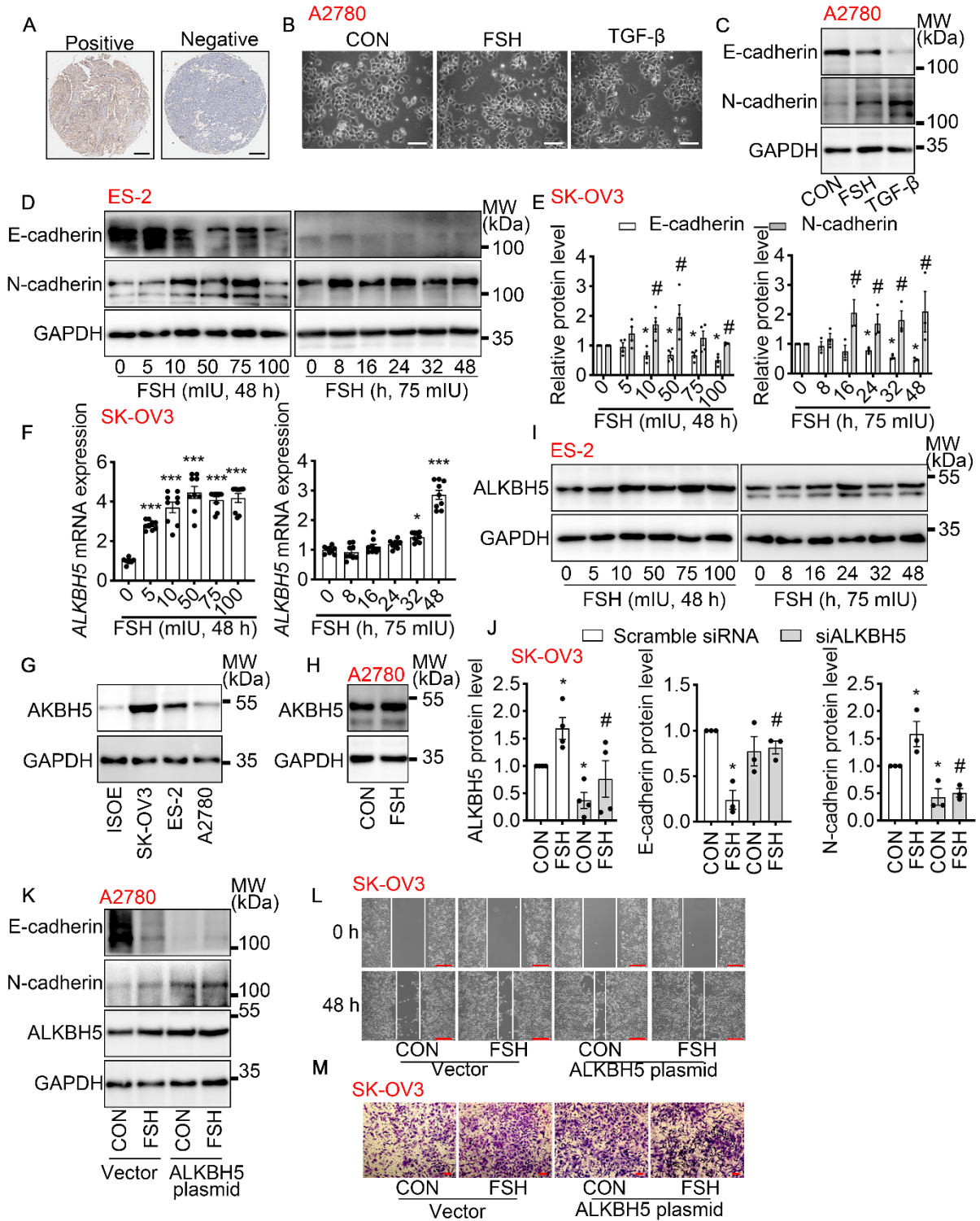


1 **Supplementary table 1.** Detailed information PCR primers

Primer name	Genbank Accession No.	Forward	Reverse	Product size (bp)
<i>Snail</i>	NM_005985.4	GGCAATTTAACAATGT CTGAAAAGG	GAATAGTTCTGGGAGA CACATCG	105
<i>ALKBH5</i>	NM_017758.4	AGTTCAGTTCAAGCC TATTCG	TGAGCACAGTCACGCT TCC	78
<i>Snail-m6A</i>	NM_005985.4	AGGTCAGCTCTGCCAC CCT	TCCCACCGTCTCGACTG GA	108
<i>E-cadherin</i>	NM_004360.5	CGAGAGCTACACGTTC ACGG	GGGTGTCGAGGGAAAA ATAGG	119
<i>GAPDH</i>	NM_002046.7	GGAGCGAGATCCCTCC AAAAT	GGCTGTTGTCATACTTC TCATGG	197

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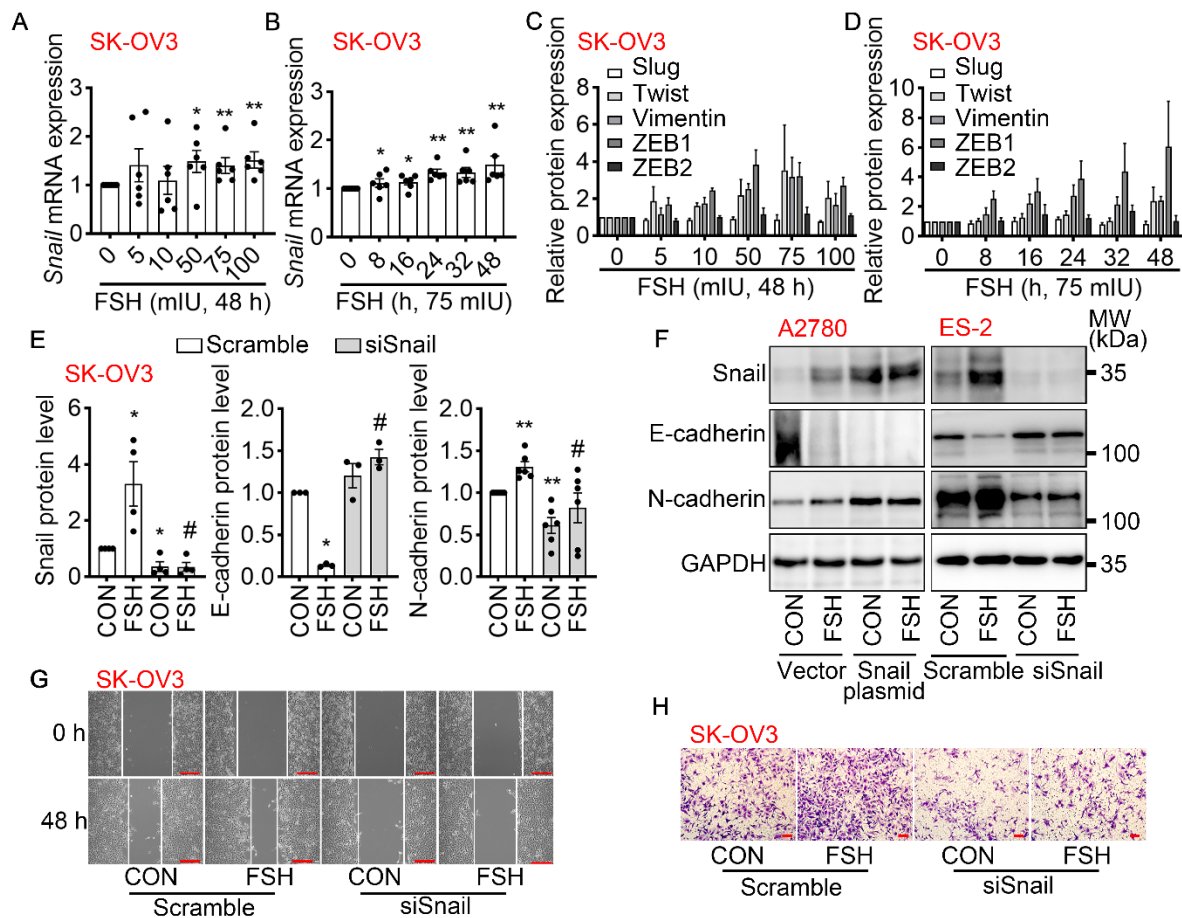


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5 **Supplementary figure 1.** FSH induced EMT in epithelial ovarian cancer cells via ALKBH5. (A) IHC of
6 FSHR on tissue microarray of ovarian tumor. Scale bar = 250 μ m. (B) Cellular morphology of A2780 cells
7 treated with FSH (75 mIU) and TGF- β (10 ng/ μ l) for 48 hours. Scale bar = 25 μ m. (C) Western blots of E-
8 cadherin and N-cadherin in A2780 cells treated with FSH (75 mIU) and TGF- β (10 ng/ μ l) for 48 hours. (D)
