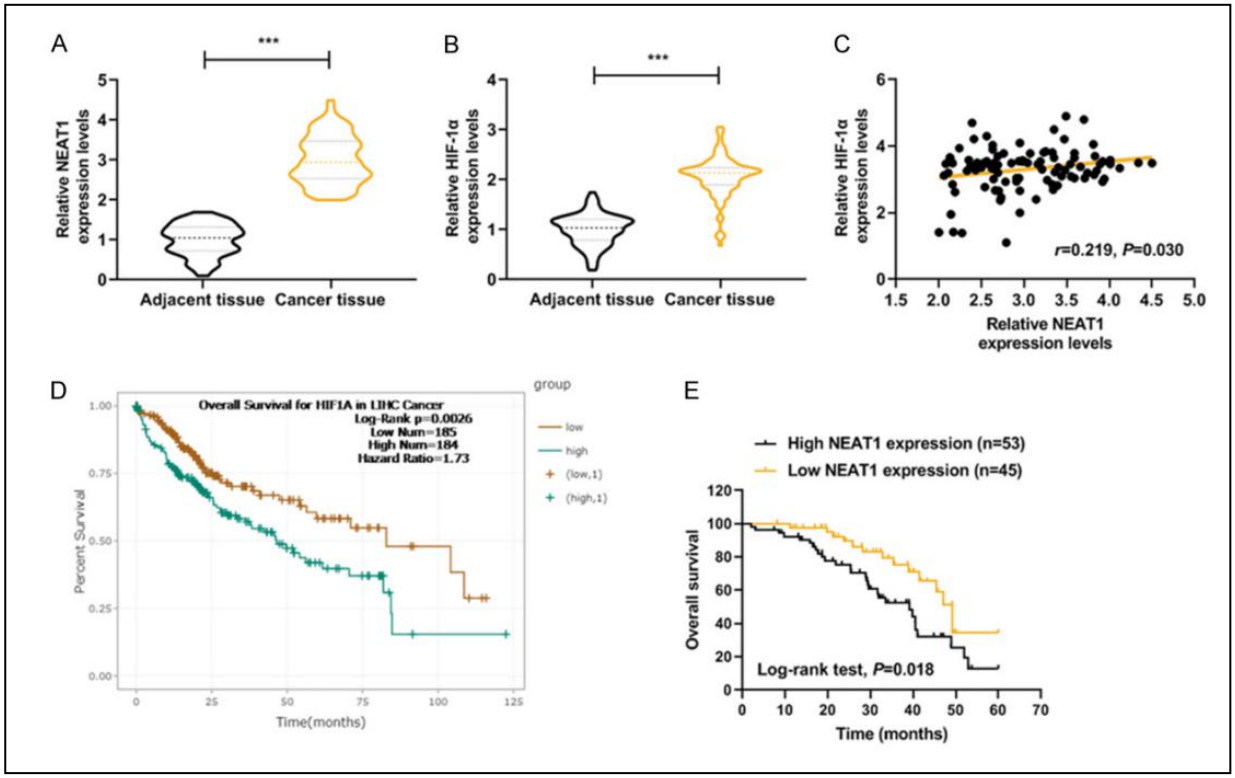

Figure 1. Correlations and relative expressions of HIF-1α and NEAT1 in HCC tissues and their relationships with overall survival of HCC patients. (A and B) HIF-1α (A) and NEAT1 (B) expressions were detected by qRT-PCR and nor malized to GAPDH expression in 98 pairs of HCC tissues compared with adjacent nontumourous liver specimens. (C) Spearman's rank correlation analysis was performed to analyze the correlations of HIF-1α and NEAT1 in HCC tissues. (D and E) Kaplan-Meier survival curve and log-rank test were used to evaluate whether HIF-1α and NEAT1 expression levels were associated with overall survival rate. ***P < 0.001 vs. Adjacent tissue. The data were shown as mean ± standard deviation (S.D.). Abbreviations: HIF-1α, hypoxia-inducible factors-1α; NEAT1, lncRNA nuclear enriched abundant transcript 1; qRT-PCR, quantitative reverse transcription-polymerase chain reaction; HCC, hepa tocellular carcinoma.

