低氧/厌氧产品应用案例——肝癌研究

文章题目：SUMOylation regulates LKB1 localization and its oncogenic activity in liver cancer
类泛素化修饰调控 LKB1 的定位及其在肝癌中的致癌活性

文章出处：EBioMedicine. 2019 Feb; 40: 406－421.西班牙肝脏和消化系统疾病网络生物医学研究中心（比斯开省德里奥）
使用气体浓度:低氧（1% O_2）,常氧（5%CO_2，95%空气）

主要内容：在人肝癌细胞中过表达肝激酶 B1（LKB1），探究与低氧相关的翻译后修饰物 SUMO 对 LKB1 致癌作用的调节作用。在低氧胁迫下的人肝癌细胞中，LKB1 的过表达增加了细胞活力和侵略性，且与 LKB1 细胞定位变化相关。

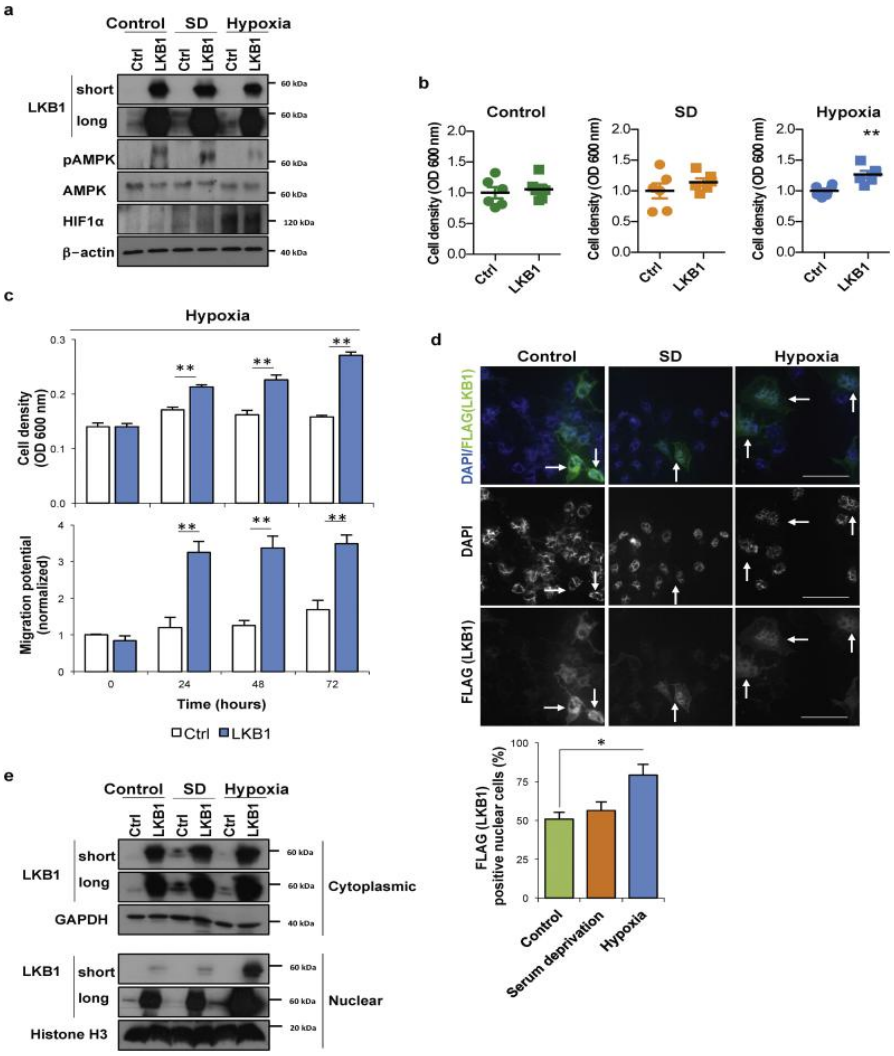

Figure 1. Liver Kinase B1 (LKB1) offers survival and invasiveness advantage to human hepatoma cells during hypoxic stress

a. Representative Western blot of LKB1, its downstream target AMP-activated protein (AMPK) and phosphorylated AMPK at Thr172 and hypoxia inducible factor (HIF1α), a hypoxic marker, are shown. [β-actin was used as loading control].

b. Cell viability as detected by staining of attached cells with crystal violet dye;

c. Time-course of cell viability and cell migration using a wound-healing scratch assay after LKB1 overexpression under hypoxia;

d. Representative immunofluorescence staining for LKB1 (FLAG) in Huh-7 hepatoma cells and quantification of the percentage of LKB1 nuclear positive staining cells. Scale bar corresponds to 50 μm; and

e. Western blot of LKB1 levels in cytoplasmic and nuclear fractions [Glyceraldehyde 3-phosphate (GAPDH) was used as loading control for cytoplasmic fractions and Histone H3 for nuclear fractions].

与常氧（20% O_2）相比，低氧(1% O_2)下过表达 LKB1 为肝癌细胞提供了生长存活率及侵略优势，表明 LKB1 受到肝癌的诱导表达，而肝癌是一种以高度缺氧环境为特征的肿瘤。

a,过表达 LKB1 能增加 THR-172 处 AMPK 的磷酸化；

b,与常氧和血清剥夺培养的细胞相比，缺氧条件下，LKB1 的上调能够增加细胞存活率；

c,尽管在缺氧期间肝癌细胞生长受到阻碍，但缺氧条件下过表达 LKB1 能够诱导细胞生长且能够释放肿瘤细胞的侵袭性潜能；

d,e,LKB1 的细胞定位在其活性中起着重要作用。在血清剥夺和常氧条件下，LKB1 在细胞核和细胞质之间主动穿梭，而在缺氧状态下，LKB1 的核质穿梭受到阻碍，LKB1 更多地存在于细胞核中。

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