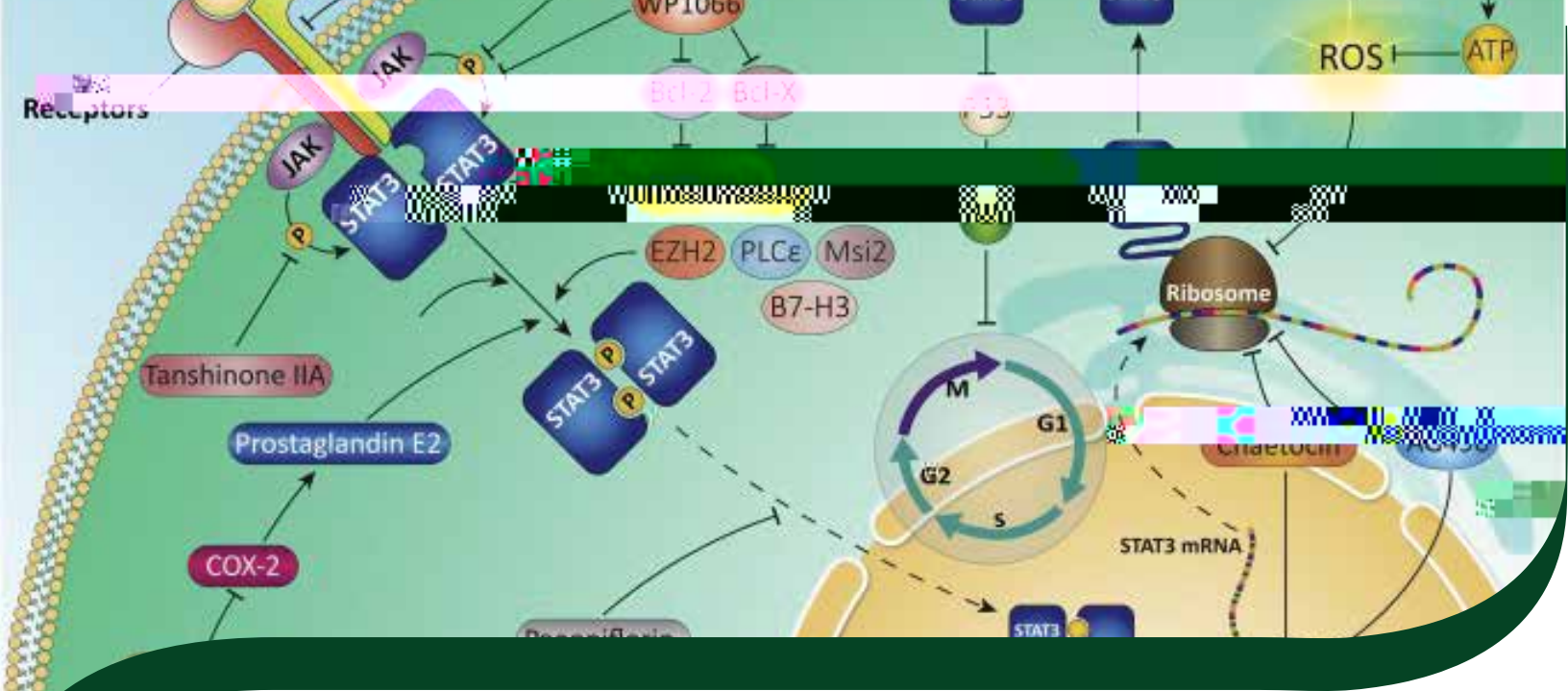


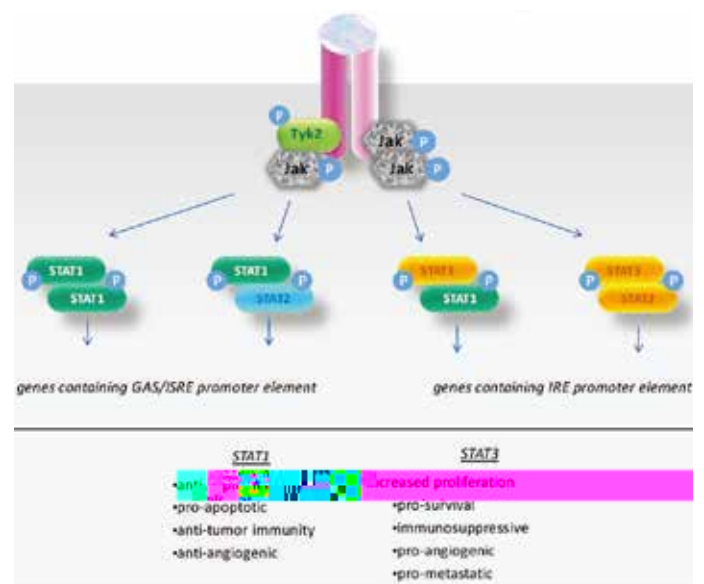


STAT3

