

MEDICILON

美迪西STAT3新药研发服务

STAT3

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STAT3 (Signal transducer and activator of transcription, STAT)

STAT3

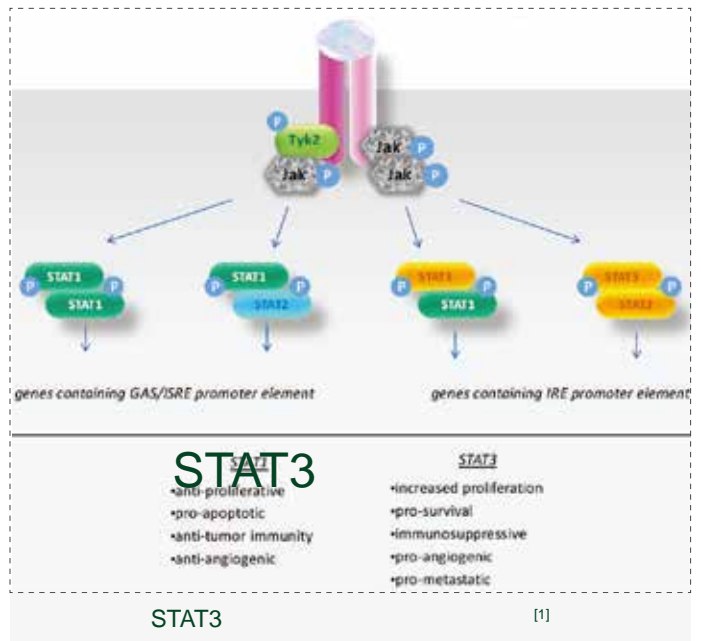
STAT3

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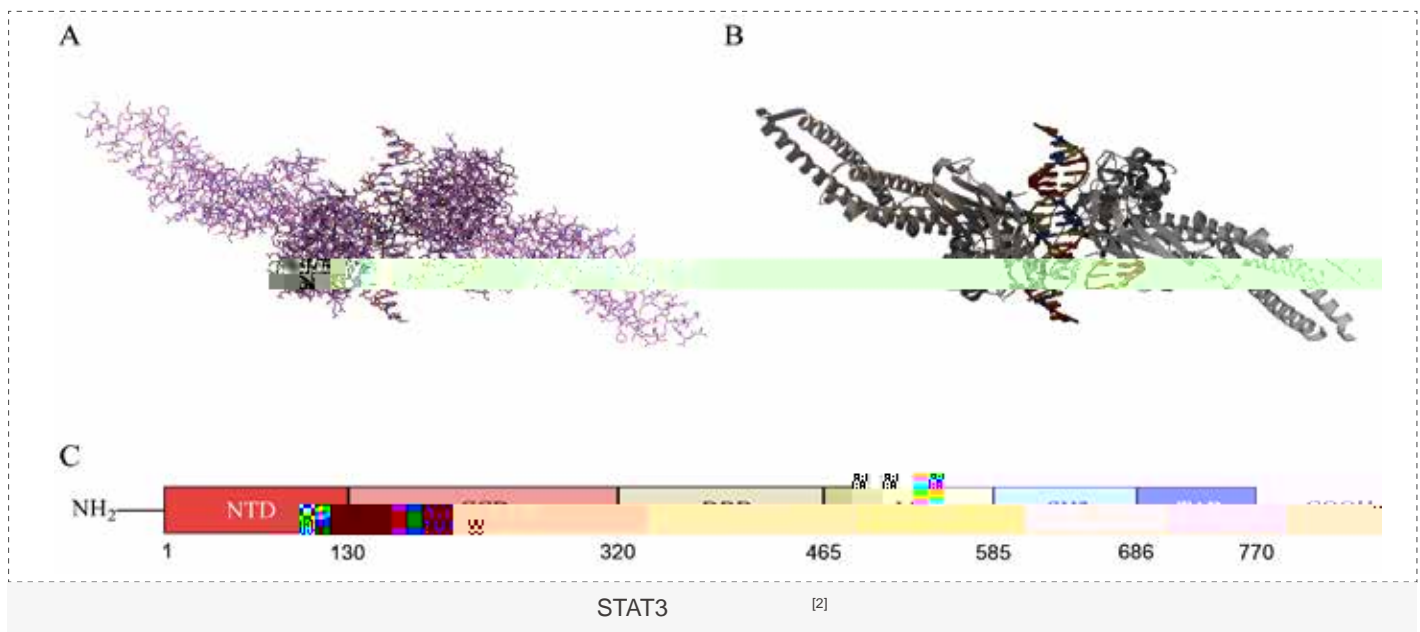