9 Western blots of E-cadherin and N-cadherin in ES-2 cells treated with different concentrations of FSH for
10 various time points. (E) Quantification of Western blot for E-cadherin and N-cadherin expression in SK-
11 OV3 cells treated with different concentrations of FSH for various time points ($n = 3 - 4$), data was analyzed

12 by Mann-Whitney U test. * $P < 0.05$ versus CON (E-cadherin), # $P < 0.05$ versus CON (N-cadherin). **(F)**
13 qRT-PCR of *ALKBH5* mRNA in SK-OV3 cells treated with different concentrations of FSH for various time
14 points ($n = 9$), data was analyzed by one-way ANOVA test. * $P < 0.05$, *** $P < 0.001$ versus CON. **(G)**
15 Western blots of ALKBH5 expression in ISOE-80 (ISOE), SK-OV3, ES-2, A2780 cell lines. **(H)** Western
16 blots of ALKBH5 expression in A2780 cells with FSH (75 mIU) treatment for 48 hours. **(I)** Western blots of
17 ALKBH5 expression in ES-2 cells were treated with different concentrations of FSH for various time points.
18 **(J)** Western blot quantification of ALKBH5, E-cadherin and N-cadherin in SK-OV3 cells treated with FSH
19 after transfection of scramble or ALKBH5 siRNA ($n = 3 - 4$), data was analyzed by Mann-Whitney U test.
20 * $P < 0.05$ versus CON group transfected with scramble siRNA, # $P < 0.05$ versus FSH group transfected
21 with scramble siRNA. **(K)** Western blots of ALKBH5, E-cadherin and N-cadherin in A2780 cell treated with
22 FSH (75 mIU, 48 h) after transfection of vector or ALKBH5 plasmid. **(L)** Representative images of wound
23 healing in SK-OV3 treated with FSH (75 mIU, 48 h) after transfection of vector or ALKBH5 plasmid. Scale
24 bar = 100 μm . **(M)** Representative images of Transwell invasion in SK-OV3 treated with FSH (75 mIU, 48
25 h) after transfection of vector or ALKBH5 plasmid. Scale bar = 250 μm .

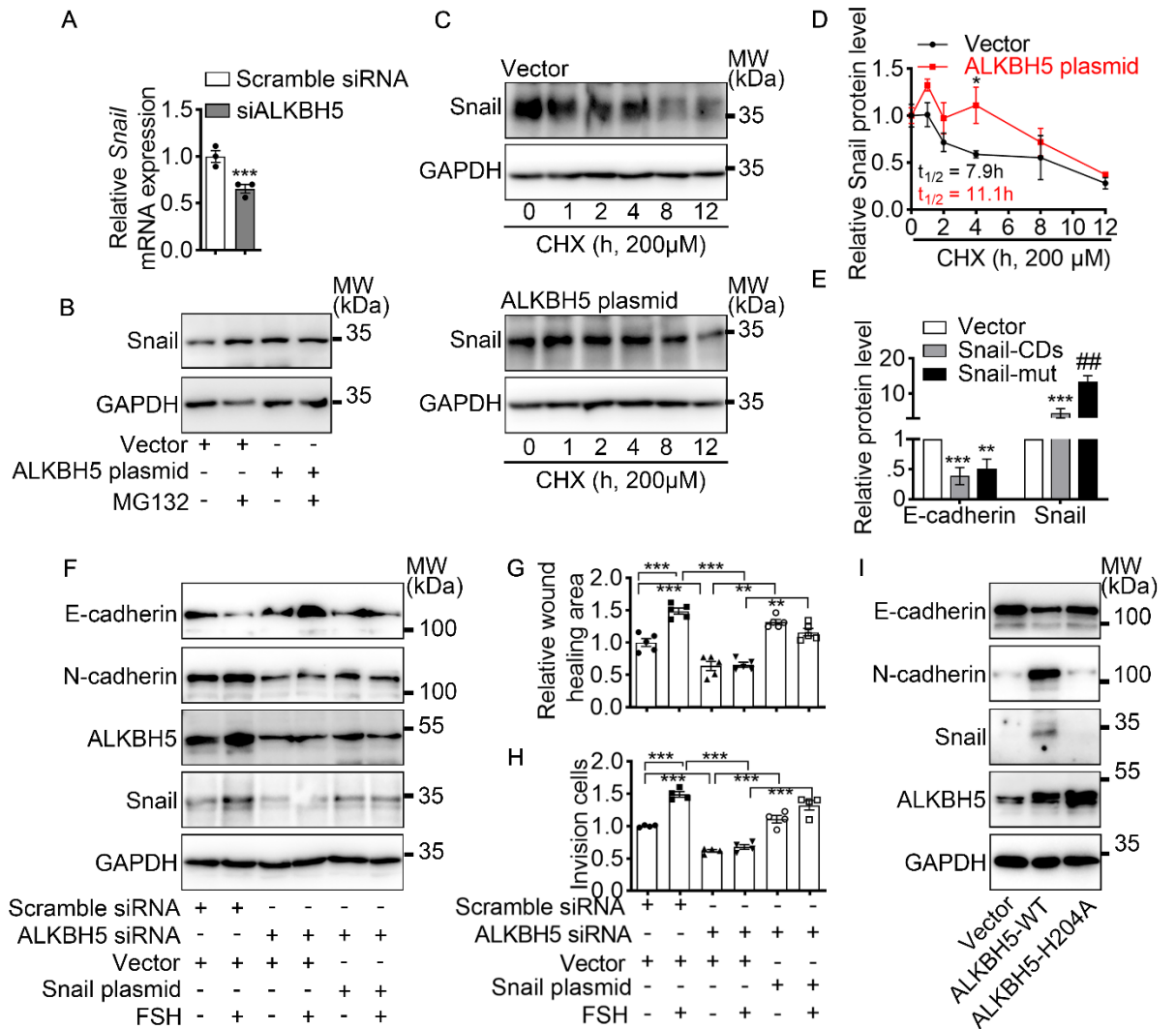
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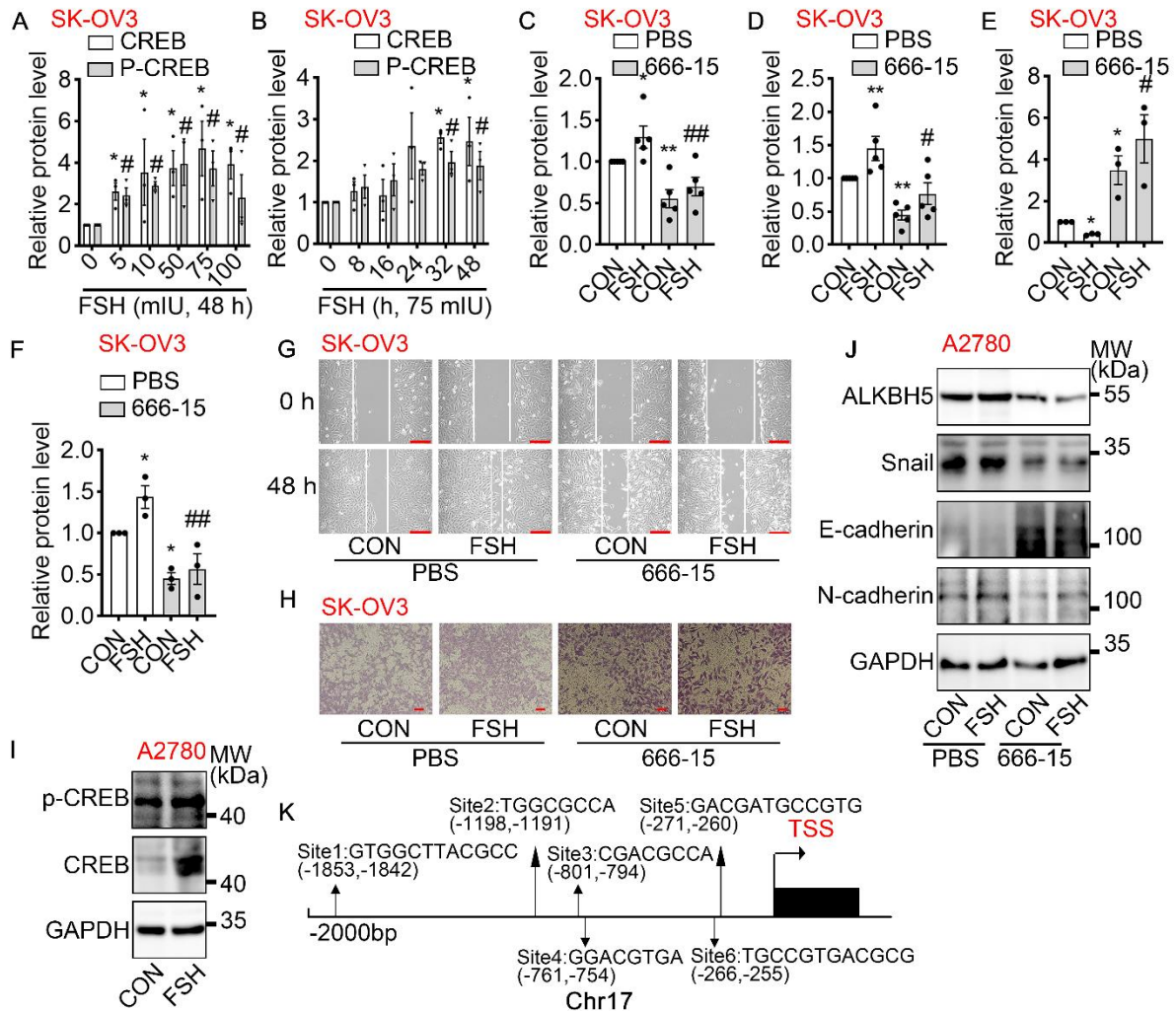
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28 **Supplementary figure 2.** Snail is a critical EMT transcription factor in FSH induces EMT progression. (A-