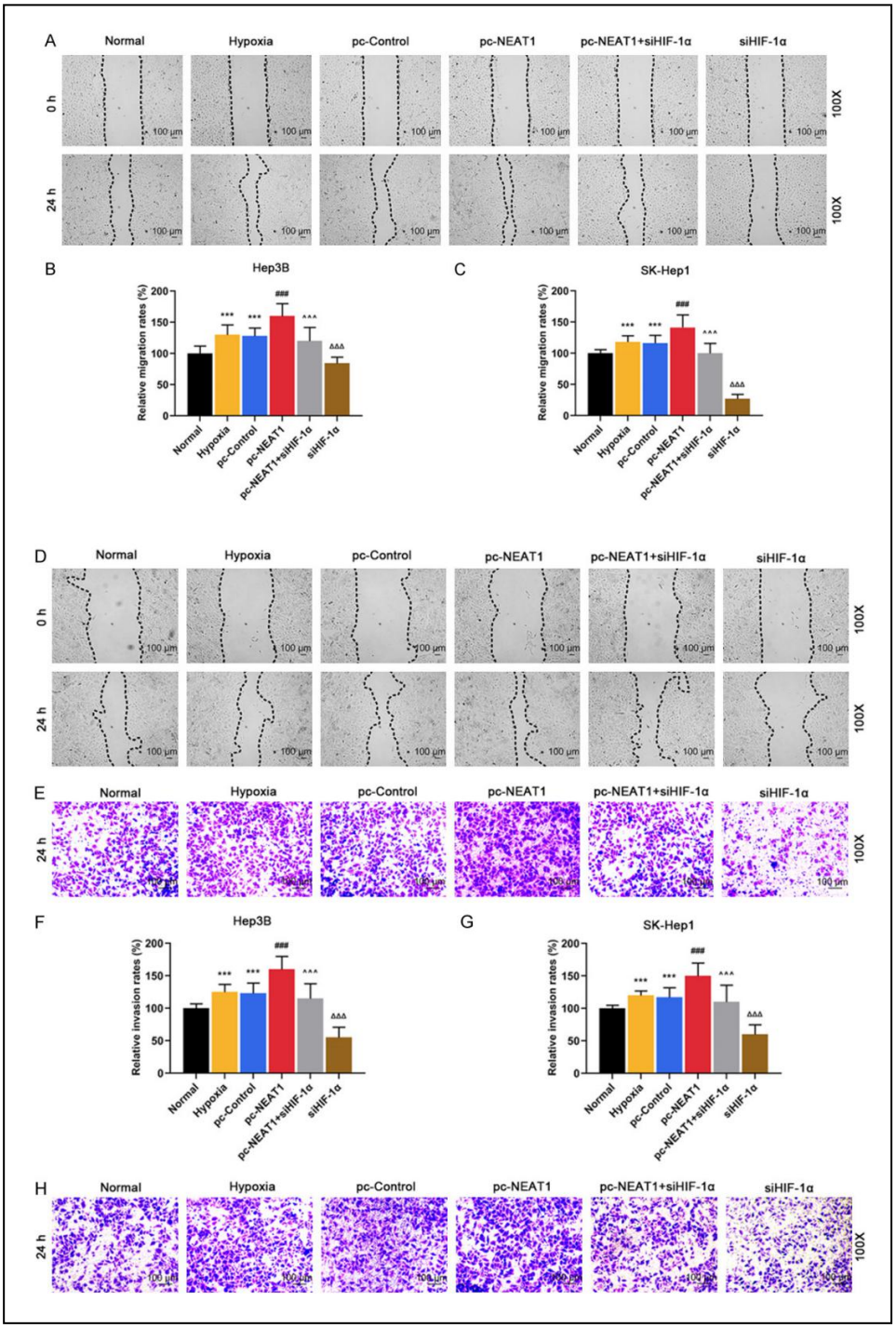

Figure 4. HIF-1α silencing suppressed the development of HCC by negatively regulating NEAT1 level in Hep3B and SK-Hep1 cells under hypoxia. (A, B) Migration rates were detected in Normal (non-transfected and non-hypoxia con trol), Hypoxia, pc-Control (non-targeting and hypoxia control), pc-NEAT1 (NEAT1 transfected and hypoxia), pc-NEAT1 + siHIF-1α (NEAT1 and siRNA-HIF-1α co-transfected under hypoxia), siHIF-1α groups in Hep3 (A and B) and SK-Hep1 cells (C and D) by scratch wound test. (E-H) Invasion rates were detected in Normal, Hypoxia, pc-Control, pc-NEAT1, pc-NEAT1 + siHIF-1α, siHIF-1α groups in Hep3 (E and F) and SK-Hep1 cells (G and H) by transwell assay. ***P < 0.001 vs. Normal. ###P < 0.001 vs. pc-Control. ^^^P < 0.001 vs. pc-NEAT1. ΔΔΔP < 0.001 vs. pc-NEAT1 + siHIF-1α. The data were shown as mean ± standard deviation (S.D.). Abbreviations: HIF-1α, hypoxia-inducible factors-1α; NEAT1, lncRNA nuclear-enriched abundant transcript 1.

HCC 组织中 NEAT1 和 HIF1α明显升高(图 1A 和 1B)；相关性分析显示 HIF-1α的表达与 NEAT1 的表达呈正相关（图 1C），HIF-1α高表达组存活的 HCC 患者比例明显低于 HIF-1α低表达组（(图 1D），提示 HIF-1α低表达的 HCC 患者预后较好；

NEAT1 过表达进一步促进了缺氧条件下的迁移和侵袭，沉默 HIF-1α显著抑制了缺氧条件下的迁移和侵袭，而 NEAT1 过表达部分逆转了沉默 HIF-1α的作用（图 4A-H）；表明 HIF-1α沉默通过负向调节缺氧条件下 Hep3B 和 SK-Hep1 细胞 NEAT1 水平抑制肝癌的发生发展。