

高表达SF3B3促进胃癌细胞恶性增殖并与患者不良预后相关

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摘要:目的 分析SF3B3在胃癌发展和预后中的作用,并探讨其潜在机制。方法 利用TIMER2.0、GEPIA和UALCAN数据库分析SF3B3在多种癌症和胃癌中的表达模式,并通过胃癌组织免疫组化验证。通过Kaplan-Meier Plotter数据库及本院队列构建K-M生存曲线,采用Cox回归筛选术后5年生存的独立危险因素,通过ROC曲线AUC值评估预测价值。生物信息学富集分析预测SF3B3在胃癌中可能参与的生物学过程。通过慢病毒介导的SF3B3干扰和过表达,结合CCK-8及Transwell迁移和侵袭方法,探究SF3B3对胃癌细胞增殖、迁移和侵袭能力的影响。免疫印迹法检测SF3B3对糖酵解关键蛋白表达的影响,通过测定细胞外酸化率(ECAR)探究SF3B3对糖酵解活性的作用。通过裸鼠成瘤实验,观察SF3B3对瘤体大小及对糖酵解关键蛋白表达的影响。结果 SF3B3在胃癌中高表达,且与患者较差的预后相关($P<0.05$)。多变量Cox回归分析显示,影响胃癌患者术后5年生存率的独立危险因素是高表达SF3B3、CEA $\geq 5 \mu\text{g/L}$ 、CA19-9 $\geq 37 \text{ kU/L}$ 、肿瘤分期的T3-4期以及淋巴结转移分期的N2-3期($P<0.05$)。生物信息学分析显示糖酵解显著富集。干扰SF3B3削弱了HGC-27细胞的增殖、迁移和侵袭能力,而过表达SF3B3相反($P<0.05$)。免疫印迹分析显示,SF3B3干扰降低HK2、PKM2、LDHA蛋白的表达,而过表达则相反($P<0.05$)。ECAR实验显示,敲低SF3B3降低HGC-27细胞的ECAR,而过表达呈升高趋势($P<0.05$)。裸鼠成瘤实验结果显示,与对照组相比,SF3B3干扰组肿瘤质量减少,HK2、PKM2、LDHA蛋白表达下调,而SF3B3过表达组显示出相反趋势($P<0.05$)。结论 SF3B3过表达与胃癌患者的不良预后密切相关,其可能通过增强糖酵解作用促进胃癌细胞的增殖、迁移和侵袭能力。

关键词:胃癌;SF3B3;不良预后;糖酵解

SF3B3 overexpression promotes proliferation of gastric cancer cells and correlates with poor patient prognosis

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Abstract: Objective To investigate the role of SF3B3 in gastric cancer (GC) progression and prognosis and its possible mechanisms. **Methods** SF3B3 expression levels in pan-cancer and GC were analyzed using TIMER2.0, GEPIA, and UALCAN databases and validated using immunohistochemistry in GC tissues. Survival curves of GC patients were established using Kaplan-Meier Plotter and the data of a patient cohort our hospital. The independent risk factors for 5-year postoperative survival were identified using Cox regression, and their predictive values were evaluated using ROC analysis. SF3B3-associated biological processes were predicted by bioinformatics enrichment analyses. In GC HGC-27 cells, the effects of lentivirus-mediated SF3B3 knockdown and overexpression on cell proliferation and migration were investigated, and the changes in the key glycolytic proteins and extracellular acidification rate (ECAR) were detected. The influence of SF3B3 expression level on tumorigenesis and glycolytic protein expression *in vivo* were evaluated in a nude mouse xenograft model. **Results** High expression of SF3B3 in GC was associated with poor patient prognosis ($P<0.05$). The factors affecting 5-year survival outcomes following gastric oncological resection included high SF3B3 expression, a CEA level $\geq 5 \mu\text{g/L}$, a CA19-9 level $\geq 37 \text{ kU/L}$, tumor stage T3-4, and lymph node metastasis stage N2-3 ($P<0.05$). Bioinformatics analysis showed significant enrichment of SF3B3 in glycolysis. In HGC-27 cells, SF3B3 knockdown significantly inhibited while SF3B3 overexpression enhanced cell proliferation, migration, and invasion. SF3B3 knockdown obviously decreased the expressions of HK2, PKM2 and LDHA proteins and ECAR in HGC-27 cells, whereas SF3B3 overexpression produced the opposite effect. In nude mouse xenograft models, SF3B3 knockdown significantly reduced tumor mass and downregulated expression of HK2, PKM2 and LDHA proteins, and SF3B3 overexpression induced the opposite changes. **Conclusion** SF3B3 overexpression is associated with poor prognosis of GC patients and promotes GC cell proliferation, migration and invasion possibly by enhancing glycolysis.

Keywords: gastric cancer; SF3B3; poor prognosis; glycolysis

胃癌作为全球高发的消化道恶性肿瘤,其防治已成

为重大公共卫生挑战。根据GLOBOCAN 2022全球癌症统计数据,胃癌的发病率与死亡率均高居恶性肿瘤第5位^[1,2]。尽管近年来以分子为导向的精准治疗策略显著提升了胃癌综合治疗水平,但患者仍面临早期诊断率低、晚期化疗耐药及5年生存率低等临床困境^[3-5]。随着高通量测序技术的突破性进展,研究者致力于通过

