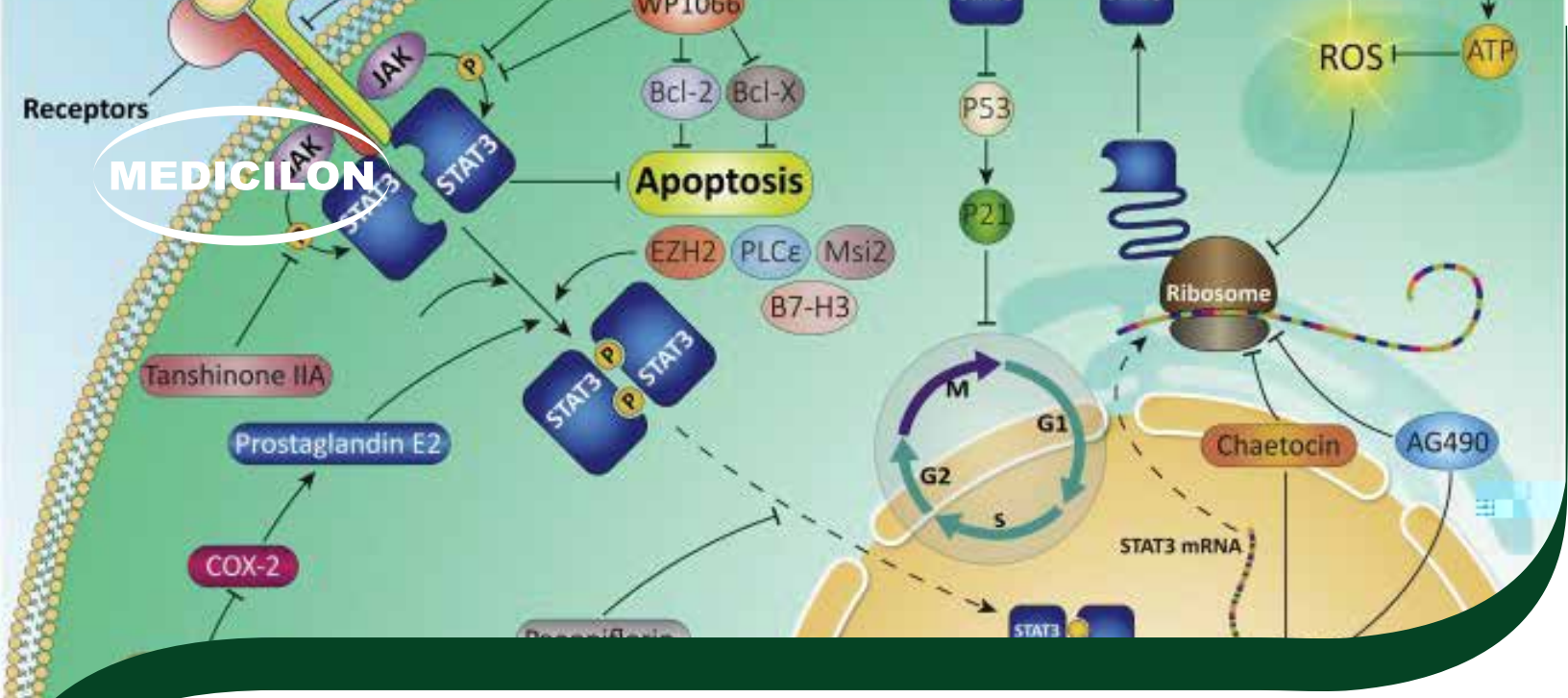
Receptors
JAK
STAT3
WP1066
Bcl-2
Bcl-X
Apoptosis
EZH2
PLCε
Msi2
B7-H3
Tanshinone IIA
Prostaglandin E2
COX-2
P53
P21
ROS
ATP
Ribosome
M
G1
G2
S
Chaetocin
AG490
STAT3 mRNA

