

# 美迪西STAT3新药研发服务

S<sub>S</sub>T<sub>A</sub>ST3

STAT3
STAT3
+ IND

# STAT3

(signal transdu**Sr A T C 3** vator of transcription, STAT)

STAT3

STAT3

STAT3

STAT3

genes containing GAS/ISRE promoter element

STATS

\*anti-proliferative
-pro-apoptotic
-anti-tumor immunity
-anti-angiogenic
-pro-metastatic

STATS

\*INCREASE Promoter element

\*pro-angiogenic
-pro-metastatic

STATS

[1]

**STAT** 

### STAT3

STAT

STAT1 STAT2 STAT3 STAT4 STAT5A STAT5B STAT6 STAT3

С

DNA STAT3

STAT3

17

JAK

JAK

770



(NTD) STAT (CCD) STAT3

DNA (DBD) DNA

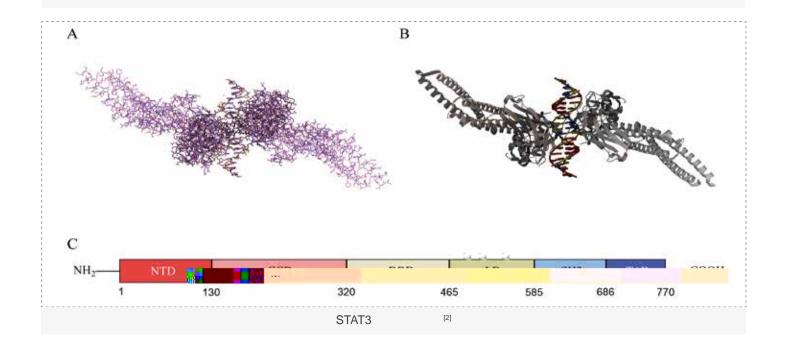
(LD) DBD SH2 DNA

2 (SH2) STAT SRC

STAT3

STAT3

(TAD)



## STAT3

JAK/STAT

(IL)

IL-6

TME IL-6

IL-6

TME

IL-6

IL-6/JAK/STAT3

IL-6 JAK/STAT3

JAK1 JAK2 JAK3 TYK2 JAK3

(JH1-7) JH1 JH2 SH2 **FERM** IL-6 IL-6 IL-6 IL-6/IL-6R/gp130 gp130 JAK JAK gp130 STAT3 STAT3 gp130 JAK STAT3 705 STAT3

Extracellular fluid IL-6/sIL-6Ra sgp130 IL-6/IL-6Ra/gp130 IL-6 Growth factor EGFR IL-6Ra CTGFR slL-6Ra miR-451a **PDGFR** gp130 Cytoplasm Tomminus. miR-133a IL-6R mRNA miR-218 JAK JAK STA miR-181d miR-124 STAT3 miR-519d STAT3 STAT3 ZNF596 **STAT3** miR-221 LINC00115 Tyrosine miR-222 phosphatase miR-147 miR-30 Nucleus STAT3 miR-551-3p **ETAT2** Target gene transcription

Vimentin

VEGF

TNF-α

[2]

IL-6/JAK/STAT3

# STAT3

STAT3 STAT3

STAT3

STAT3

NCT Number	Inhibitors	Cancer Types	Targets	Phase
NCT03382340	IMX-110	Solid Tumor *	STAT3/NF-kB	I/II
NCT02983578	AZD9150	PC, NSCLC, CRC	STAT3	II
NCT02993731	Napabucasin	PC	STAT3	Ш

#### **❖** STAT3-HDAC

histone deacetylase HDAC

HDAC HDACi

HDACi

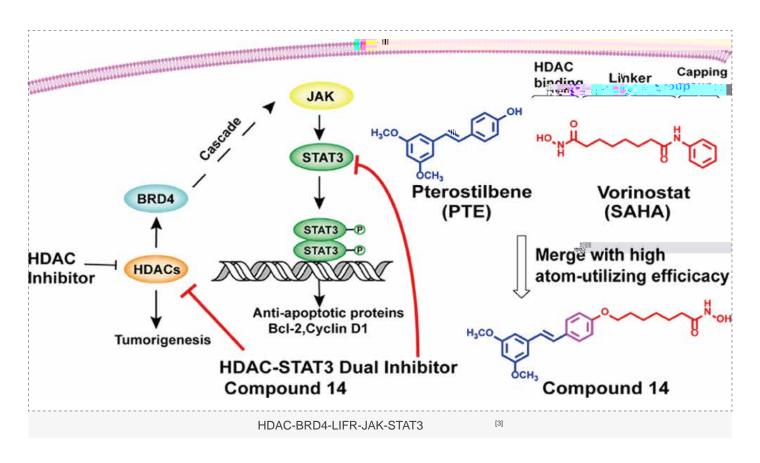
**HDACi** 

HDAC STAT3 HDAC HDACi STAT3-HDAC

BRD4-HDAC JAK1-HDAC STAT3-HDAC

STAT3 (Pterostilbene PTE) PTE

HDAC SAHA PTE STAT3-HDAC



Compound 14 STAT3  $K_D=33 \text{ nM}$ HDAC IC<sub>50</sub> 23.15 nM Compound 14 MDA-MB-231 IC50 HCT116 Compound 14  $IC_{50}$ Compound 14 Compound 14 15 mg/kg 54% 62% Compound 14 53% 30 mg/kg 64% Compound 14 Compound 14 SD (PK) Compound 14 PΚ Compound 14 2 mg/kg 1.65 L/kg (CI) 63.89 mL/min/kg  $T_{1/2}$  0.47h Compound 14 20 mg/kg 5.81% 0.88h  $T_{1/2}$ 

