Supplemental Figure 1: ELISA expression detection of LysoA, Indole sulfate, L-Malic acid, and Ethyl glucuronide in the plasma of *VHL*-mutant RCC patients

Supplemental Figure 2：Supplemental experimental results of Fig.2F

Supplemental Figure 3: Evaluation of the clinical relevance of ASNS using TCGA-KIRC data

(A) Analysis of ASNS expression levels in ccRCCs compared to their AN tissues, along with its correlation to various tumor stages, grades, and metastasis. (B) Comparison of overall survival (OS) and disease-free survival (DFS) in ccRCC patients categorized by high and low ASNS expression. (C) Comparison of OS in metastatic ccRCC patients based on ASNS expression levels. (D) Comparison of ASNS mRNA expression between *VHL*-mutant ccRCC and *VHL* wild-type ccRCC. (E) Prognostic analysis results for patients with *VHL*-mutant ccRCC.

Supplemental Figure 4: Evaluation of the clinical relevance of ASNS using TCGA-KIRP and TCGA-KICH data

(A) Comparative analysis of the expression level of ASNS in pRCC compared to their AN tissues, as well as its relationship with various tumor stages, lymph node invasion, distant metastasis, and the OS and DFS of patients. (B) Comparative analysis of the expression level of ASNS in chRCC compared to their AN tissues, as well as its relationship with various tumor stages, lymph node invasion, distant metastasis, and patient OS and DFS.

Supplemental Figure 5：Supplemental experimental results of Fig.2M

Supplemental Figure 6：Supplemental experimental results of Fig.3A

Supplemental Figure 7: The impact of VHL overexpression on ASNS mRNA level in 786-O and RCC4 cell lines

Supplemental Figure 8：Supplemental experimental results of Fig.4B and C

(A) Supplemental experimental results of Fig.4B. (B) Supplemental experimental results of Fig.4C.

