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*Research Article*

# LATS1 Exerts Tumor-Suppressive Effects in Colorectal Cancer via Activating the Hippo Signaling Pathway

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## ABSTRACT

**Objective:** To explore the role of LATS1 (large tumor suppressor 1) in colorectal cancer (CRC) cell proliferation, migration, invasion and its regulation of the Hippo signaling pathway.

**Methods:** LATS1 expression in CRC cell lines (HCT116, SW480) and normal colonic epithelial cell line (NCM460) was detected by Western blot and qRT-PCR. LATS1 was overexpressed via plasmid or knocked down via siRNA in HCT116 cells. Cell proliferation (CCK-8), migration (scratch assay), invasion (Transwell) and Hippo-related proteins (YAP1, p-YAP1, TEAD4) were analyzed.

**Results:** LATS1 was downregulated in CRC cells ($P<0.01$). LATS1 overexpression reduced proliferation (OD450 at 72h: 0.62±0.06 vs. 1.28±0.10, $P<0.05$), migration (24h rate: 28.5±3.8% vs. 67.2±5.6%, $P<0.01$), invasion (cell number: 38±5 vs. 118±8, $P<0.01$), upregulated p-YAP1 ($P<0.05$) and downregulated YAP1/TEAD4 ($P<0.05$). LATS1 knockdown showed opposite effects.

**Conclusion:** LATS1 inhibits CRC progression via Hippo signaling, serving as a potential therapeutic target.

**Keywords:** Colorectal Cancer; Cell Proliferation; Transwell; Large Tumor Suppressor 1

## Introduction

Colorectal cancer (CRC) causes ~935,000 annual deaths globally[1]. The Hippo pathway regulates cell growth and tumorigenesis, with dysregulation driving CRC progression[2,3]. LATS1, a core Hippo kinase, phosphorylates YAP1 to inhibit its oncogenic activity[4]. LATS1 is downregulated in liver, breast and gastric cancers, correlating with poor prognosis[5-7]. However, LATS1's role in CRC remains understudied. This study investigates LATS1's function in CRC cells and its link to Hippo signaling.

## Materials and Methods

### Cell culture

HCT116, SW480 (CRC) and NCM460 (normal colonic epithelial) cells (ATCC) were cultured in RPMI-1640 (Gibco) with 10% FBS and 1% penicillin-streptomycin at 37°C, 5% $CO_2$.

### Transfection

pcDNA3.1-LATS1 (overexpression) and si-LATS1 (knockdown) (Thermo Fisher) were transfected into HCT116 cells via Lipofectamine 3000 (Invitrogen). LATS1 expression

was verified by Western blot/qRT-PCR 48h post-transfection.

## qRT-PCR and western blot

qRT-PCR: TRIzol-extracted RNA was reverse-transcribed; LATS1primers:Forward5'-GCTGCTGCTGCTGTTTCTGA-3', Reverse 5'-CAGCAGCAGCAGCTTCTTCT-3' (GAPDH as control). Western blot: RIPA-extracted protein (30μg) was probed with anti-LATS1, YAP1, p-YAP1 (Ser127), TEAD4 and GAPDH antibodies (Abcam/Cell Signaling Technology).

### Functional assays

- CCK-8: $2\times10^3$ transfected cells/well; OD450 measured at 24/48/72h.
- Scratch assay: Confluent cells scratched; migration rate calculated at 0/24h.
- Transwell invasion: Matrigel-coated chambers; invasive cells counted at 24h.

### Statistical analysis

Data (mean±SD, triplicate) were analyzed via SPSS 26.0 (t-test); $P<0.05$ was significant.

## Results

### LATS1 is downregulated in CRC cells

**qRT-PCR:** LATS1 mRNA in HCT116/SW480 was 0.27±0.03/0.35±0.04 folds of NCM460 ($P<0.01$). Western blot: LATS1 protein in HCT116/SW480 was 0.30±0.04/0.38±0.05 folds of NCM460 ($P<0.01$).

### LATS1 inhibits CRC cell proliferation

LATS1 overexpression reduced OD450 at 48h (0.54±0.06 vs. 0.91±0.08, $P<0.05$) and 72h (0.62±0.06 vs. 1.28±0.10, $P<0.05$). LATS1 knockdown increased OD450 at 48h (1.08±0.09 vs. 0.89±0.07, $P<0.05$) and 72h (1.39±0.11 vs. 1.26±0.09, $P<0.05$).

### LATS1 suppresses CRC cell migration

LATS1 overexpression reduced migration rate (28.5±3.8% vs. 67.2±5.6%, $P<0.01$). LATS1 knockdown increased rate (75.1±6.0% vs. 66.5±5.5%, $P<0.01$).

### LATS1 inhibits CRC cell invasion

LATS1 overexpression reduced invasive cells (38±5 vs. 118±8, $P<0.01$). LATS1 knockdown increased cells (135±10 vs. 116±7, $P<0.01$).

### LATS1 activates the hippo pathway

LATS1 overexpression upregulated p-YAP1 (2.02±0.18 vs. 1.00±0.08, $P<0.05$) and downregulated YAP1 (0.38±0.04 vs. 1.00±0.09, $P<0.05$) and TEAD4 (0.35±0.03 vs. 1.00±0.07, $P<0.05$). LATS1 knockdown showed opposite effects.

## Discussion

LATS1 is downregulated in CRC cells and its overexpression inhibits CRC cell proliferation, migration and invasion by activating Hippo signaling (upregulating p-YAP1, downregulating YAP1/TEAD4)-consistent with LATS1's tumor-suppressive role in other cancers[5-7]. LATS1 phosphorylates YAP1 to block nuclear translocation[4], which aligns with our data. Limitations include lack of in vivo validation and clinical sample analysis; future studies should address these. Restoring LATS1 may be a promising CRC therapy[8,9].

## Conclusion

LATS1 is downregulated in CRC cell lines. It inhibits CRC cell proliferation, migration and invasion by activating the Hippo signaling pathway, highlighting its potential as a therapeutic target.

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