STAT3

| | | | | | | | | | |
|-------|-------|-------|-------|-------|-------|--------|--------|-------|-------|
| STAT | | STAT1 | STAT2 | STAT3 | STAT4 | STAT5A | STAT5B | STAT6 | STAT3 |
| | STAT3 | STAT3 | STAT3 | | STAT3 | STAT3 | C | 55 | STAT3 |
| STAT3 | | DNA | | STAT3 | | | | STAT3 | 17 |
| | | 770 | | | | | | | |



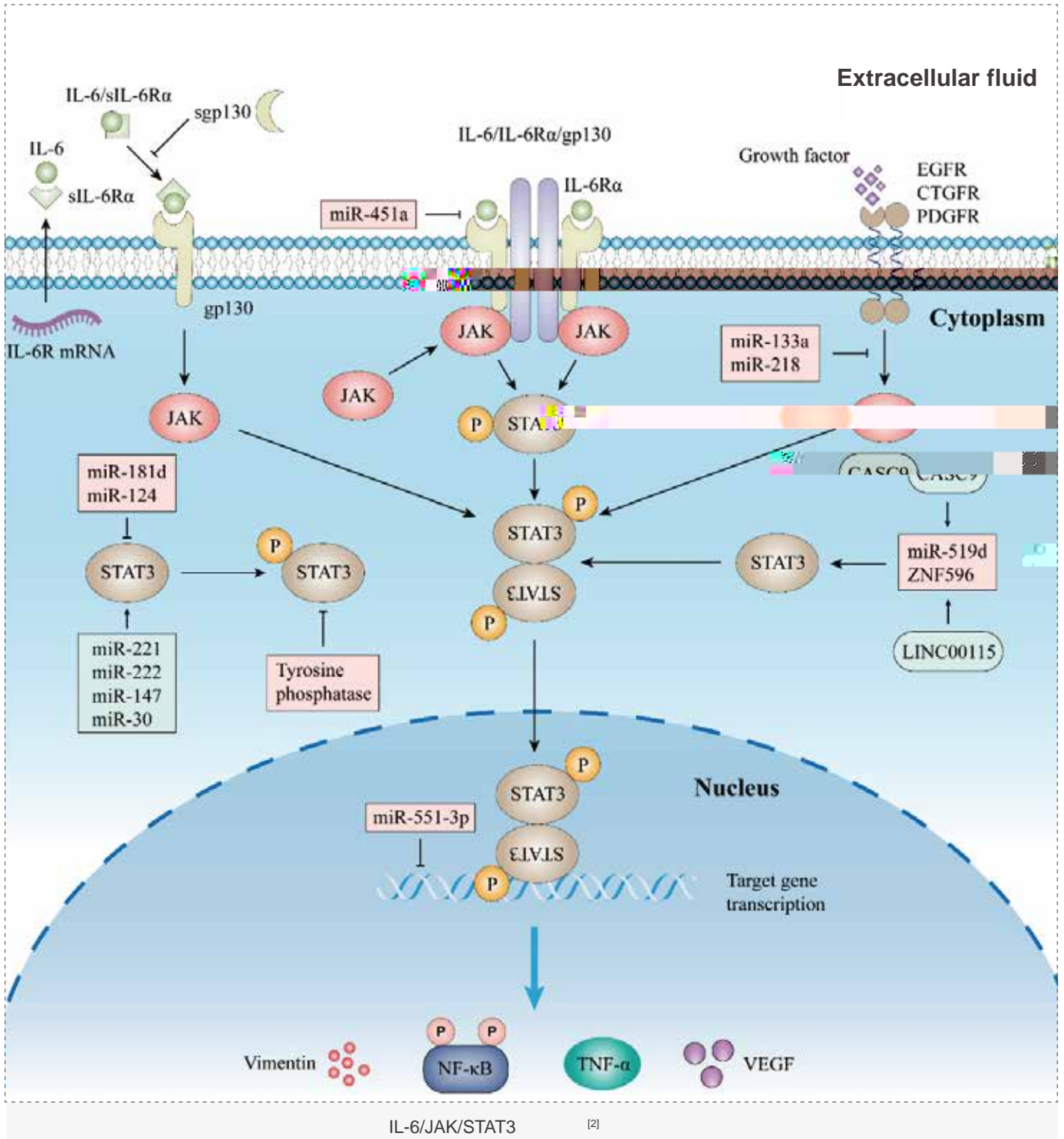
| | | | | | | | | | |
|-------|-------|-------|-------|------|--|-------|--|--|--|
| ● N | (NTD) | STAT | | | | | | | |
| ● | (CCD) | | STAT3 | | | | | | |
| ● DNA | (DBD) | | | DNA | | | | | |
| ● | (LD) | DBD | SH2 | DNA | | | | | |
| ● SRC | 2 | (SH2) | | STAT | | STAT3 | | | |
| | | STAT3 | | | | | | | |
| ● | (TAD) | | | | | | | | |