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组学及生信分析挖掘具有临床转化价值的分子标志物,以期实现胃癌的早期预警、疗效预测及预后评估^[6-9]。肿瘤代谢重编程作为癌症的显著特征之一,其核心机制在于癌细胞通过重调代谢途径满足快速增殖的能量需求和生物大分子合成^[10]。其中,Warburg效应(即有氧糖酵解)的激活尤为突出,表现为葡萄糖摄取激增及乳酸过量生成^[11]。乳酸脱氢酶A(LDHA)作为该代谢途径的限速酶,在胃癌等多种实体瘤中异常高表达,其催化产生的肿瘤微环境酸化不仅促进血管新生和免疫逃逸,更与患者总生存期显著缩短呈正相关^[12,13]。这种代谢特征的动态演变提示,靶向糖酵解关键调控分子可能为胃癌治疗提供新维度^[14]。剪接因子SF3B复合体作为pre-mRNA剪接体的核心组成单元,其亚基SF3B3通过调控可变剪接过程影响多种致癌信号通路的激活^[15-17]。近年来,研究揭示了SF3B3与乳腺癌、肾癌等多种癌症的恶性进展和不良预后相关,并将其视为这些癌症的预后标志物^[18-21]。最新研究指出,在结直肠癌中,SF3B3高表达与患者生存期缩短密切相关,沉默SF3B3可有效抑制结直肠肿瘤细胞的增殖和转移^[22]。然而迄今为止,尚无文献报道SF3B3在胃癌中的表达水平及其对胃癌患者预后的具体影响。本研究整合胃癌临床数据库与患者生物标本库信息,结合分子生物学及病理学等实验技术,系统解析SF3B3在胃癌中的表达特征及其预后价值。通过建立SF3B3基因敲除/过表达模型,深入探讨SF3B3通过调控糖酵解途径影响胃癌增殖侵袭的分子机制。旨在从代谢重编程的角度剖析胃癌演进规律,为患者早期干预与预后监测提供理论依据。

1 资料和方法

1.1 研究对象与资料收集

本项研究采用回顾性研究方法,搜集2014年5月~2019年6月于本院接受胃癌根治术的患者临床病理资料。纳入标准:经组织病理学确诊的原发性胃癌患者;手术实现R0切除。排除标准:合并其他恶性肿瘤;关键临床数据缺失;非胃癌相关死亡病例。最终确定纳入107例患者,完整采集基线临床病理参数,涵盖性别、年龄、术前CEA和CA19-9水平、肿瘤病理分类、肿瘤最大径以及肿瘤病理分期等。采用结构化随访(电话访谈、门诊复诊及电子病历系统追踪)获取术后5年生存结局数据。所有入组病例的福尔马林固定石蜡包埋组织标本均通过标准化免疫组化染色流程进行蛋白表达定量评估。本研究经蚌埠医科大学第一附属医院伦理委员会审批(伦理批号:伦科批字[2023]399)。

1.2 数据库分析

运用TIMER2.0在线数据库对SF3B3基因在人类多种恶性肿瘤中的表达情况进行分析。采用UALCAN

和GEPIA数据库分析SF3B3在胃癌样本与癌旁正常组织的表达差异。利用Kaplan-Meier Plotter数据库在线分析SF3B3表达与胃癌患者总体生存期(OS)及首次进展生存期(FPS)的相关性。

1.3 免疫组织化学检测

对107对胃癌及配对的癌旁正常组织标本采用标准化免疫组化技术流程:石蜡包埋组织切片经梯度脱蜡水化后,通过高压热修复法进行抗原表位暴露,依次完成内源性过氧化物酶活性抑制、血清封闭、SF3B3(1:100,Proteintech)—抗孵育、二抗孵育及DAB显色体系构建,苏木素复染后树脂封片。通过双盲评估模式,应用ImageJ图像分析系统对染色切片进行定量病理学分析,计算目标蛋白的累积光密度值(IOD)作为定量指标^[23]。

1.4 生物信息学分析

利用cBioPortal在线平台获得SF3B3基因及其潜在的共表达基因,采用DAVID数据库进行GO及REACTOME通路富集分析,采用Bioinformatics平台进行数据的可视化处理。通过UCSCXena在线资源库获取TCGA胃癌数据集。根据SF3B3表达量中位数将样本划分高低表达组,利用sangerbox3.0平台提供的GSEA在线分析工具对其进行GSEA功能富集和可视化展示^[24]。

1.5 细胞转染

采用含10%胎牛血清的DMEM培养基(Gibco)培养HGC-27细胞至指数生长期,0.25%胰酶(Beyotime,上海)消化细胞,接种于6孔板(Corning)。通过慢病毒转染的方法对HGC-27细胞系进行SF3B3基因的过表达及干扰实验。分别设置阴性对照载体组(sh-NC)和SF3B3干扰组(sh-SF3B3),过表达空载体组(LV-NC)和SF3B3过表达组(LV-SF3B3)。慢病毒转染步骤如下^[25]:将对数生长期细胞接种于96孔板继续培养24 h,根据感染复数(MOI值)加入1 μL /孔的病毒悬液($1 \times 10^8 \text{ TU/mL}$),继续培养并观察转染效果。使用2 $\mu\text{g/mL}$ 嘌呤霉素(Beyotime)进行筛选稳转细胞株,用于后续实验验证。

1.6 CCK-8实验

将各组细胞进行消化制备成细胞悬液,接种至96孔板(1×10^3 /孔), 37°C 、5% CO_2 培养箱中继续培养24、48、72 h,于目标孔室中添加CCK-8试剂(10 μL /孔),培养箱中培养2 h后用酶标仪检测各孔吸光度值 $A_{450\text{nm}}$ 。

1.7 Transwell侵袭与迁移实验

于Transwell小室的上室内均匀铺设50 μL 的基质胶(Corning)。调整HGC-27细胞悬液密度浓度至 2×10^4 /孔。将200 μL 的细胞悬液加入上室,而下室则加入600 μL 含有10%胎牛血清的DMEM培养基,继续培养48 h。4%多聚甲醛对细胞进行固定,0.2%的结晶

紫对细胞进行染色,观察并记录细胞侵袭数。迁移实验步骤与侵袭实验相似,区别在于迁移实验中不添加基质胶。

1.8 Western blotting 实验

采用RIPA裂解液对各组细胞进行裂解提取细胞总蛋白,BCA法对蛋白浓度进行定量分析。将蛋白通过10%的SDS-PAGE凝胶进行电泳分离后,以湿转法将蛋白质转移到膜上。室温下使用5%脱脂奶粉对膜进行封闭处理,4℃条件下对一抗SF3B3(1:1000)、 β -actin(1:1000)、HK2(1:1000)、PKM2(1:1000)、LDHA(1:1000,Proteintech)进行过夜孵育。孵育结束后,以TBST进行膜的洗涤,随后进行二抗(1:4000,中杉金桥)孵育。最后,利用凝胶成像系统对膜进行曝光,并运用ImageJ软件对所得免疫印迹结果进行图像处理与数据分析。

