revealed that *Lysinibacillus sphaericus* significantly reduced the aspirin levels in aspirin-containing medium. Moreover, the germ-free mice monocolonized with *Lysinibacillus sphaericus* showed significantly lower plasma aspirin levels post aspirin administration relative to the intact germ-free mice, confirming a role of this bacterium in reducing aspirin bioavailability.

Conclusions Gut microbiota modulates the chemopreventive efficacy of aspirin on CRC through impact on aspirin bioavailability in mice. *Lysinibacillus sphaericus* may play a critical role in aspirin degradation in the gut.

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LONG NON-CODING RNA LOC148709 REGULATES PFKFB3-MEDIATED GLYCOLYTIC REPROGRAMMING IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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Background Rapid proliferation and glucose metabolism remodeling are hallmarks of cancers. Long non-coding RNAs (lncRNAs) are potentially involved in Warburg effect. We aimed to identify oncogenic lncRNAs that significantly affect the development of esophageal squamous cell carcinoma (ESCC) and investigate the metabolism-related mechanisms.

Methods Bioinformatics analysis and siRNA library screening were used to pinpoint lncRNAs that significantly affected cell glycolysis and proliferation. RNAscope(R) in situ hybridization and qRT-PCR assays were performed in clinical samples to investigate expression levels and clinical relevance of the lncRNA. RNA interference and CRISPR-Cas9 were used to explore the functional roles of the lncRNA. *In vivo*, cell-based and patient-derived xenograft (PDX) models were used. Extracellular acidification rate and ¹³C-labeled intracellular metabolites were determined. RNA pull-down, MS2-Tagged RNA affinity purification, RNA-binding protein immunoprecipitation and cross-linking immunoprecipitation were performed to identify lncRNA associated proteins and related mechanisms.

Results The lncRNA *LOC148709* was identified as a metabolism-related lncRNA. Increased expression of *LOC148709* was observed in ESCC and was correlated with poor prognosis. *LOC148709* knockdown significantly decreased cell proliferation and glycolysis. Mechanistically, *LOC148709* was directly associated with PFKFB3 and significantly affected PFKFB3 stability. *LOC148709* interacted mainly with the C-terminal fragment of PFKFB3 and the T5 (2031–2321) fragment of *LOC148709* mediated the interaction with PFKFB3. Through inhibiting K302 ubiquitination, *LOC148709* protected PFKFB3 from proteasomal degradation, which subsequently activated glycolytic flux and promoted cell cycle progression by regulating p27 and CDK1. P53 could bind to the *LOC148709* promoter and repress its transcription, p53 loss or mutation triggered striking *LOC148709* upregulation. Multiple micro-environmental factors, including hypoxia and oncogenic stress, were also involved in the *LOC148709* regulatory network via affecting the status of p53. Notably, our patient-derived xenograft (PDX) model studies demonstrated that *LOC148709* knockdown dramatically impaired tumor growth.

Conclusions The lncRNA *LOC148709* plays an essential role in glycolytic reprogramming by binding to and stabilizing

PFKFB3. This study identified a novel metabolism-related lncRNA and revealed a novel mechanism underlying lncRNA-mediated cancer metabolism remodeling. Translational studies further implicated that *LOC148709* is a promising biomarker for cancer diagnosis and therapy.

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SCNN1B FUNCTIONS AS A TUMOR SUPPRESSOR IN COLORECTAL CANCER BY INHIBITING RAS-RAF-MEK-ERK PATHWAY

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Background The incidence of colorectal cancer (CRC) is rapidly rising worldwide. Understanding the molecular mechanism underlying CRC pathogenesis is critical to uncover novel drug targets and diagnostics for this disease. Our preliminary work identified SCNN1B as an outlier down-regulated in CRC. SCNN1B mRNA and protein expression were down-regulated in primary CRC and CRC cell lines, suggesting that it might function as a tumor suppressor in CRC.

Methods Clinical significance of SCNN1B in evaluated using tissue microarray (N=153). Biological function of SCNN1B was investigated in CRC cell lines using cell proliferation, apoptosis, cell cycle, cell migration and subcutaneous xenograft assays. Molecular mechanism of SCNN1B was evaluated by Gene Set Enrichment Analysis (GSEA), and assessment of Ras-Raf-MEK-ERK pathways.

Results In a pilot tissue microarray cohort of CRC (N=153), SCNN1B protein expression was an independent prognostic factor predicting favorable patient survival. Ectopic expression of SCNN1B in two CRC cell lines inhibited cell proliferation, induced apoptosis and cell cycle arrest, and suppressed cell migration. Gene Set Enrichment Analysis (GSEA) revealed that SCNN1B expression was associated with KRAS signaling pathway. SCNN1B inhibited p-MEK/p-ERK and SRE luciferase activity, confirming blockade of Ras-Raf-MEK-ERK oncogenic signaling. Mechanistically, SCNN1B suppressed the activation of c-Raf by inducing its inhibitory phosphorylation. Ectopic expression of c-Raf rescued cell proliferation and colony formation in SCNN1B-overexpressed CRC cells, confirming c-Raf as a molecular target of SCNN1B.

Conclusions SCNN1B inhibits colorectal tumorigenesis via inhibition of RAS-MEK-ERK signalling. SCNN1B expression may serve as an independent prognostic biomarker for CRC patients.

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THE IMPACT OF INTENSIVE PATIENT EDUCATIONAL PROGRAMME ON QUALITY OF BOWEL PREPARATION FOR COLONOSCOPY: A RANDOMISED CONTROL TRIAL

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Background Optimal bowel preparation prior to colonoscopy leads to good quality of visualisation. However, achieving