Supplemental Figure 9：Supplemental experimental results of Fig.7I

Supplemental Figure 10：Supplemental experimental results of Fig.7J

Supplemental Figure 1

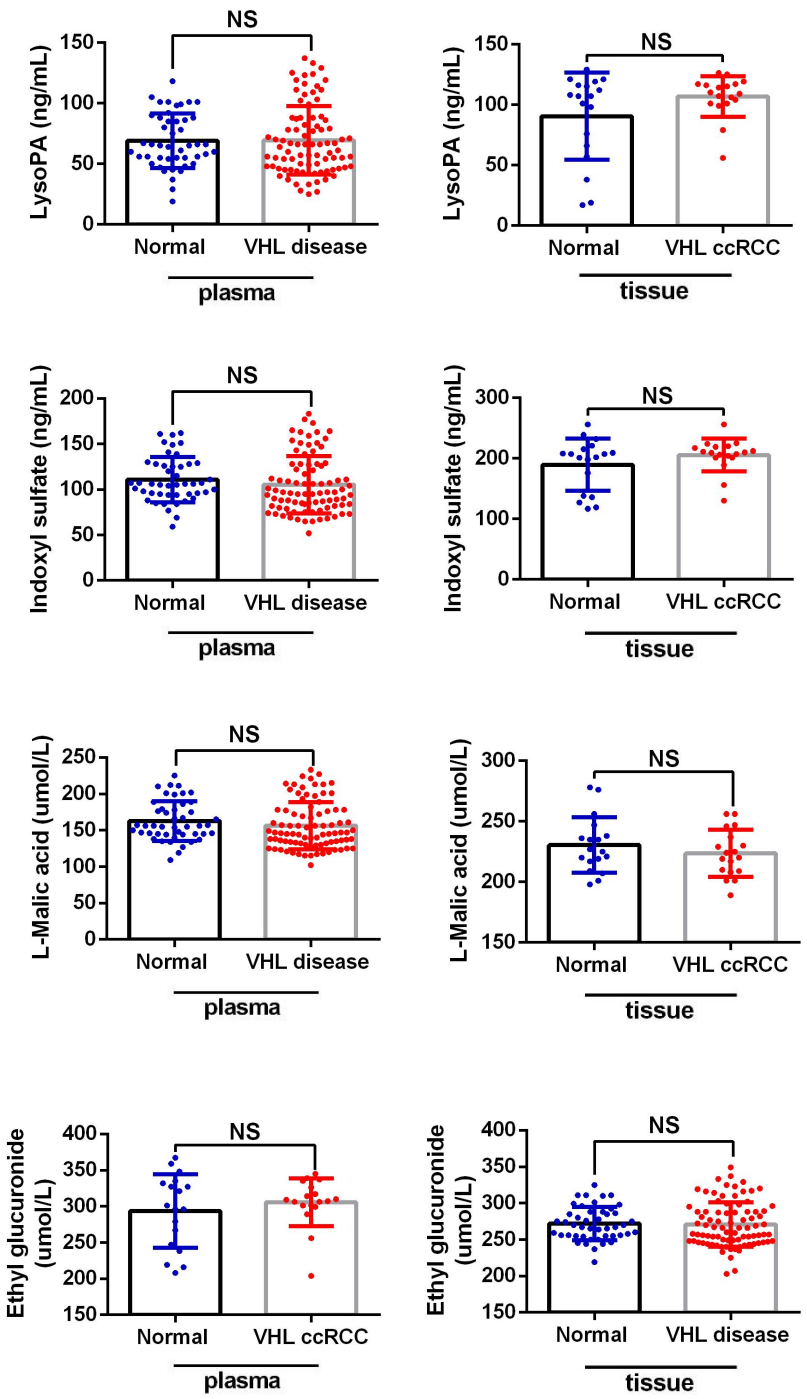
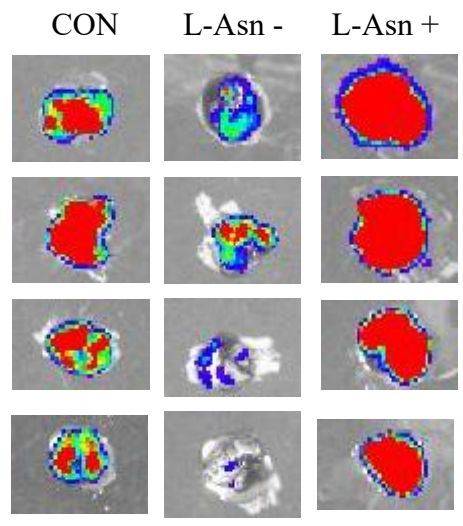
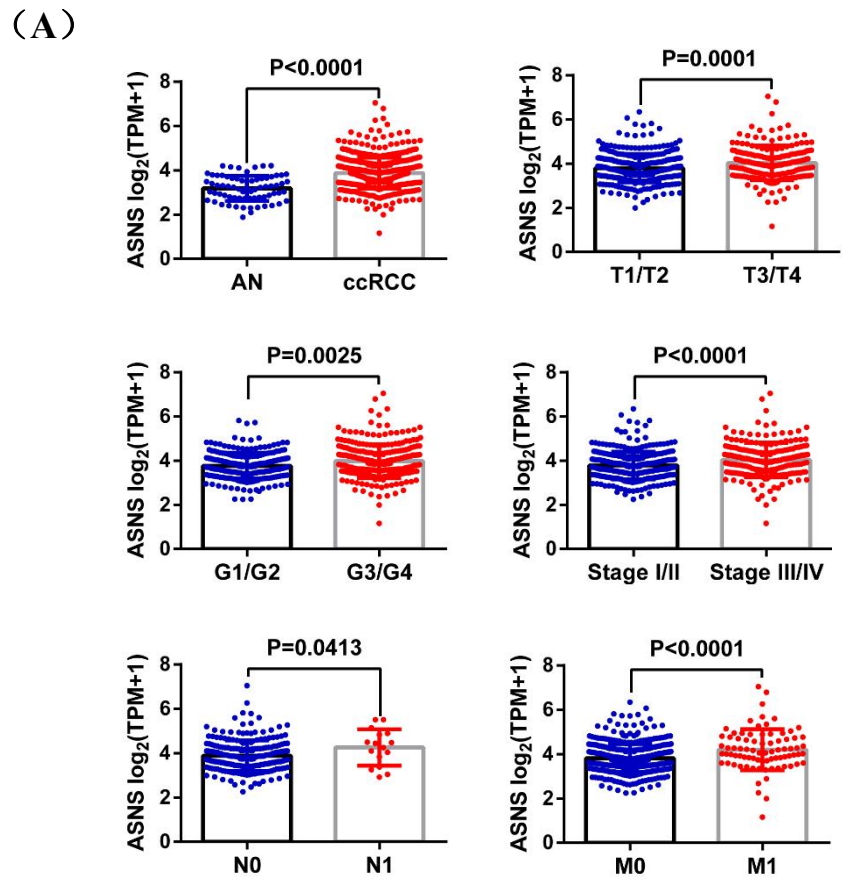
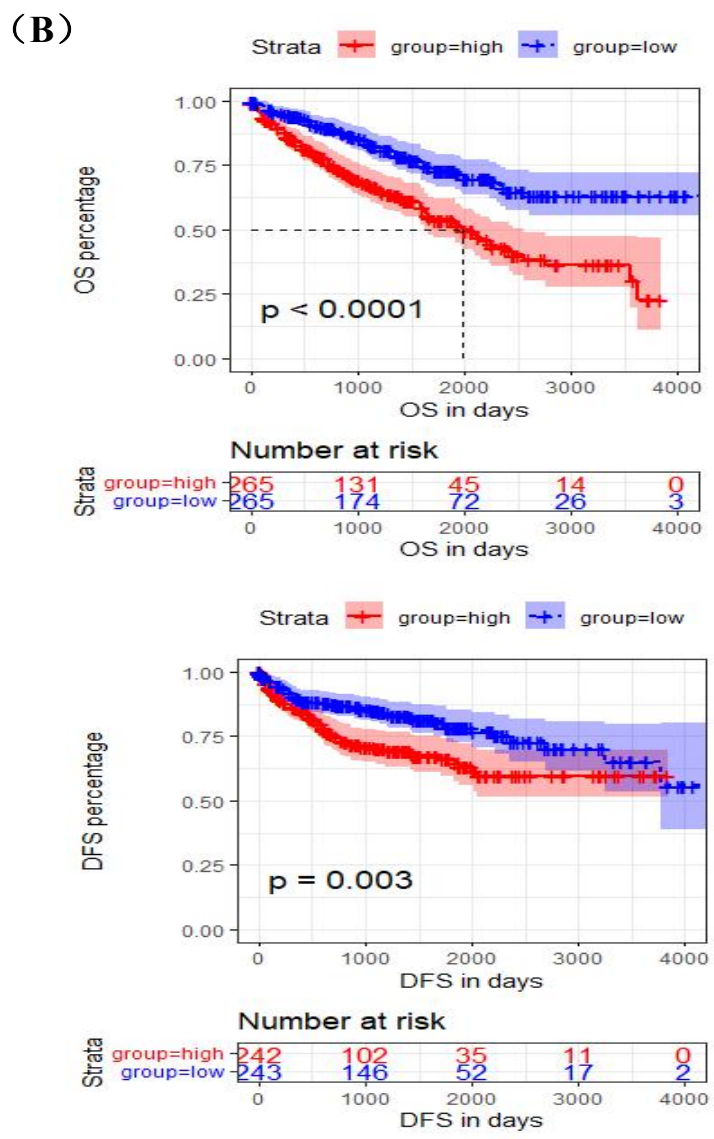
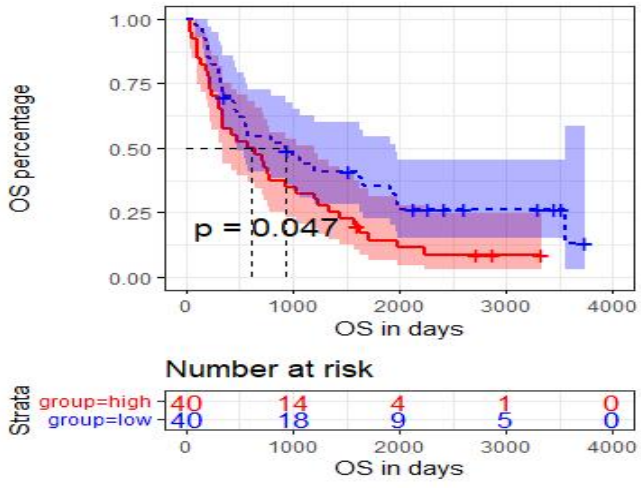