1.9 裸鼠皮下成瘤实验

6~8周龄雄性BALB/c裸鼠(江苏集萃药康有限公司),随机分为4组:sh-NC组、sh-SF3B3组、LV-NC组和LV-SF3B3组,3只/组,进行无特定病原体(SPF)级饲养。将各组稳定转染的细胞重悬至浓度为 1×10^6 mL,于裸鼠背部皮下区域接种100 μ L细胞悬液。接种后第14天,对小鼠实施安乐死,取检肿瘤组织,进行拍照记录,称量,计算瘤体体积,成瘤体积=(长径 \times 短径²)/2。免疫印迹法检测小鼠肿瘤组织中HK2、PKM2、LDHA蛋白的表达水平。体内实验经蚌埠医科大学第一附属医院伦理委员会审批(伦理批号:伦动科批字[2023]第430号)。

1.10 细胞外酸化率(ECAR)检测

使用ECAR荧光法测定试剂盒(Elabscience)测定ECAR水平^[22]。实验步骤如下:将各组细胞以 2×10^4 /孔的密度接种到96孔黑色透底培养板中,加入100 μ L/孔的工作溶液。在37℃的避光条件下孵育30 min,使用多功能酶标仪检测A,激发波长为490 nm,发射波长为535 nm。

1.11 统计学分析

采用SPSS 26.0和GraphPad Prism 9进行数据分析与图形绘制。分类变量采用 $n(\%)$ 表示,组间比较采用卡方检验。连续变量采用均数 \pm 标准差表示,正态分布数据组间比较采用独立样本 t 检验,非正态分布数据选用非参数检验Mann-Whitney U test。本研究通过K-M生存曲线(Log-rank检验)与多因素Cox比例风险模型,重点评估术后5年生存的独立预后因子。 $P < 0.05$ 表示差异具有统计学意义。

2 结果

2.1 胃癌组织中SF3B3的表达上调

TIMER2.0泛癌分析显示,SF3B3在包括胃癌在内

的多种恶性肿瘤中表达上调($P < 0.001$,图1A)。UALCAN和GEPIA数据库证实胃癌组织SF3B3表达量较配对正常组织明显升高($P < 0.05$,图1B、C)。免疫组化结果显示,SF3B3在胃癌中的表达量高于癌旁组织($P < 0.05$,图1D、E)。

2.2 SF3B3表达量与胃癌恶性进展相关

胃癌中SF3B3表达量与血液中CEA和CA19-9、T分期及N分期呈现出相关性($P < 0.05$,表1)。

2.3 SF3B3表达量影响患者术后5年生存率

K-M Plotter数据库分析显示,与SF3B3低表达组相比,SF3B3高表达组患者OS和FPS均降低($P < 0.01$,图2A、B)。K-M生存曲线分析示,SF3B3高表达组患者术后5年生存率低于低表达组(Log-rank $\chi^2 = 28.541$, $P < 0.001$,图2C)。

2.4 影响胃癌患者术后5年生存率的单变量与多变量分析

患者生存数据的Cox单变量与多变量分析显示,影响胃癌患者术后5年生存率的独立风险因素包括高表达SF3B3、CEA ≥ 5 μ g/L、CA19-9 ≥ 37 kU/L、T3-4期以及N2-3期($P < 0.05$,图3)。

2.5 SF3B3表达对患者术后5年生存率的预测意义

ROC曲线分析显示,SF3B3评估胃癌患者术后5年生存率的敏感度为89.3%,特异度为66.7%,曲线下面积为0.807($P < 0.001$,图4)。

2.6 SF3B3在胃癌生物学功能调控中的潜在作用

GO富集分析显示,SF3B3参与糖酵解、RNA剪接、细胞周期、代谢过程等生物学过程;SF3B3主要富集于剪接复合体、细胞核、染色体、线粒体和细胞质等细胞组分;SF3B3与ATP酶活性和蛋白结合等分子功能相关(图5A)。REACTOME富集分析表明SF3B3参与糖酵解进程(图5B)。GSEA分析结果表明SF3B3在糖酵解过程中显著富集(图5C)。

2.7 SF3B3促进胃癌HGC-27细胞增殖、迁移和侵袭功能

CCK-8结果显示,与对照组相比,sh-SF3B3处理组抑制HGC-27细胞的增殖活性;LV-SF3B3处理组促进HGC-27细胞的增殖($P < 0.05$,图6A、B)。Transwell实验结果显示,与对照组相比,sh-SF3B3干预的胃癌细胞迁移和侵袭活性降低;LV-SF3B3干预的胃癌细胞呈现出迁移和侵袭活性的提升($P < 0.05$,图6C~F)。

2.8 SF3B3促进胃癌细胞糖酵解

免疫印迹结果显示,敲低SF3B3抑制胃癌细胞中HK2、PKM2、LDHA蛋白的表达,而过表达呈相反趋势($P < 0.05$,图7A~C)。ECAR实验显示,SF3B3敲低降低胃癌细胞的ECAR水平,而过表达SF3B3增强($P < 0.05$,图7D、E)。