STAT3

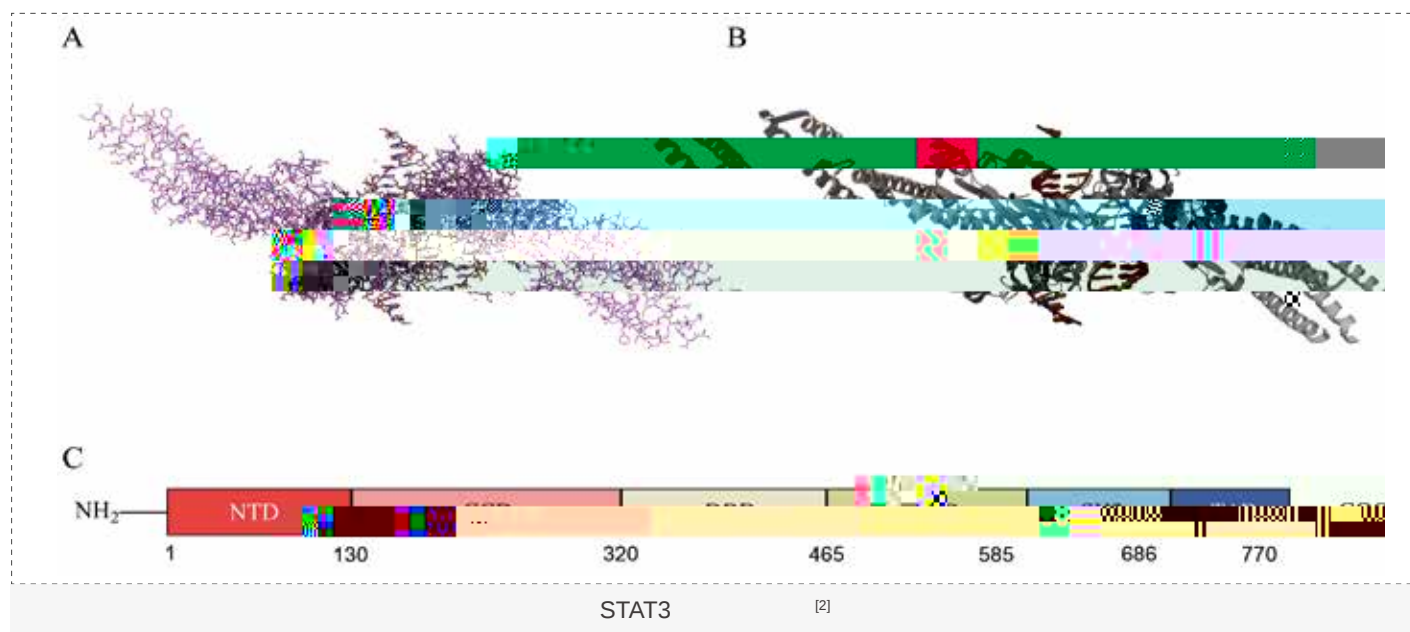
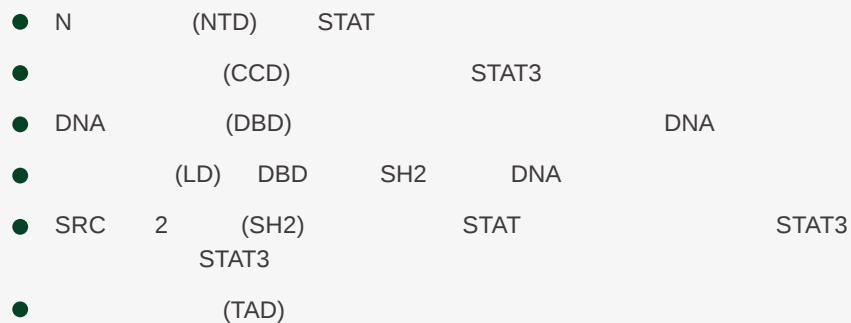
STAT3