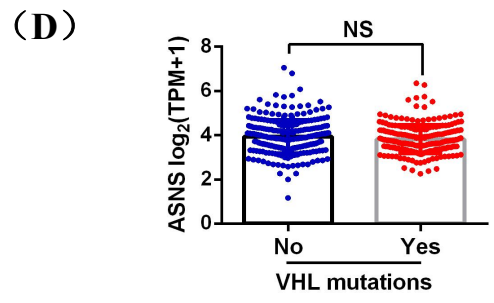
Fig.2F repeats

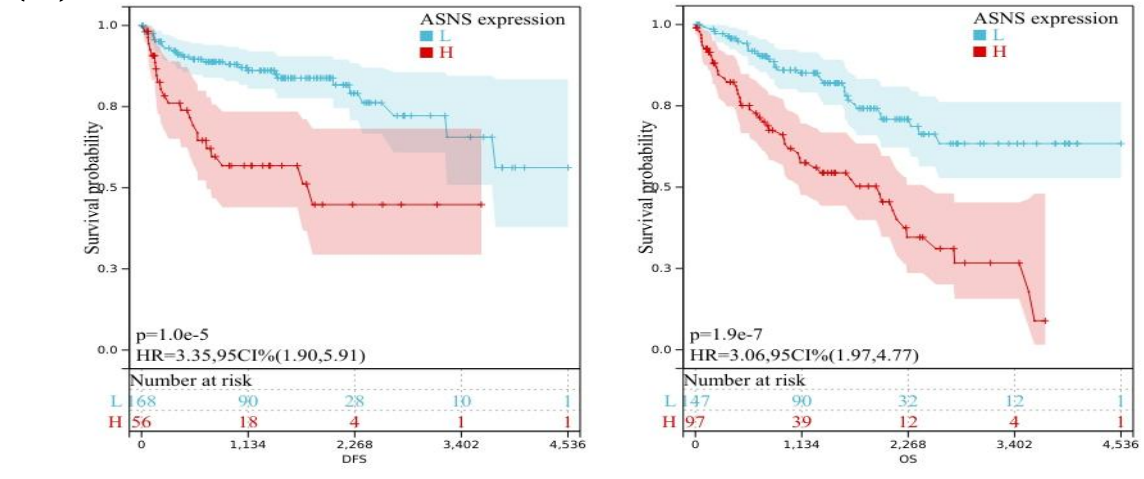



（A）
P<0.0001
ASNS log2(TPM+1)
AN
ccRCC
P=0.0001
T1/T2
T3/T4
P=0.0025
G1/G2
G3/G4
P<0.0001
Stage I/II
Stage III/IV
P=0.0413
N0
N1
P<0.0001
M0
M1