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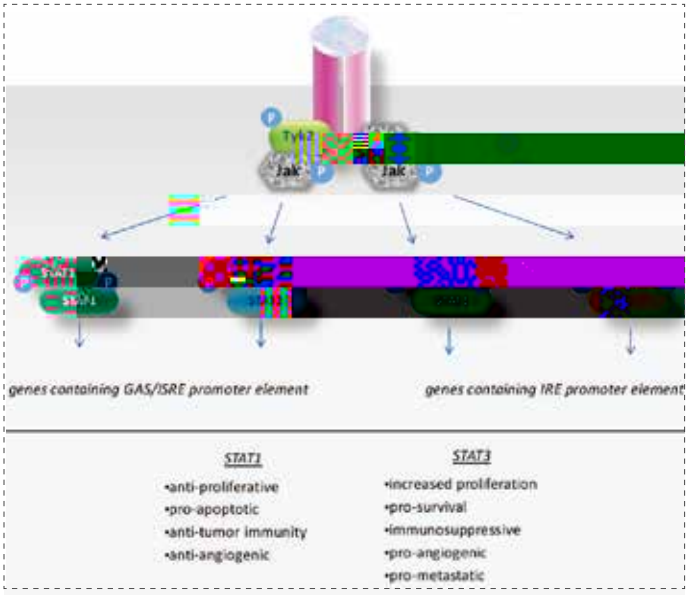