 29 **D**) SK-OV3 cells treated with different concentrations of FSH for various time points. (A, B) qRT-PCR of
 30 *Snail* mRNA transcripts, $n = 6$ per group, data was analyzed for statistical difference by Mann-Whitney U
 31 test. $*P < 0.05$, $**P < 0.01$. (C, D) Quantification of Western blot for Slug, Twist, Vimentin and ZEB1/2 (n
 32 = 3). (E) Quantification of Western blot for Snail, E-cadherin and N-cadherin in SK-OV3 cells treated with
 33 FSH (75 mIU, 48 h) after transfection of scramble or Snail siRNA (siSnail). ($n = 3 - 5$), data was analyzed
 34 by Mann-Whitney U test. $*P < 0.05$, $**P < 0.01$ versus CON group transfected with scramble siRNA, $\#P <$
 35 0.05 versus FSH group transfected with scramble siRNA. (F) Western blots of Snail, E-cadherin and N-
 36 cadherin in A2780 (left) or ES-2 cells (right) treated with FSH (75 mIU, 48 h) after transfection of Snail
 37 plasmid or Snail siRNA. (G, H) SK-OV3 cells were treated with FSH (75 mIU, 48 h) after transfection of
 38 scramble or Snail siRNA. (G) Representative images of wound healing (scale bar = 100 μm) and (H)
 39 Transwell invasion (scale bar = 250 μm).

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 42 **Supplementary figure 3.** Increased Snail expression induced by ALKBH5 is essential for FSH-triggered
 43 EMT. **(A)** qRT-PCR of *Snail* mRNA transcripts in SK-OV3 cells transfected with Scramble and ALKBH5
 44 siRNA (siALKBH5), ($n = 3$). Data was analyzed by two-tailed unpaired t test. $***P < 0.001$. **(B)** Western
 45 blots of Snail in SK-OV3 cells transfected with vector or ALKBH5 plasmid with treatment of proteasome
 46 inhibitors MG132. **(C)** Western blots of Snail in SK-OV3 cells transfected with Vector or ALKBH5 plasmid
 47 with treatment of cycloheximide (CHX), quantitative analysis was present in the right panel **(D)**. **(E)**
 48 Quantification of Western blot for E-cadherin and N-cadherin in SK-OV3 cells transfected with Vector,
 49 Snail-CDs and Snail-mut plasmid ($n = 3$), data was analyzed by one-way ANOVA test. $**P < 0.01$, $***P <$
 50 0.001 versus Vector, $##P < 0.01$ versus Snail-CDs. **(F-H)** SK-OV3 cells were solely transfected with