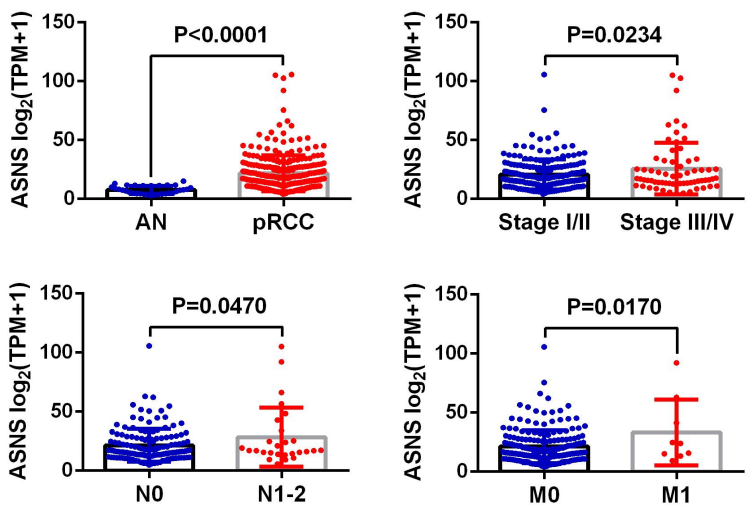

（B）
Strata
group=high
group=low
OS percentage
p < 0.0001
OS in days
Number at risk
group=high 265 131 45 14 0
group=low 265 174 72 26 3
DFS percentage
p = 0.003
DFS in days
Number at risk
group=high 242 102 35 11 0
group=low 243 146 52 17 2


（C）
Strata
group=high
group=low
OS percentage
p = 0.047
OS in days
Number at risk
group=high 40 14 4 1 0
group=low 40 18 9 5 0