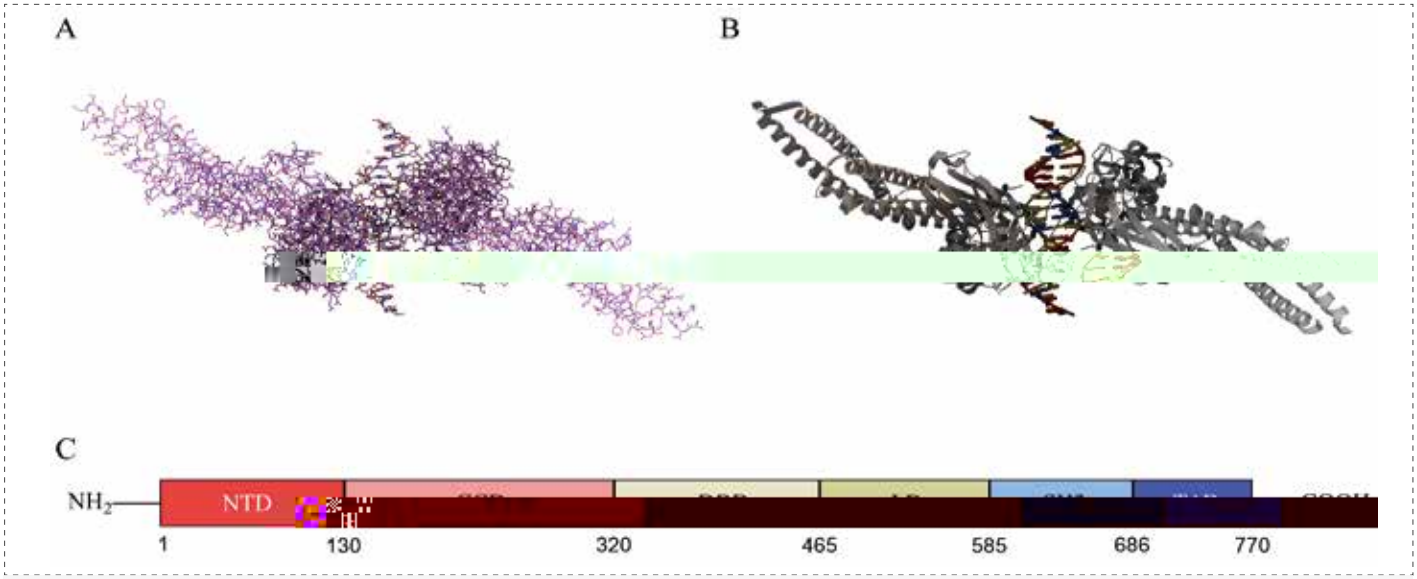
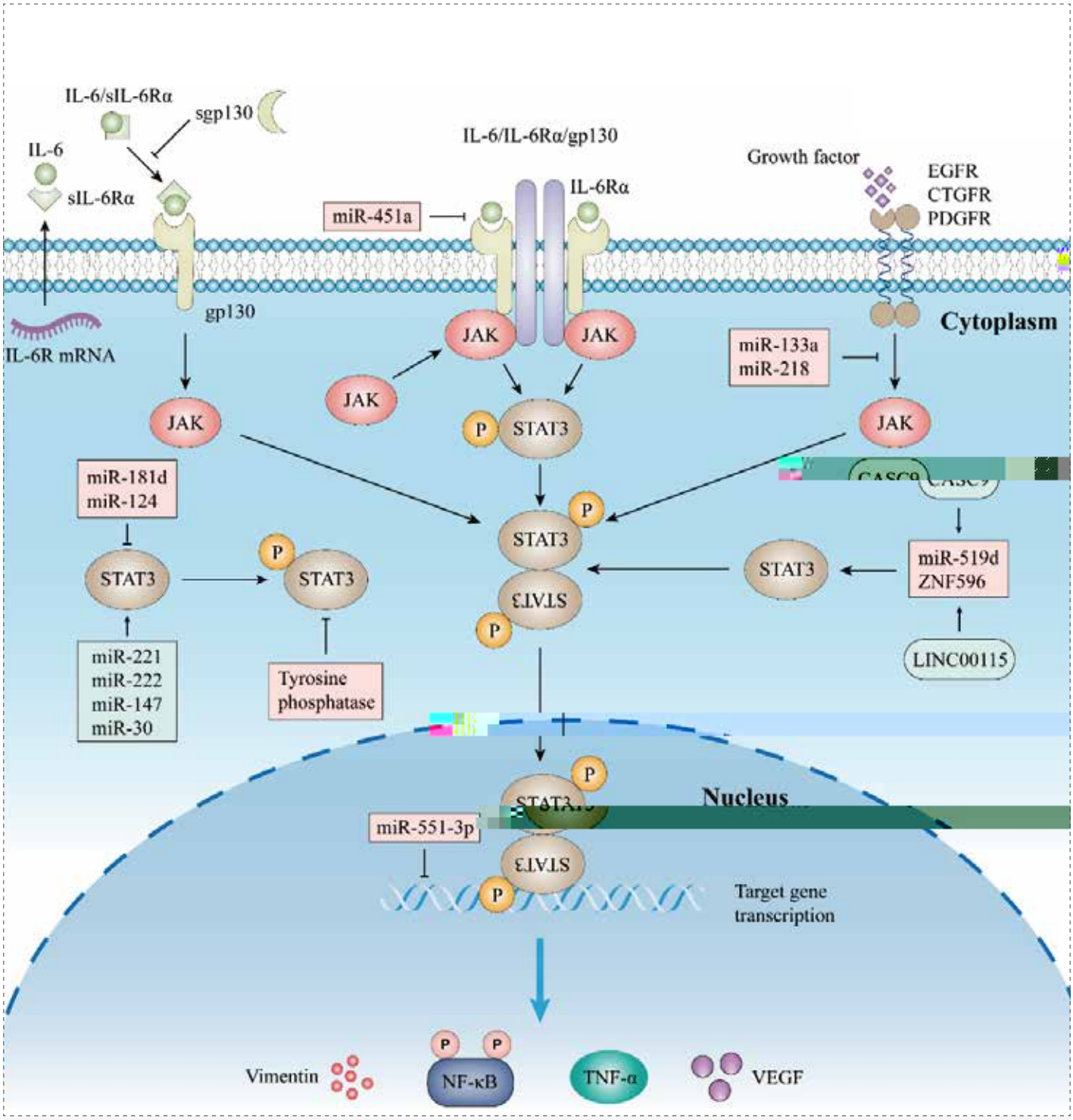