 51 ALKBH5 siRNA or co-transfected with ALKBH5 siRNA and Snail plasmid followed by treatment of FSH.
 52 **(F)** Protein expression of E-cadherin, N-cadherin, ALKBH5 and Snail were assessed by Western blot. **(G)**
 53 Cell migration was assessed by wound healing assay ($n = 5$). Data was analyzed by one-way ANOVA test.
 54 $**P < 0.01$, $***P < 0.001$. **(H)** Cell invasion was measured by Transwell assay ($n = 4$). Data was analyzed
 55 for statistical difference by one-way ANOVA test. $***P < 0.001$. **(I)** Western blots of E-cadherin, N-cadherin,
 56 Snail and ALKBH5 in SK-OV3 cells transfected with empty vector (Vector), wild type ALKBH5 (ALKBH5-
 57 WT) and inactive mutant H204A ALKBH5 (ALKBH5-H204A) plasmid.



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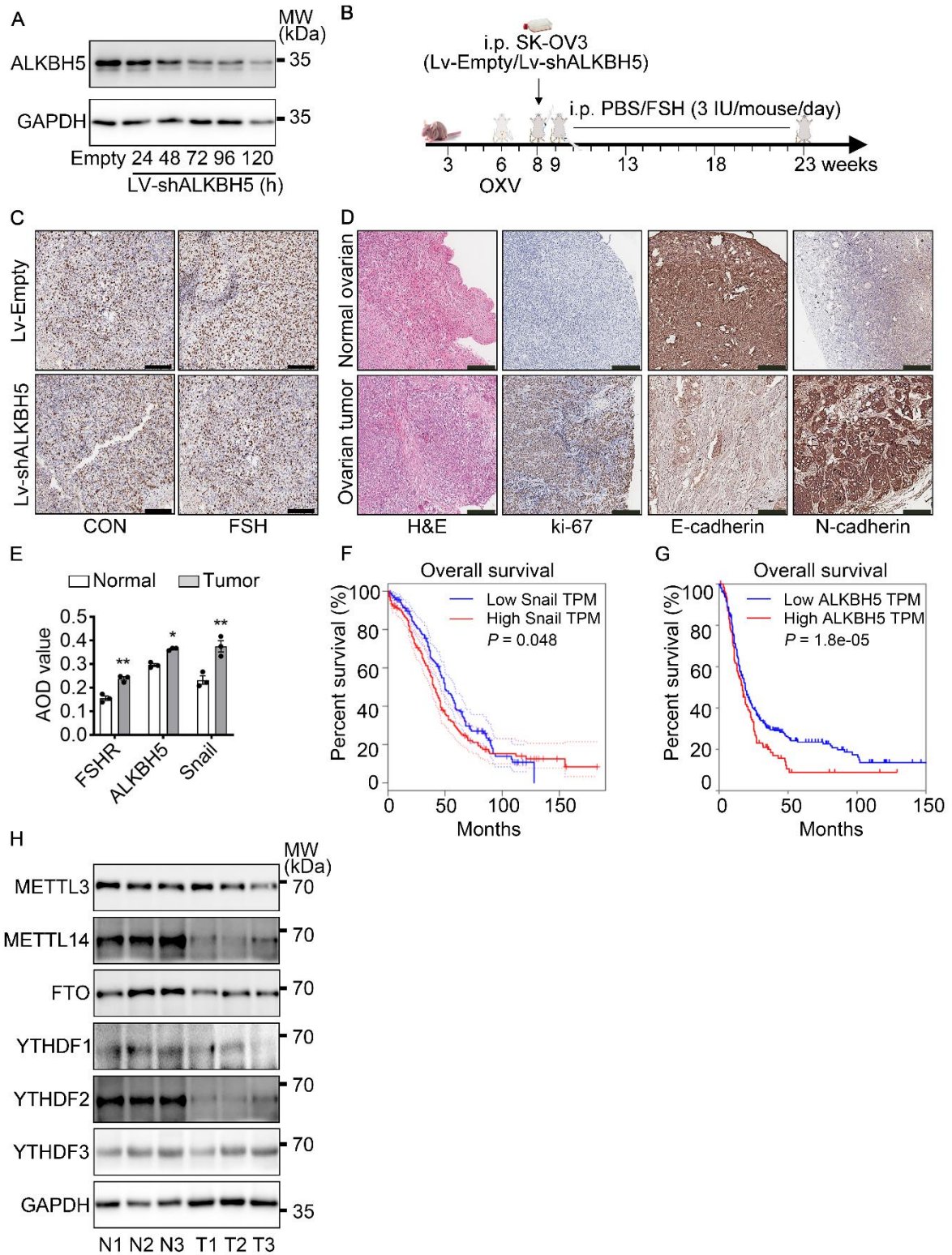
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Supplementary figure 4. FSH activates CREB to elevate ALKBH5 expression. **(A, B)** Western blot quantification of p-CREB/CREB in SK-OV3 cells were treated with different concentrations of FSH for various time points ($n = 3$), data was analyzed by Mann-Whitney U test. $*P < 0.05$ versus CON (CREB), $\#P < 0.05$ versus CON (p-CREB). Western blot quantification of Snail **(C)**, ALKBH5 **(D)** E-cadherin **(E)** and N-cadherin **(F)** in SK-OV3 cells pretreated with CREB inhibitor, followed by treatment of FSH ($n = 3 - 5$), data was analyzed by Mann-Whitney U test. $*P < 0.05$, $**P < 0.01$ versus CON group transfected with scramble siRNA, $\#P < 0.05$, $\#\#P < 0.01$ versus FSH group transfected with scramble siRNA. **(G)** Representative images of wound healing in SK-OV3 cells pretreated with 666-15, followed by treatment of FSH (75 mIU, 48 h). Scale bar = 100 μm. **(H)** Representative images of Transwell invasion in SK-OV3 cells pretreated with 666-15, followed by treatment