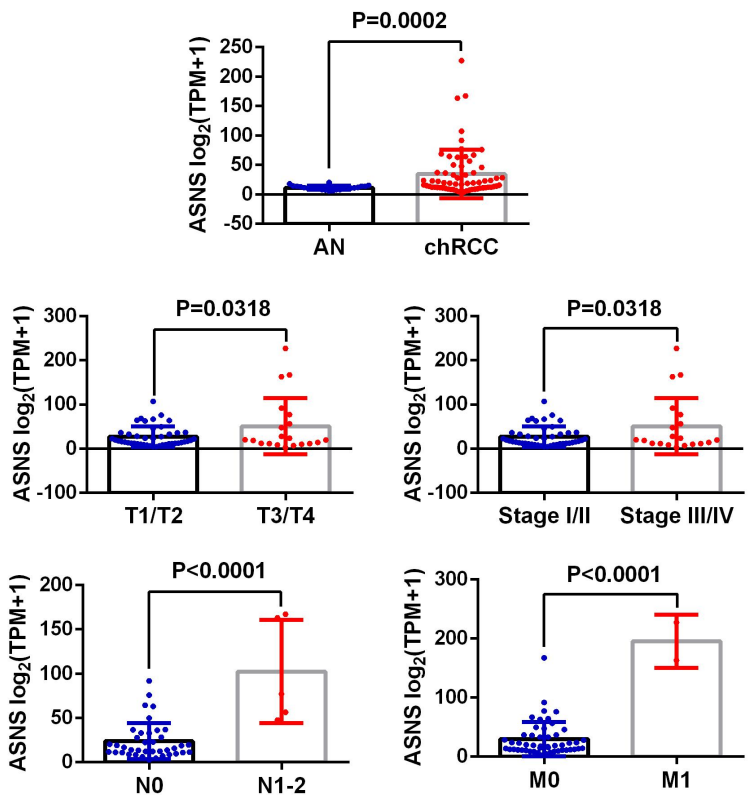

（D）
NS
ASNS log2(TPM+1)
No
Yes
VHL mutations

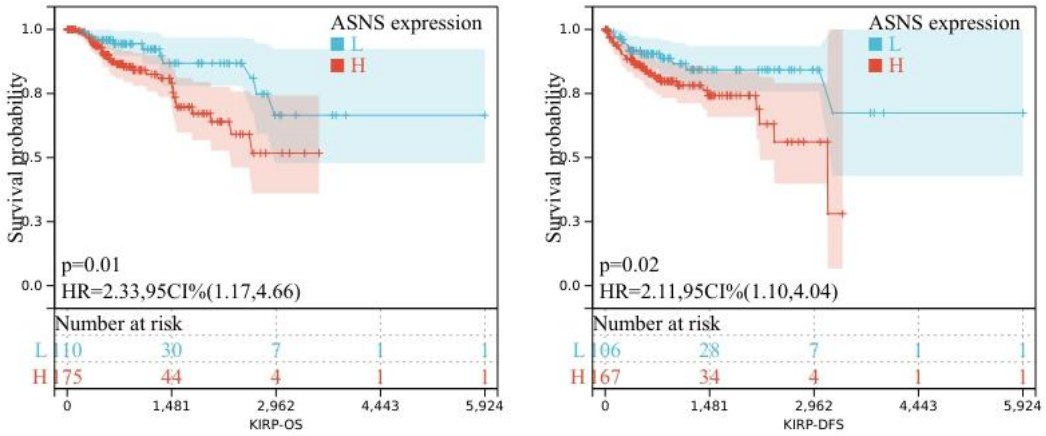

（E）
ASNS expression
L
H
Survival probability
p=1.0e-5
HR=3.35,95CI%(1.90,5.91)
Number at risk
L 168 90 28 10 1
H 56 18 4 1 1
DFS
p=1.9e-7
HR=3.06,95CI%(1.97,4.77)
Number at risk
L 147 90 32 12 1
H 97 39 12 4 1
OS

（A）


ASNS log2(TPM+1)
P<0.0001
AN
pRCC
P=0.0234
Stage I/II
Stage III/IV
P=0.0470
N0
N1-2
P=0.0170
M0
M1

（B）


ASNS log2(TPM+1)
P=0.0002
AN
chRCC
P=0.0318
T1/T2
T3/T4
P=0.0318
Stage I/II
Stage III/IV
P<0.0001
N0
N1-2
P<0.0001
M0
M1


ASNS expression
L
H
Survival probability
p=0.01
HR=2.33,95CI%(1.17,4.66)
Number at risk
L 110 30 7 1 1
H 175 44 4 1 1
KIRP-OS
p=0.02
HR=2.11,95CI%(1.10,4.04)
Number at risk
L 106 28 7 1 1
H 167 34 4 1 1
KIRP-DFS

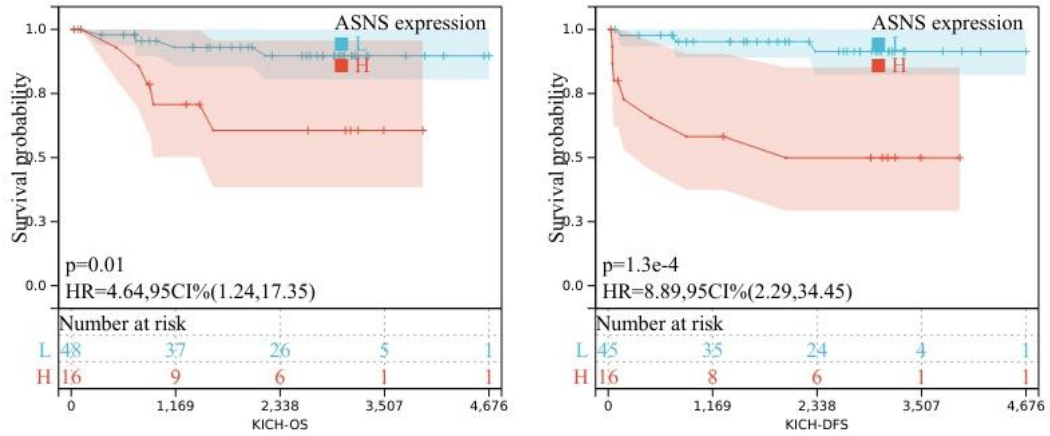

ASNS expression
L
H
Survival probability
p=0.01
HR=4.64,95CI%(1.24,17.35)
Number at risk
L 48 37 26 5 1
H 16 9 6 1 1
KICH-OS
p=1.3e-4
HR=8.89,95CI%(2.29,34.45)
Number at risk
L 45 35 24 4 1
H 16 8 6 1 1
KICH-DFS