genes containing GAS/ISRE promoter element
genes containing IRE promoter element
STAT1
•anti-proliferative
•pro-apoptotic
•anti-tumor immunity
•anti-angiogenic
STAT3
•increased proliferation
•pro-survival
•immunosuppressive
•pro-angiogenic
•pro-metastatic

STAT3α STAT3β STAT3α STAT3β STAT3α STAT3β
STAT3α

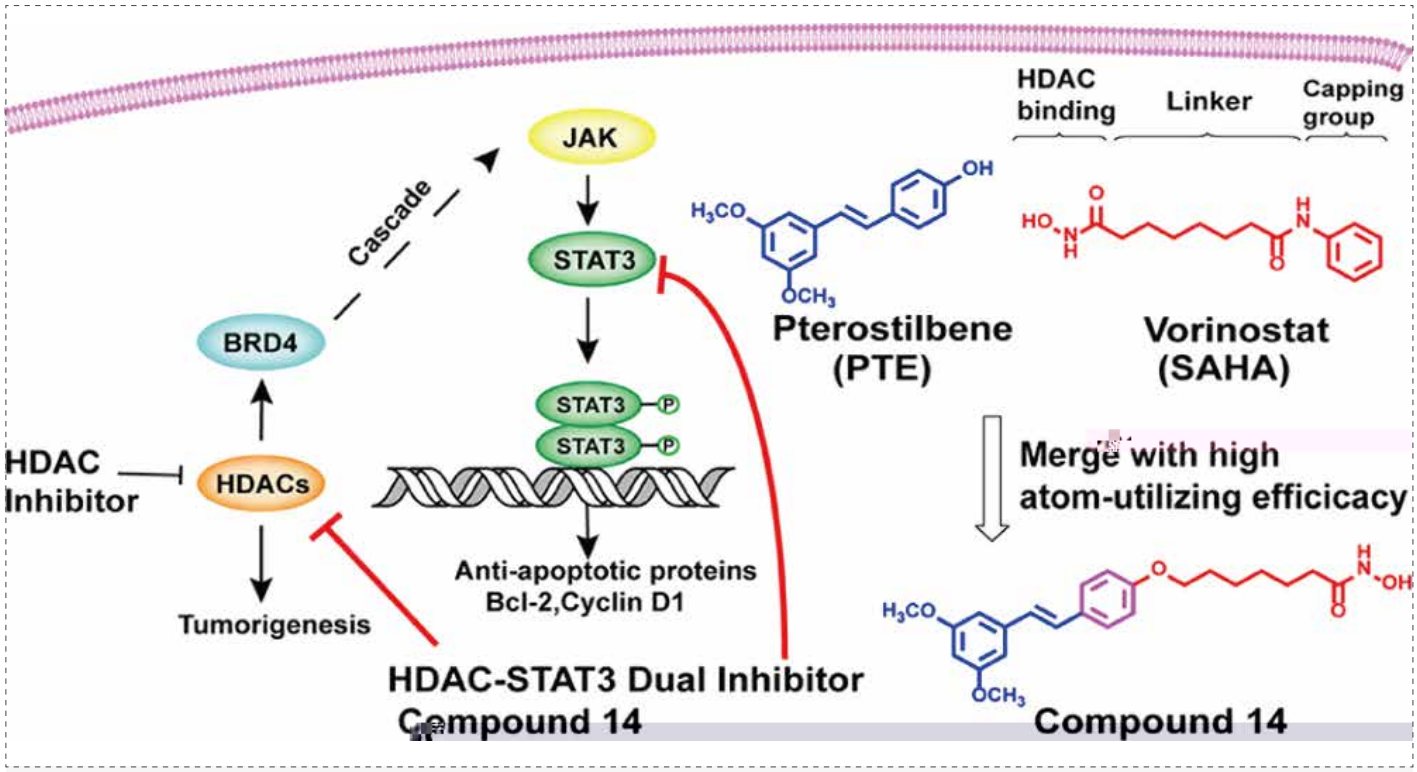


α (IL-6Rα)