STAT3

| | | | | | | | | | |
|----------------|------|------|--|------|-----------|--|--|--|-----|
| JAK/STAT | | | | | | | | | |
| (IL) | | IL-6 | | TME | IL-6 | | | | |
| | | IL-6 | | | TME | | | | |
| IL-6 | | | | IL-6 | JAK/STAT3 | | | | JAK |
| IL-6/JAK/STAT3 | | | | | | | | | JAK |
| JAK1 JAK2 JAK3 | TYK2 | JAK3 | | | | | | | JAK |

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



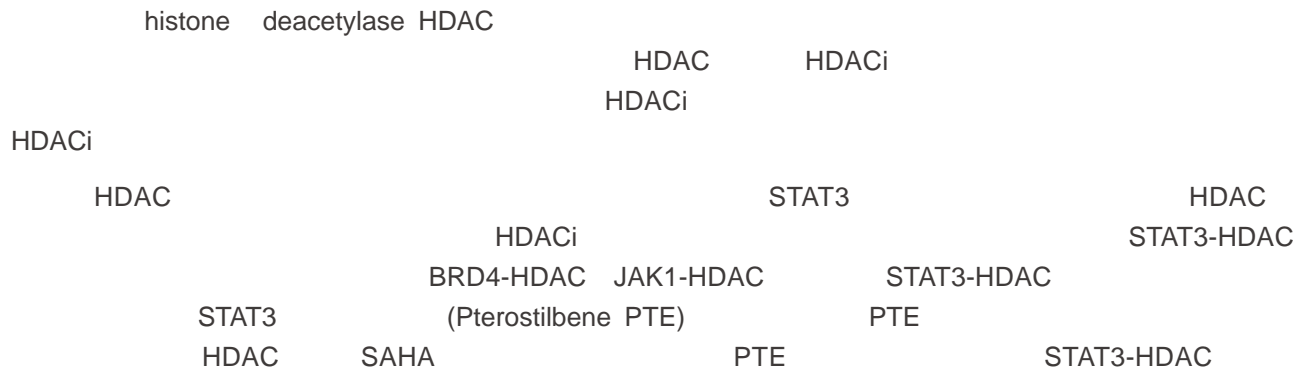
STAT3

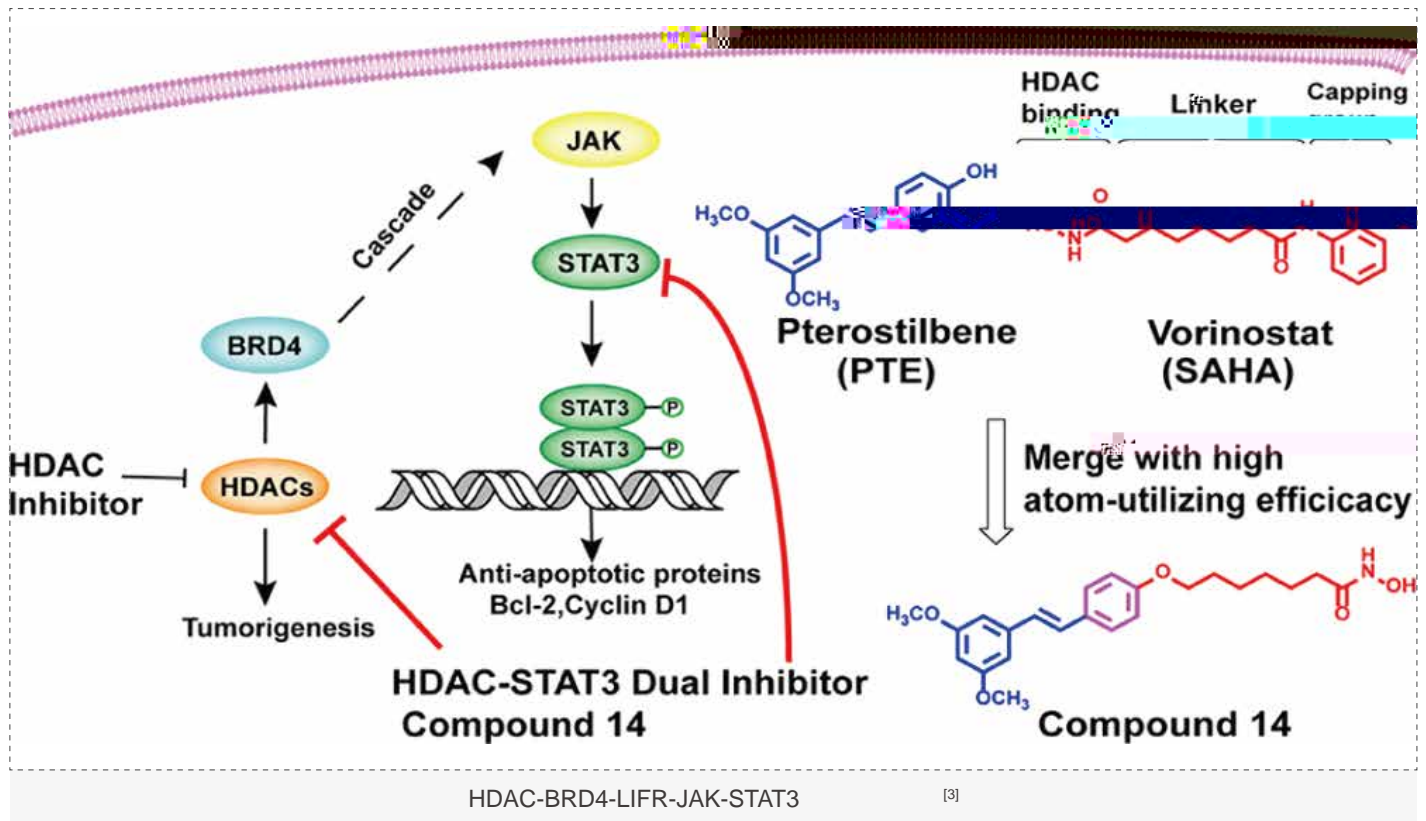
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| NCT Number | HDAC Inhibitors | Cancer Types | Targets | Phase |
|-------------|-----------------|-------------------|-------------|-------|
| NCT02382340 | IMY 110 | Colorectal Cancer | STAT3, HDAC | I/II |
| NCT02989578 | AZD9150 | PC, NSCLC, CRC | STAT3 | |
| NCT02992721 | Nonohydroxy | PC | STAT3 | |

STAT3 [2]

STAT3-HDAC





Compound 14
 HDAC IC₅₀ 23.15 nM
 HCT116 IC₅₀=1.07 μM
 Compound 14
 53% 30 mg/kg
 Compound 14
 64%
 Compound 14
 62%
 Compound 14
 54%
 Compound 14
 62%
 Compound 14
 15 mg/kg
 Compound 14
 54%
 Compound 14 SD
 Compound 14 2 mg/kg
 T_{1/2} 0.47h
 Compound 14 20 mg/kg
 Compound 14
 5.81%
 T_{1/2} 0.88h
 STAT3
 K_D=33 nM
 MDA-MB-231 IC₅₀=0.78 μM
 (PK)
 V_{ss} 1.65 L/kg
 F