Fig.2M repeat 2, 3

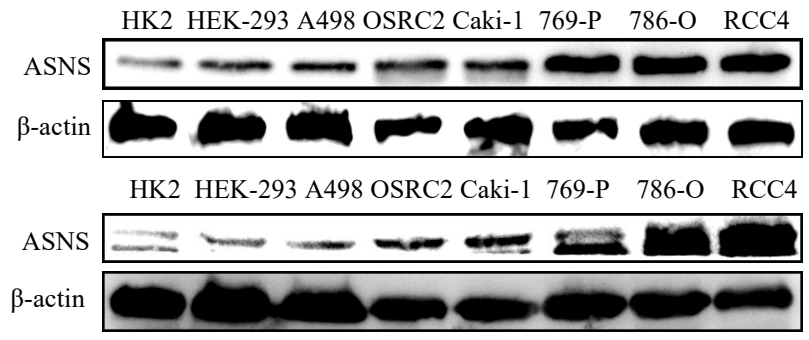
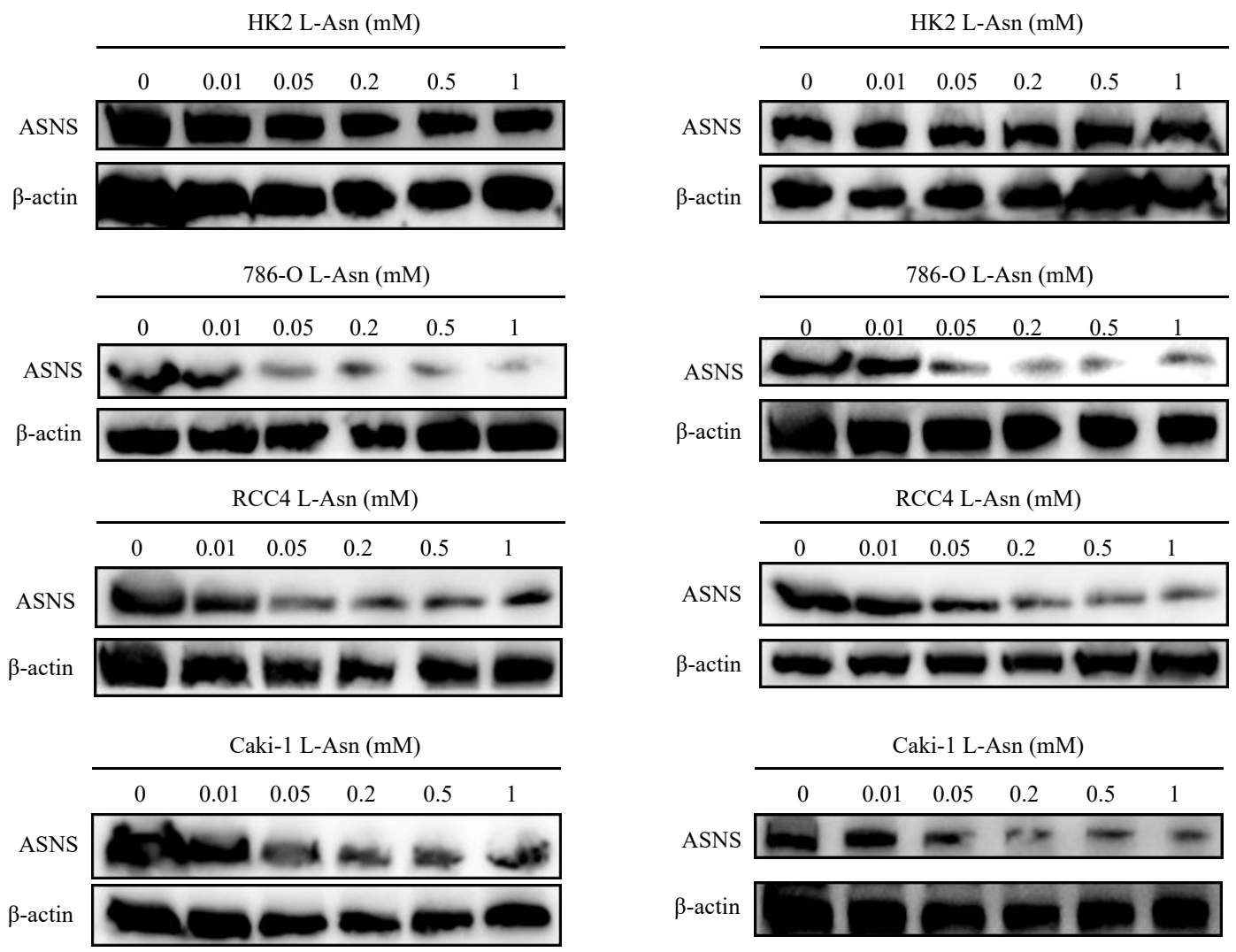