IL-6/sIL-6Rα
sgp130
IL-6
sIL-6Rα
gp130
IL-6R mRNA
IL-6/IL-6Rα/gp130
IL-6Rα
miR-451a
Growth factor
EGFR
CTGFR
PDGFR
Cytoplasm
JAK
JAK
JAK
JAK
JAK
P
STAT3
miR-133a
miR-218
miR-181d
miR-124
STAT3
STAT3
STAT3
STAT3
STAT3
miR-519d
ZNF596
LINC00115
miR-221
miR-222
miR-147
miR-30
Tyrosine
phosphatase
Nucleus
miR-551-3p
Target gene
transcription
Vimentin
NF-κB
TNF-α
VEGF

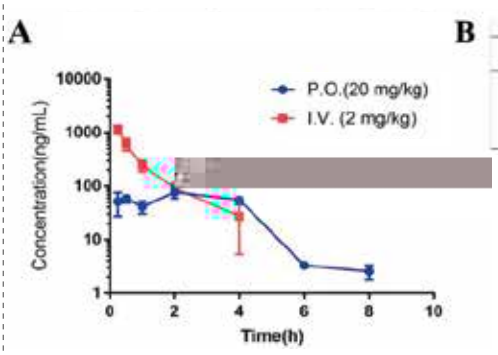
STAT3 Inhibitors	Cancer Types	Targets	Phase	NCT Number
IMX-110	Solid Tumor*	STAT3 /NF-kB	I/II	NCT03382340
AZD9150	PC, NSCLC, CRC	STAT3	II	NCT0399355
Napabucasin	PC	STAT3	III	NCT0290037

[redacted]



=0.78 μM

=1.07 μM



B

Animal code	Route of Dosing	Dose Level mg/kg	$T_{1/2}$ h	T_{max} h	C_{max} ng/mL	$AUC_{(0-t)}$ h*ng/mL	$AUC_{(0-\infty)}$ h*ng/mL	$MRT_{(0-t)}$ h	$MRT_{(0-\infty)}$ h	C_0 ng/mL	V_{ss_obs} L/kg	V_{z_obs} L/kg	Cl_obs mL/min/kg
101	IV	2	0.59	0.083	1279.29	617.12	659.48	0.41	0.50	1660.90	1.71	2.59	50.54
102	IV	2	0.55	0.083	1303.09	514.48	536.51	0.32	0.43	1868.68	1.59	2.98	62.13
103	IV	2	0.27	0.083	945.00	419.55	422.04	0.34	0.35	1369.83	1.66	1.87	78.98
Mean			**0.47**	**0.08**	**1175.79**	**517.18**	**539.34**	**0.36**	**0.45**	**1633.16**	**1.65**	**2.48**	**63.89**
SD			**0.17**	**0.00**	**200.23**	**98.61**	**118.75**	**0.04**	**0.11**	**250.58**	**0.09**	**0.56**	**14.30**

C

Group	Route of Dosing	Dose Level mg/kg	$T_{1/2}$ h	T_{max} h	C_{max} ng/mL	$AUC_{(0-t)}$ h*ng/mL	$AUC_{(0-\infty)}$ h*ng/mL	$MRT_{(0-t)}$ h	$MRT_{(0-\infty)}$ h	F %
201	PO	20	0.89	0.3	78.64	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
202	PO	20	0.90	2.0	67.77	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
203	PO	20	0.85	2.0	98.98	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Mean			**0.88**	**1.42**	**81.80**	**300.69**	**304.11**	**2.55**	**2.62**	**5.81**
SD			**0.03**	**1.01**	**15.84**	**27.83**	**27.12**	**0.24**	**0.25**	**0.54**