STAT3



STAT3

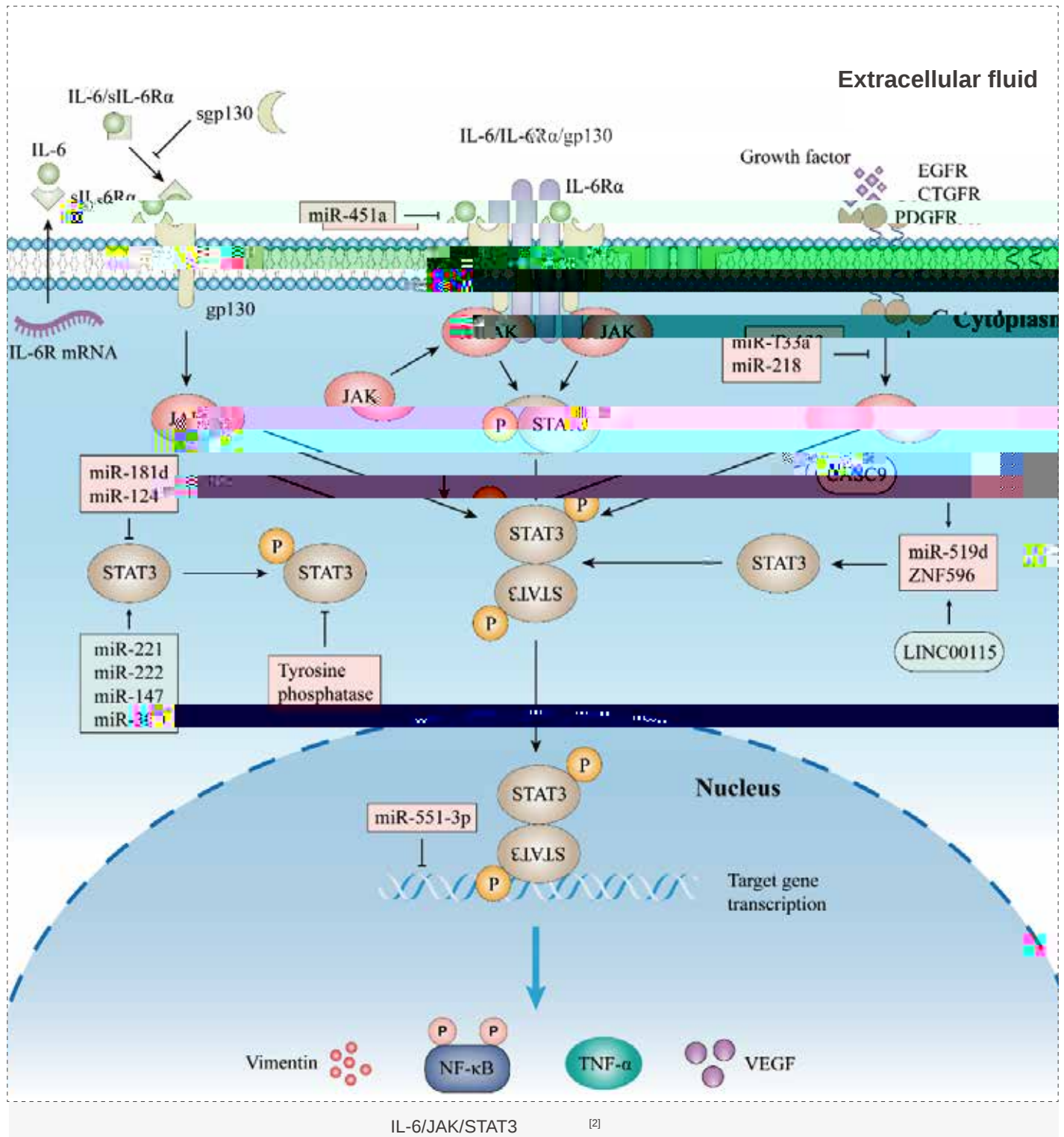
STAT	STAT1	STAT2	STAT3	STAT4	STAT5A	STAT5B	STAT6	STAT3
STAT3α	STAT3β	STAT3α	STAT3β	STAT3α	C	55	STAT3β	17
STAT3α	DNA	STAT3	STAT3					
	770							