Fig.3A repeat 2, 3



Supplemental Figure 7

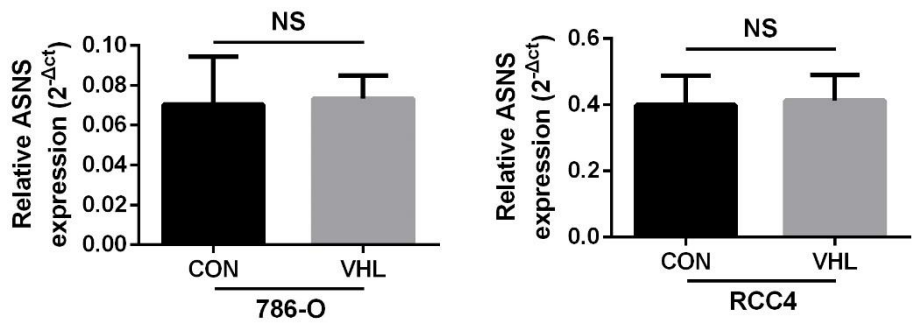


Fig.4B repeat 2, 3

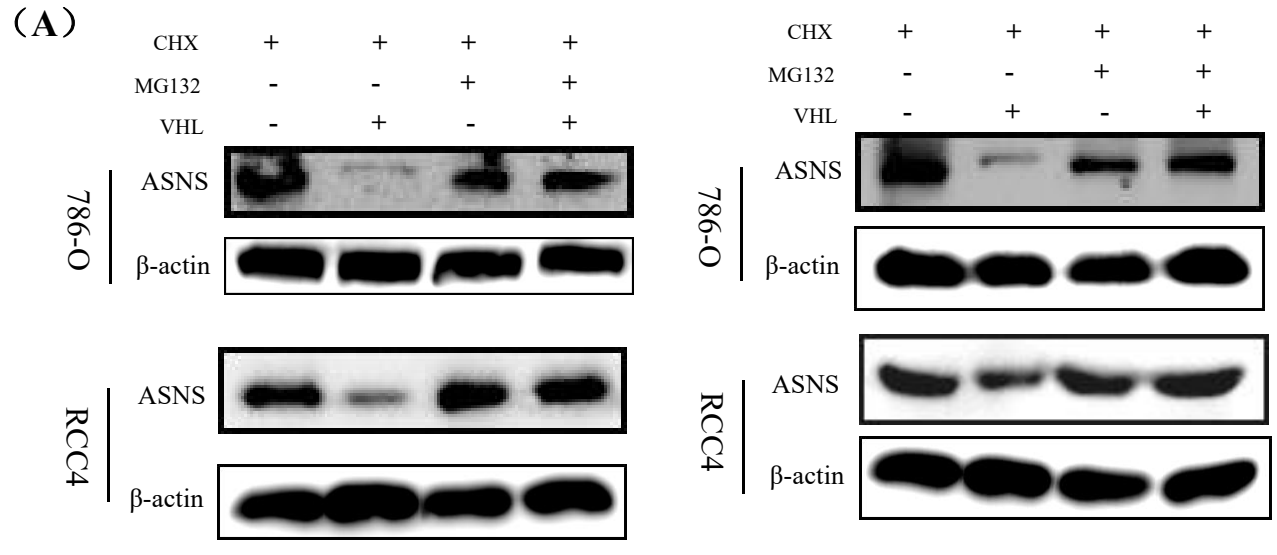


Fig.4C repeat 2, 3