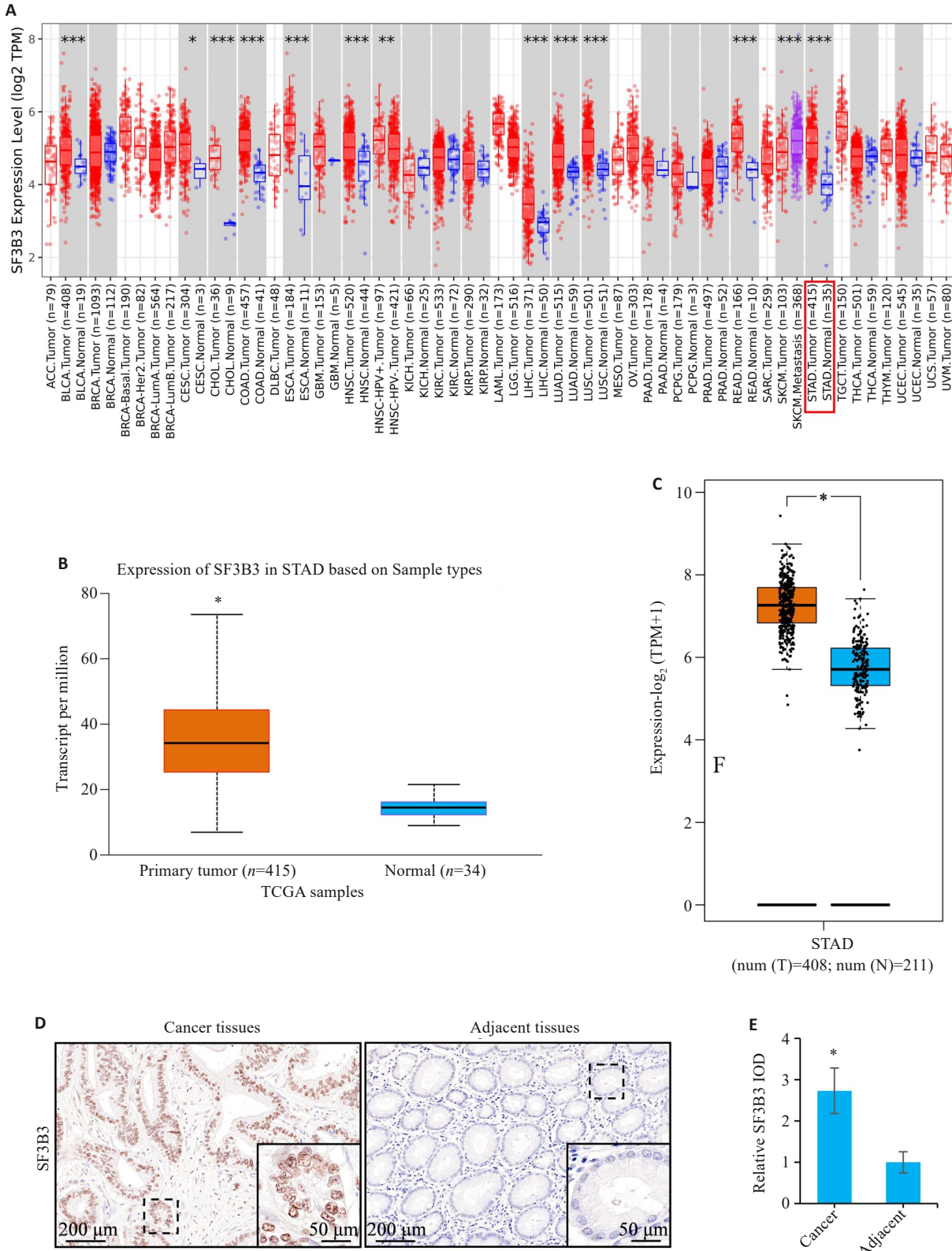


图1 胃癌组织中SF3B3表达升高

Fig.1 Overexpression of SF3B3 in stomach adenocarcinoma. A: Differential expression profiles of SF3B3 in diverse cancerous lesions. B, C: Analysis of SF3B3 expression between gastric cancer and adjacent benign tissues. D, E: Immunohistochemistry for SF3B3 in paired gastric carcinoma and adjacent normal tissues. *P<0.05, **P<0.01, ***P<0.001.

2.9 SF3B3促进裸鼠皮下成瘤能力,体内促进糖酵解

裸鼠皮下成瘤实验结果显示,经 sh-SF3B3 干预的肿瘤体积与质量低于 sh-NC 对照组,经 LV-SF3B3 干预的肿瘤体积与质量高于 LV-NC 对照组 (P<0.05,

图8A~E)。免疫印迹分析显示,敲低 SF3B3 抑制胃癌组织 HK2,PKM2,LDHA 蛋白水平;而过表达相反 (P<0.05, 图8F~H)。

表1 SF3B3表达模式与胃癌临床病理特征的关系

Tab.1 SF3B3 expression patterns in relation to clinicopathological features of gastric cancer patients

Factor	n	SF3B3 expression (n, %)		χ^2	P
		Low (n=53)	High (n=54)		
Gender					
Male	45	26 (57.78%)	19 (42.22%)	2.112	0.146
Female	62	27 (43.55%)	35 (56.45%)		
Age (year)					
<60	36	18 (50.00%)	18 (50.00%)	0.005	0.945
≥60	71	35 (49.30%)	36 (50.70%)		
CEA (μg/L)					
<5	51	36 (70.59%)	15 (29.41%)	17.282	<0.001
≥5	56	17 (30.36%)	39 (69.64%)		
CA19-9 (kU/L)					
<37	53	36 (67.92%)	17 (32.08%)	14.211	<0.001
≥37	54	17 (31.48%)	37 (68.52%)		
Tumor size (cm)					
<5	49	28 (57.14%)	21 (42.86%)	2.094	0.148
≥5	58	25 (43.10%)	33 (56.90%)		
Histological type					
Adenocarcinoma	84	44 (52.38%)	40 (47.62%)	1.268	0.260
Other	23	9 (39.13%)	14 (60.87%)		
Pathological grading					
G1-G2	53	27 (50.94%)	26 (49.06%)	0.084	0.772
G3-G4	54	26 (48.15%)	28 (51.85%)		
T stage					
T1-T2	48	31 (64.58%)	17 (35.42%)	7.888	0.005
T3-T4	59	22 (37.29%)	37 (62.71%)		
N stage					
N0-N1	63	40 (63.49%)	23 (36.51%)	11.943	<0.001
N2-N3	44	13 (29.55%)	31 (70.45%)		

3 讨论

本研究首次揭示剪接因子SF3B3通过代谢重编程驱动胃癌恶性进展的分子机制。跨平台验证(TIMER2.0/GEPIA/本院队列)证实,SF3B3在胃癌组织中的异常高表达与T、N分期、血清CEA/CA19-9水平及术后5年生存率相关。这提示,SF3B3可作为一种新型且高效的预后生物标志物^[27],尤其对于常规标志物阴性的患者具有补充诊断价值。