STAT3

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

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



STAT3

🏆 STAT3-HDAC

histone deacetylase HDAC

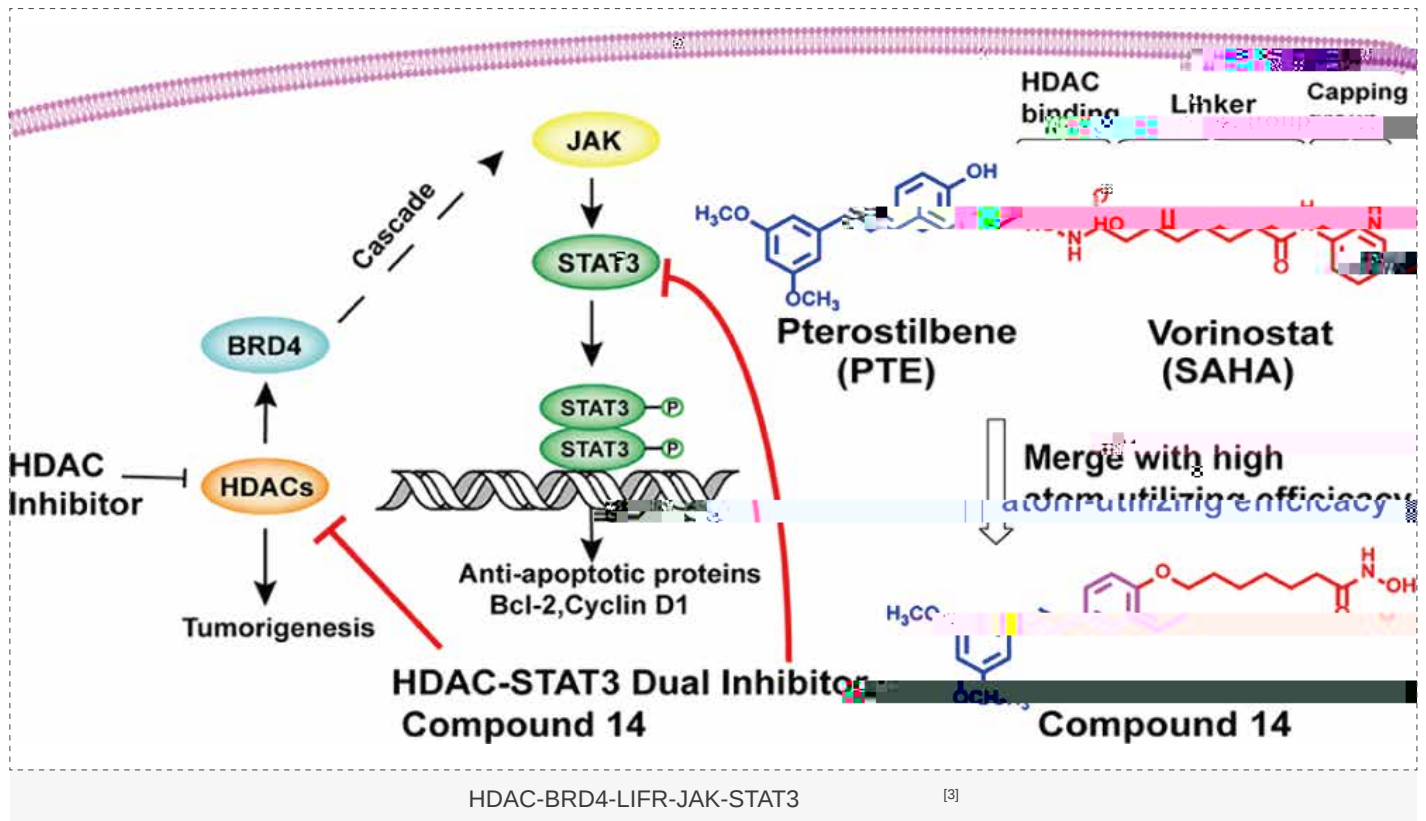
HDAC HDACi HDACi

HDACi HDAC

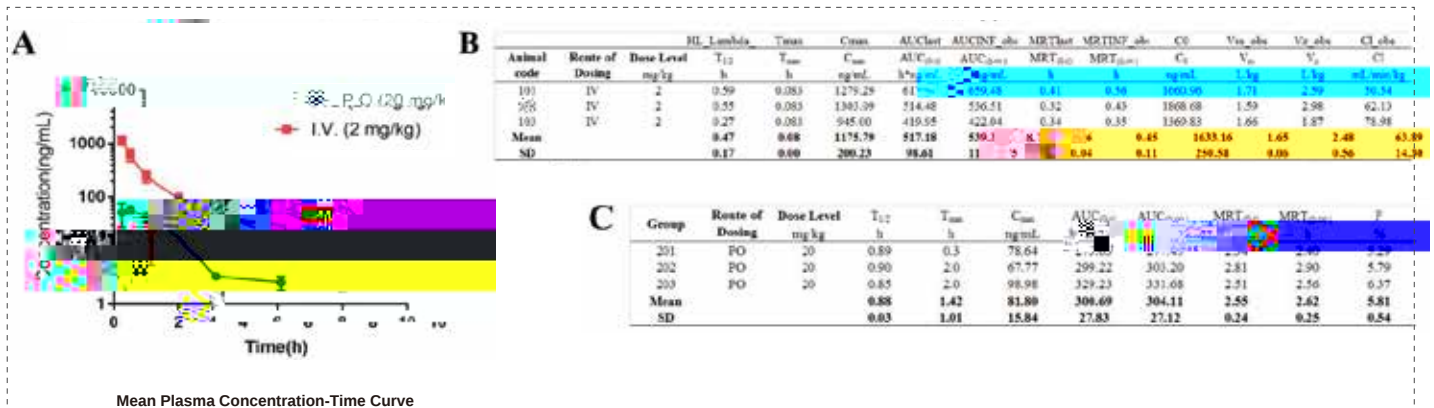
HDACi STAT3 HDAC

BRD4-HDAC JAK1-HDAC STAT3-HDAC

S0 Td[37700B4AR-11 056F5001 1 J0.008 T



Compound 14	HDAC	IC ₅₀	23.15 nM	Compound 14	STAT3	K _D =33 nM	
HCT116	IC ₅₀	1.07 μM	Compound 14	MDA-MB-231	IC ₅₀	0.78 μM	
Compound 14			Compound 14				
53%	30 mg/kg		64%	Compound 14	15 mg/kg		54%
Compound 14			62%	Compound 14			
Compound 14				Compound 14			
Compound 14	PK		Compound 14	SD			(PK)
(CI)	63.89 mL/min/kg		Compound 14	2 mg/kg	V _{ss}		1.65 L/kg
5.81%	T _{1/2}	0.88h	T _{1/2}	0.47h	Compound 14	20 mg/kg	F



Pharmacokinetics of Compound 14 in SD rats^[3]

YY201

2023 7

STAT3

—YY201

NMPA

AI

STAT3

"YY201"

First-in-class

STAT3

STAT3

Tyr705

Ser727

STAT3

YY201 STAT3

1-10

1-10 nM

YY201

STAT3

STAT3

STAT3

STAT3

PROTAC

STAT3-PROTAC

STAT3

STAT3

STAT3

[1]Courtney Nicholas and Gregory B. Lesinski. The Jak-STAT Signal Transduction Pathway in Melanoma. Breakthroughs in Melanoma Research.

[2]Xin Li, et al. STAT3 Inhibitors: A Novel Insight for Anticancer Therapy of Pancreatic Cancer. Biomolecules. 2022 Oct 9;12(10):1450. doi: 10.3390/biom12101450.

[3]Yuhao Ren, et al. Discovery of STAT3 and Histone Deacetylase (HDAC) Dual-Pathway Inhibitors for the Treatment of Solid Cancer. J Med Chem. 2021 Jun 10;64(11):7468-7482. doi: 10.1021/acs.jmedchem.1c00136.

[4]Sailan Zou, et al. Targeting STAT3 in Cancer Immunotherapy. Mol Cancer. 2020 Sep 24;19(1):145.DOI: 10.1186/s12943-020-01258-7.