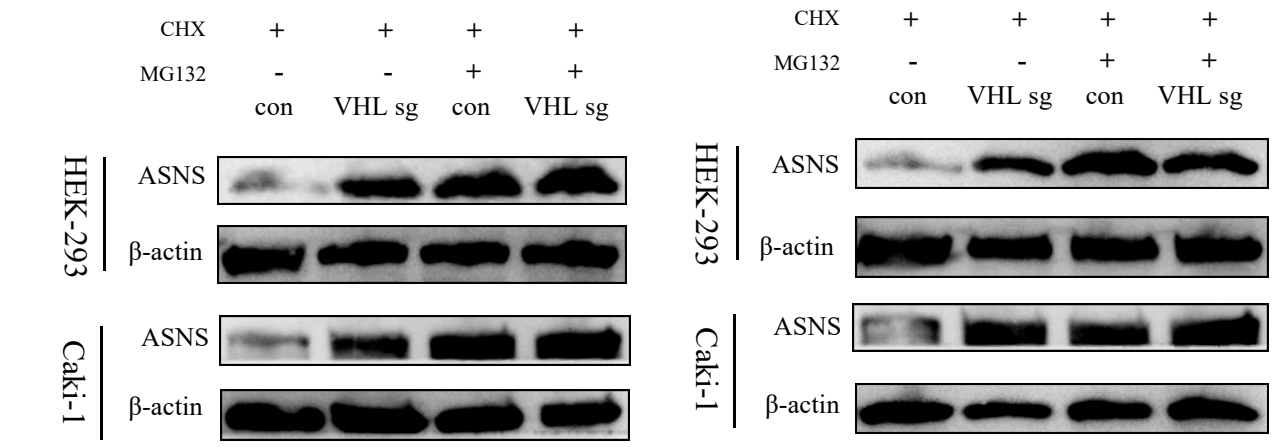


Fig.7I repeat 2, 3

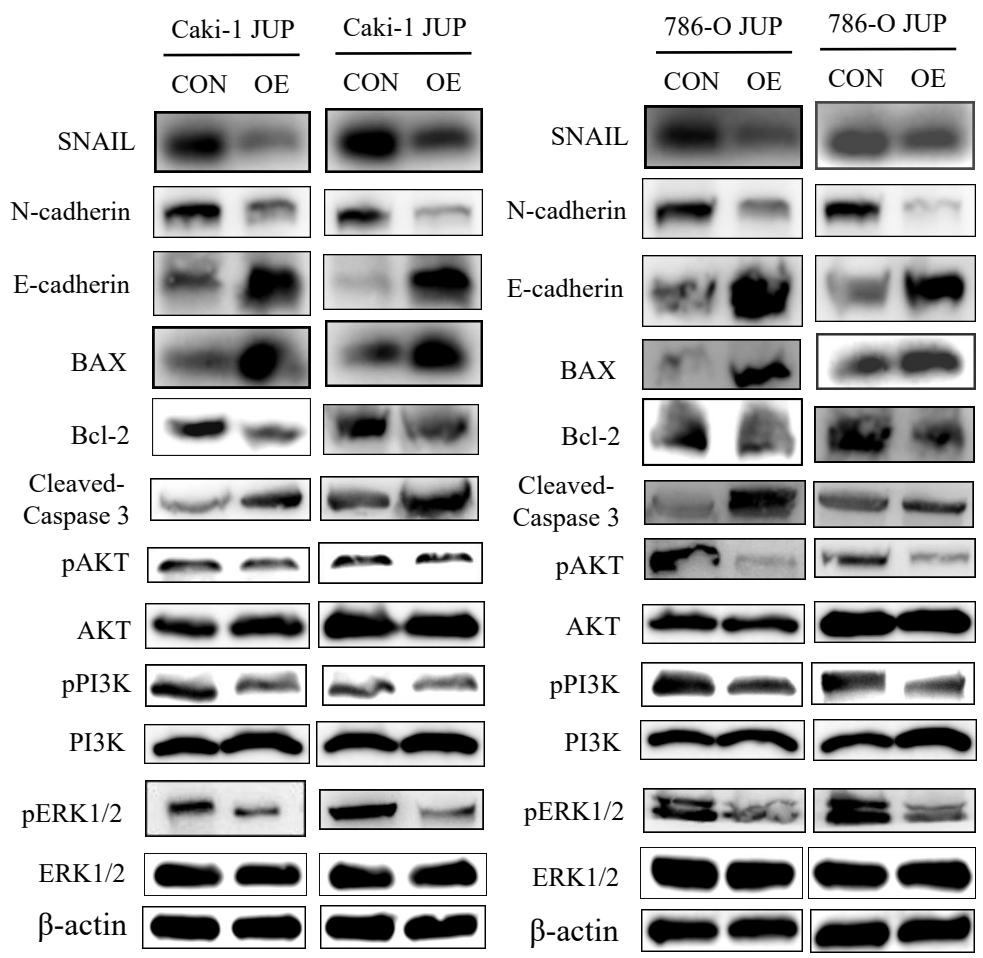
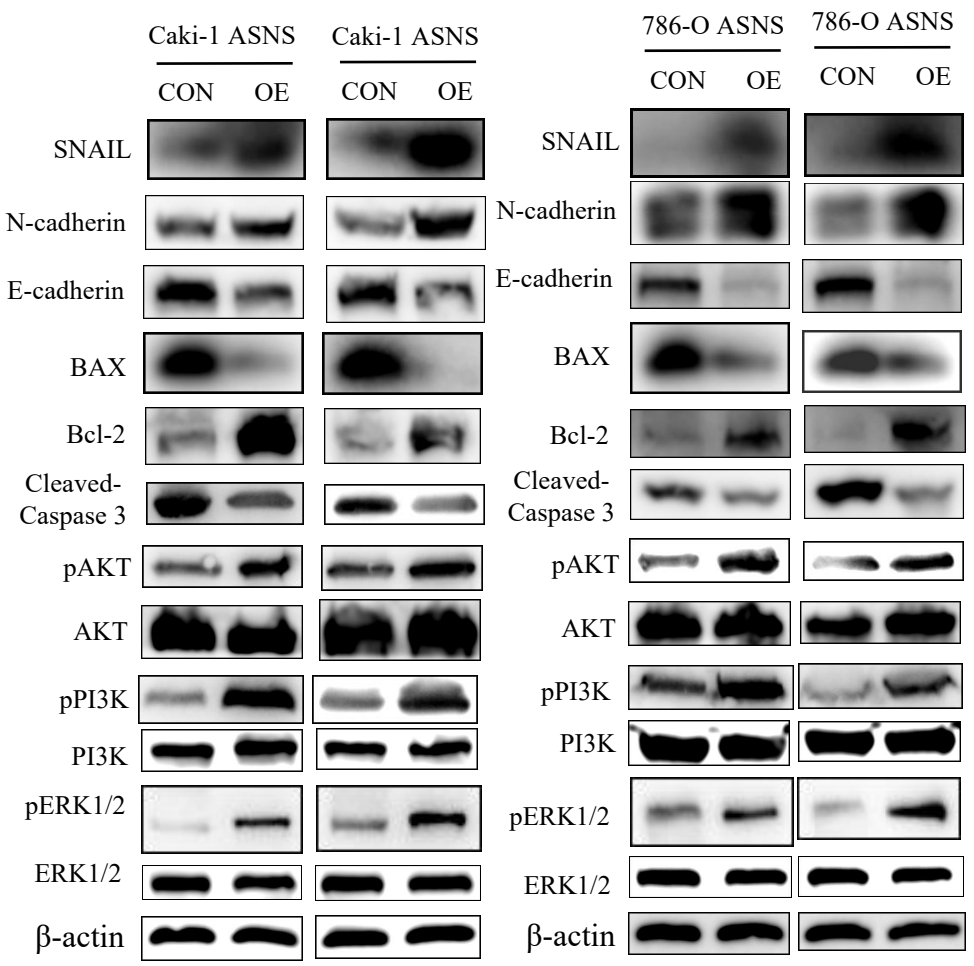



Fig.7J repeat 2, 3