既往研究报道SF3B3在乳腺癌、肾癌、结直肠癌等多种肿瘤中的高表达,并揭示了其与这些肿瘤的发生、发展及不良预后之间的紧密联系^[18-22]。本研究首次在胃癌中验证其促癌作用:通过构建SF3B3表达下调和上调的胃癌细胞株,并结合体内外实验明确观察到

SF3B3表达量的增加显著促进了胃癌细胞的增殖、迁移及侵袭活性,进一步证实了SF3B3在胃癌恶性进展中的关键作用。结合K-M Plotter数据库分析结果显示,SF3B3高表达与患者不良生存结果密切相关,而针对本院患者的术后生存资料分析则进一步发现,高表达SF3B3患者的生存率较低表达患者显著下降。上述证据从临床-基础多维度证实,SF3B3表达水平与胃癌进展及预后不良呈强相关性,为其转化为新型预后评估工具提供了理论支撑。

为进一步探究SF3B3在胃癌细胞中的作用机制,本研究借助生物信息学分析发现,SF3B3与糖酵解、细胞代谢及细胞周期等关键生物学功能及信号通路存在相关性。有氧糖酵解(Warburg效应)作为肿瘤细胞代

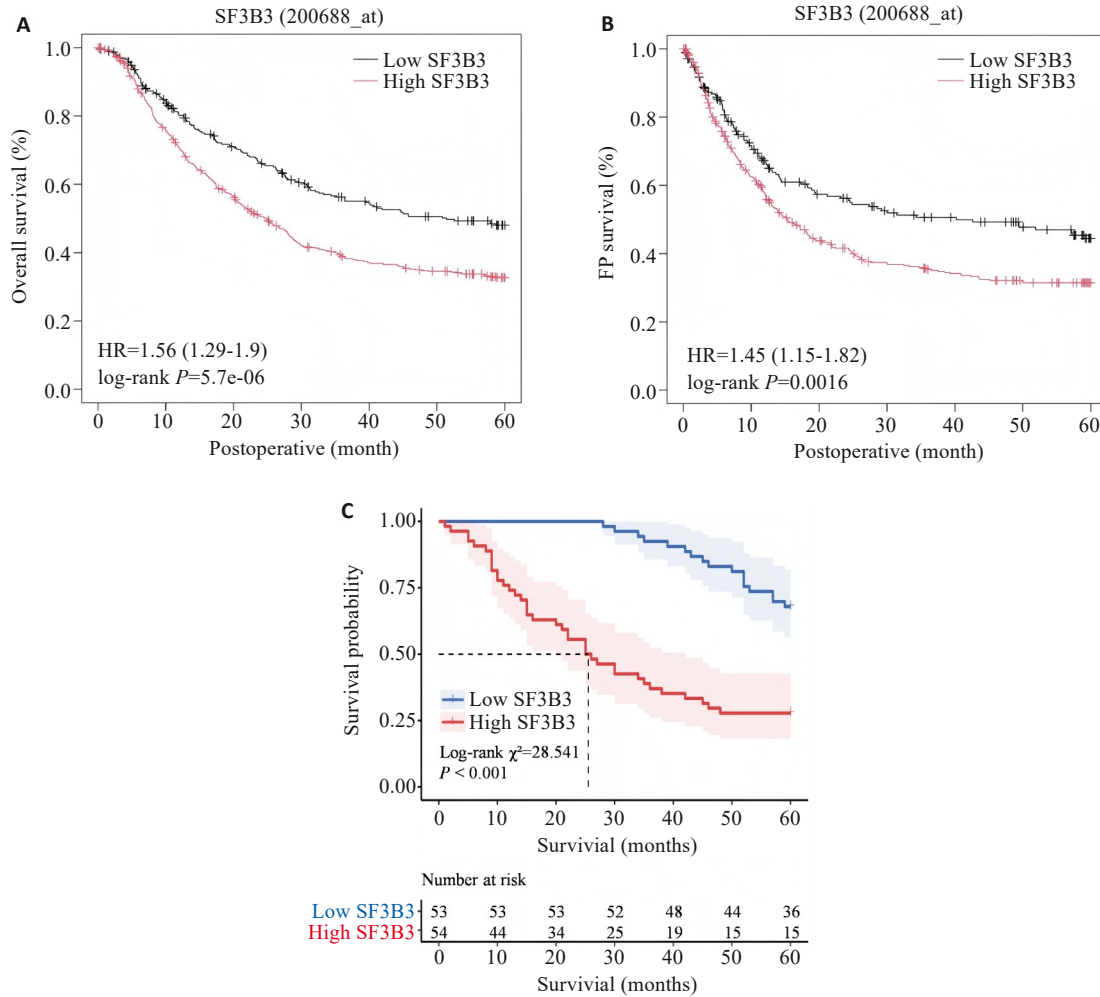


图2 SF3B3表达量影响术后5年生存率

Fig. 2 SF3B3 expression levels affect 5-year postoperative survival rate of gastric cancer patients. **A:** K-M Plotter analysis reveals the correlation between SF3B3 expression and 5-year overall survival in gastric cancer patients. **B:** K-M Plotter analysis reveals the association between SF3B3 expression and 5-year first progression survival in gastric cancer patients. **C:** K-M survival analysis depicts the 5-year survival rate post-radical gastrectomy in gastric cancer patients.

Characteristic	Univariate Cox analysis		Multivariate Cox analysis	
	P	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)
Gender	0.105	0.365-1.105		
Age	0.188	0.821-2.684		
Tumor size	0.140	0.874-2.540		
Histological type	0.201	0.808-2.711		
Pathological grading	0.106	0.907-2.657		
CEA level	<0.001	3.417-12.507	<0.001	1.840-7.843
CA19-9 level	<0.001	3.893-14.926	0.006	1.345-5.995
T Stage	<0.001	3.251-12.968	<0.001	2.041-9.509
N Stage	<0.001	3.325-10.266	<0.001	1.915-6.386
SF3B3 expression	<0.001	2.381-7.546	0.003	1.425-5.269

图3 SF3B3表达水平是影响胃癌患者预后的独立危险因素

Fig.3 SF3B3 expression level is an independent risk factor for prognosis of gastric cancer patients.