of FSH (75 mIU, 48 h) or PBS. Scale bar = 250 μm. **(I)** Western blots of p-CREB and CREB in A2780 cells with treatment of FSH. **(J)** Western blots of ALKBH5, Snail, E-cadherin and N-cadherin expression in A2780 cells pretreated with 666-15, followed by treatment of FSH (75 mIU, 48 h). **(K)** Schematic graph of the genomic locations of ALKBH5 and CREB potential binding sites in the promoter region of ALKBH5 host gene chromosome 17.



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Supplementary figure 5. FSHR and Snail expression are positively associated with ALKBH5 expression. **(A)** Western blots of ALKBH5 in SK-OV3 cells transfected with a control (Lv-Empty) or shALKBH5 (Lv-shALKBH5) luciferase-tagged lentivirus. **(B)** Experimental timeline of bilateral ovariectomy (OVX) surgery, xerograph and FSH administration. **(C)** SK-OV3 xenografts were sectioned and stained for Ki-67 expression using IHC. Scale bar = 200 μ m. **(D)** H&E, ki-67, E-cadherin and N-cadherin in tissue sections of normal and tumor ovarian tissues. Scale bar = 200 μ m. **(E)** Histograms of average optical density (AOD) showed

80 the average immunoreactivity of FSHR, ALKBH5 and Snail in tissue sections of normal and tumor ovarian
81 tissues ($n = 3$), data was analyzed by Student's t tests. $*P < 0.05$, $**P < 0.01$. **(F)** Survival analysis of ovarian
82 cancer with high or low *Snail* mRNA using Gene Expression Profiling Interactive Analysis (GEPIA,
83 <http://gepia.cancer-pku.cn/index.html>). **(G)** Kaplan-Meier analysis of overall survival in 614 ovarian cancer
84 patients with various *ALKBH5* mRNA expression (<https://kmplot.com/analysis/index.php?p=service>). **(H)**
85 Western blots of METTL3, METTL14, FTO and YTHDF1/2/3 protein in normal ovarian tissue (N) and
86 ovarian tumors (T).
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