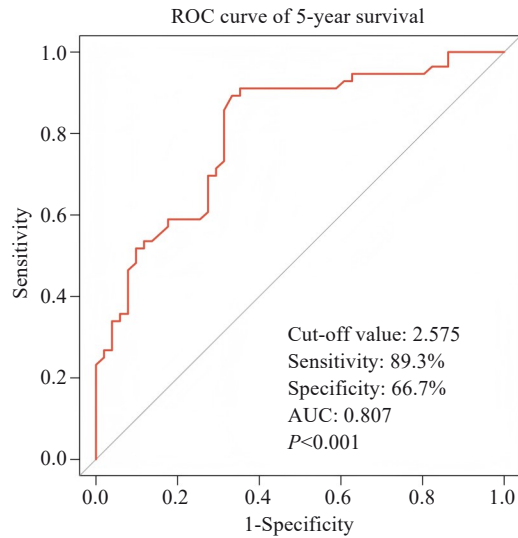


图4 SF3B3表达对胃癌患者术后5年生存率的预测意义
Fig. 4 Prognostic value of SF3B3 expression for 5-year survival outcomes of gastric cancer patients following surgical intervention.

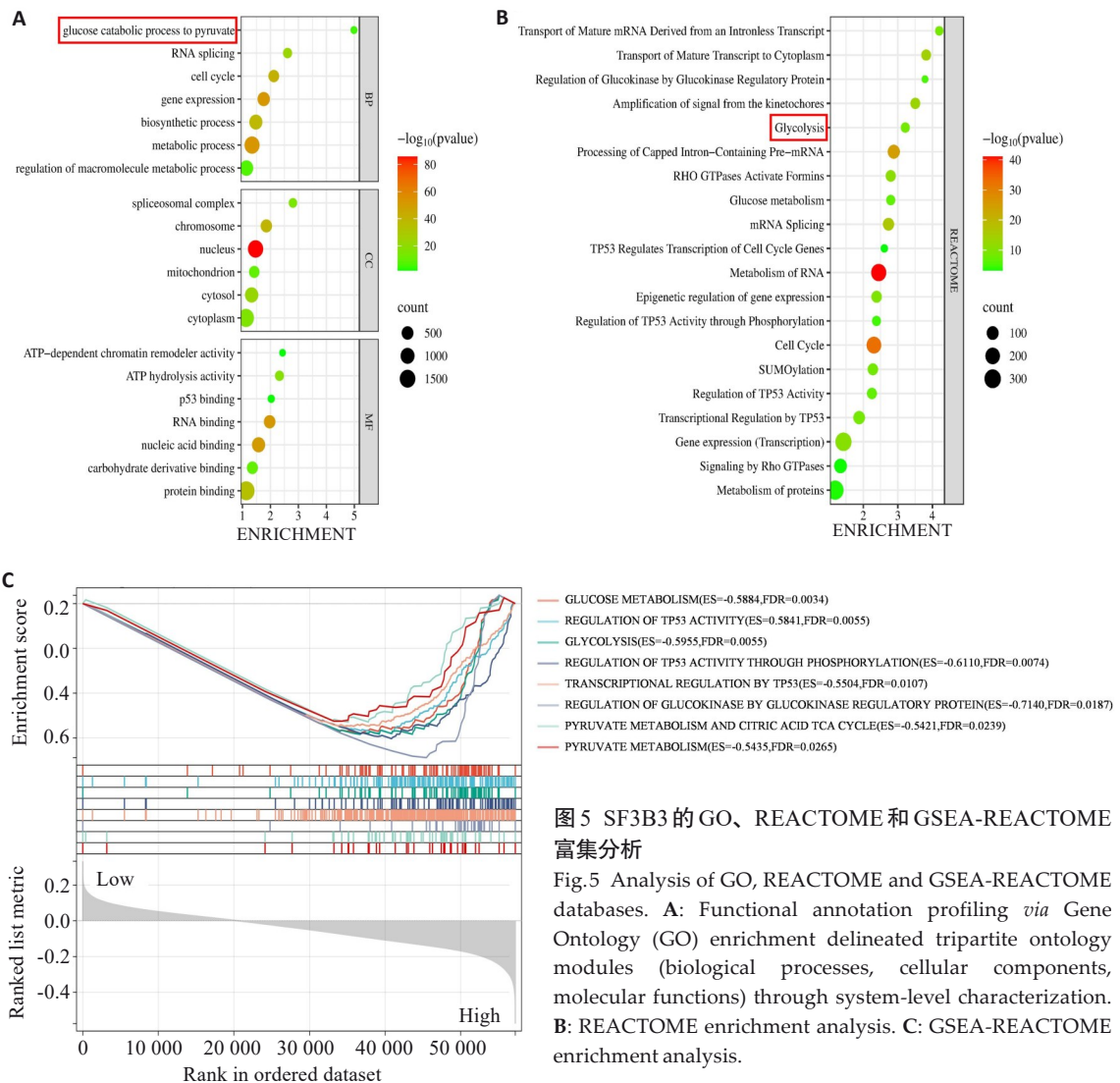


图5 SF3B3的GO、REACTOME和GSEA-REACTOME富集分析

Fig.5 Analysis of GO, REACTOME and GSEA-REACTOME databases. **A:** Functional annotation profiling *via* Gene Ontology (GO) enrichment delineated tripartite ontology modules (biological processes, cellular components, molecular functions) through system-level characterization. **B:** REACTOME enrichment analysis. **C:** GSEA-REACTOME enrichment analysis.

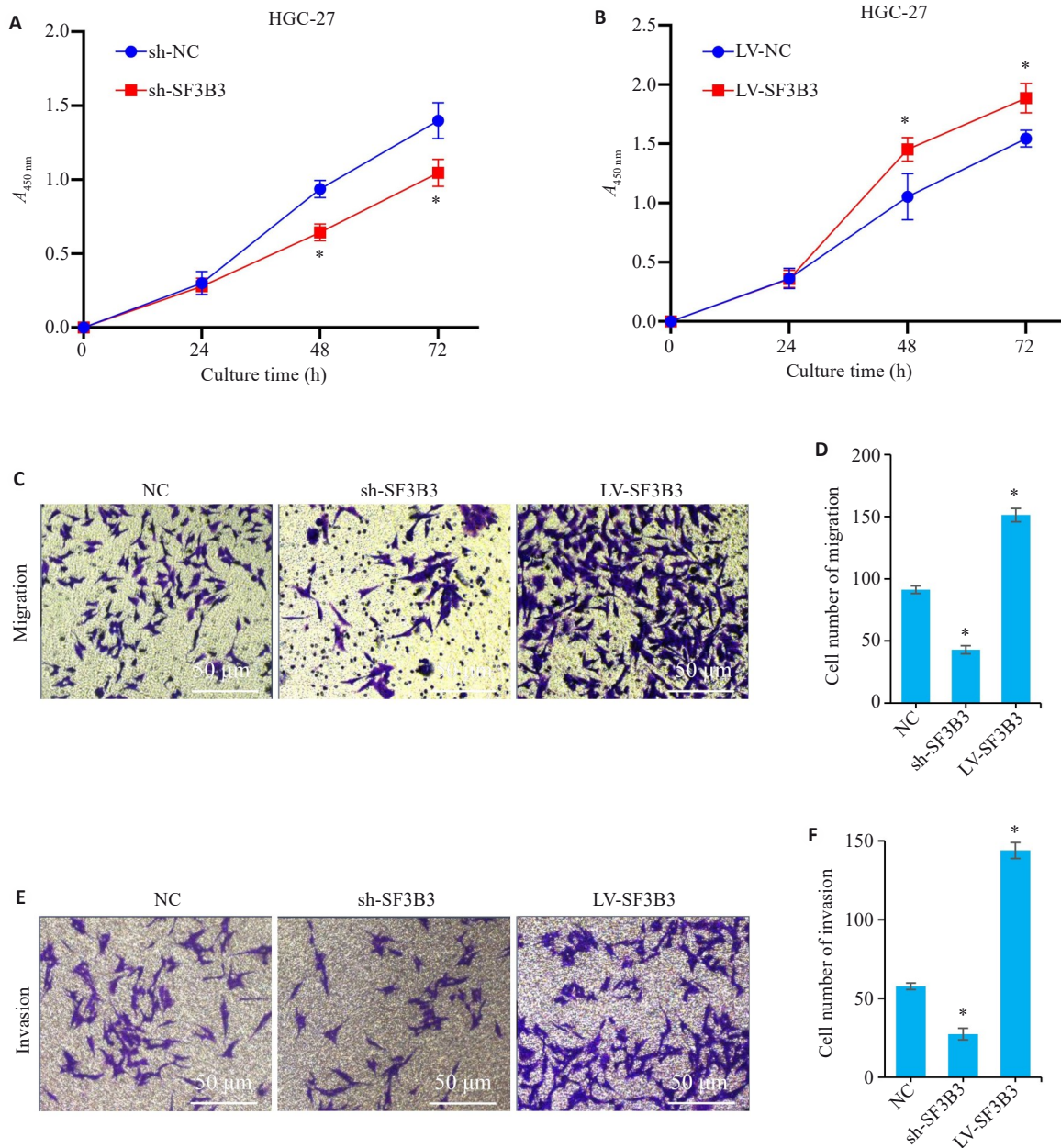


图6 SF3B3促进胃癌HGC-27细胞的增殖、迁移和侵袭能力

Fig.6 Elevated SF3B3 levels enhance proliferative, migration, and invasive abilities of HGC-27 cells. A: Impact of SF3B3 knockdown on proliferation of HGC-27 cells. B: Impact of SF3B3 overexpression on proliferation of HGC-27 cells. C-F: Assessment of migration and invasion of HGC-27 cells. NC: Negative control; sh-NC: Short hairpin RNA negative control; LV-NC: Lentivirus negative control. * $P < 0.05$ vs NC.

谢重编程的典型特征,对于肿瘤细胞的快速生长、增殖及逃逸等恶性过程至关重要^[11,27-30]。本研究通过免疫印迹检测发现,上调SF3B3可提升HK2、PKM2、LDHA等糖酵解关键酶的表达水平。ECAR实验进一步证实SF3B3对糖酵解活性的调控作用。上述结果提示SF3B3可能通过增强Warburg效应促进胃癌细胞的恶性进展。

本研究虽已取得初步成果,但仍存在一些局限性。首先,由于本研究采用回顾性设计,可能存在患者选择

偏差及数据收集不完整的问题。其次,纳入的样本量相对较少,后续研究有必要通过多中心协作纳入更具代表性的群体样本以验证研究结果的可靠性和普适性。尽管如此,本研究仍为SF3B3在胃癌中的作用机制提供了新的见解,并为其作为潜在生物标志物和靶向治疗靶点的临床应用价值奠定了基础。未来,我们将继续通过更多的实验和临床研究,深入挖掘SF3B3的确切分子机制和潜在的临床应用价值,以期胃癌的精准治疗和预后评估提供新的策略和方法。

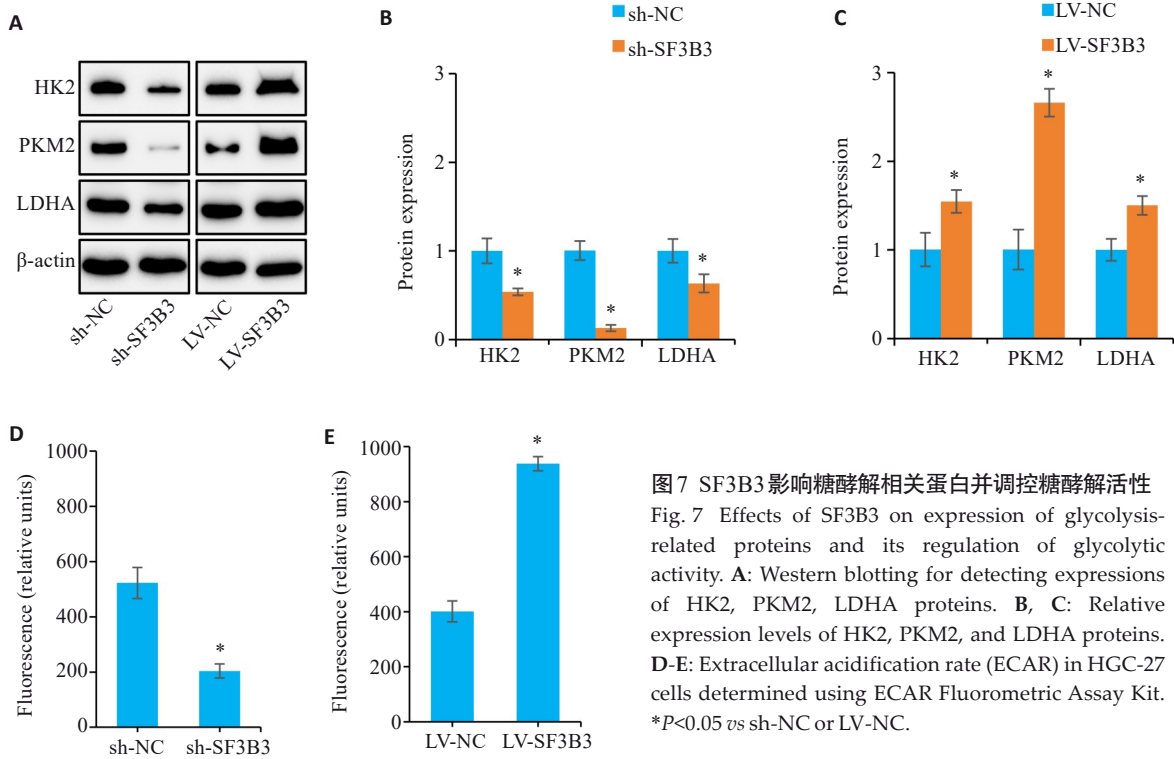


图7 SF3B3影响糖酵解相关蛋白并调控糖酵解活性
 Fig. 7 Effects of SF3B3 on expression of glycolysis-related proteins and its regulation of glycolytic activity. **A:** Western blotting for detecting expressions of HK2, PKM2, LDHA proteins. **B, C:** Relative expression levels of HK2, PKM2, and LDHA proteins. **D-E:** Extracellular acidification rate (ECAR) in HGC-27 cells determined using ECAR Fluorometric Assay Kit. * $P < 0.05$ vs sh-NC or LV-NC.

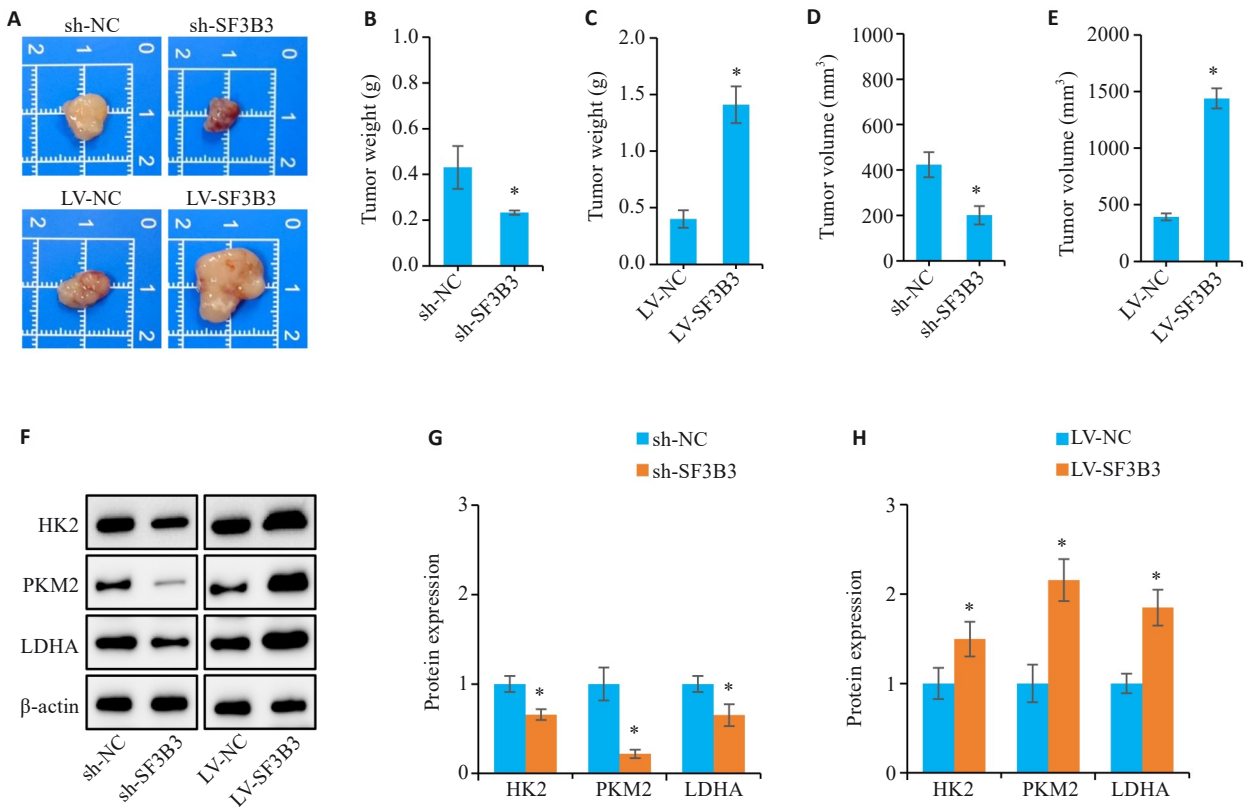


图8 SF3B3促进裸鼠皮下成瘤能力,体内促进糖酵解
 Fig. 8 Role of SF3B3 in augmenting tumorigenesis in nude mice and its impact on glycolytic activity *in vivo*. **A:** Comparison of xenograft growth among the groups. **B, C:** Measurement of tumor weight in nude mice. **D, E:** Quantification of tumor volume in nude mice. **F-H:** Assessment of HK2, PKM2, and LDHA protein expression using Western blotting in tumor xenografts. * $P < 0.05$ vs sh-NC or LV-NC group.

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