

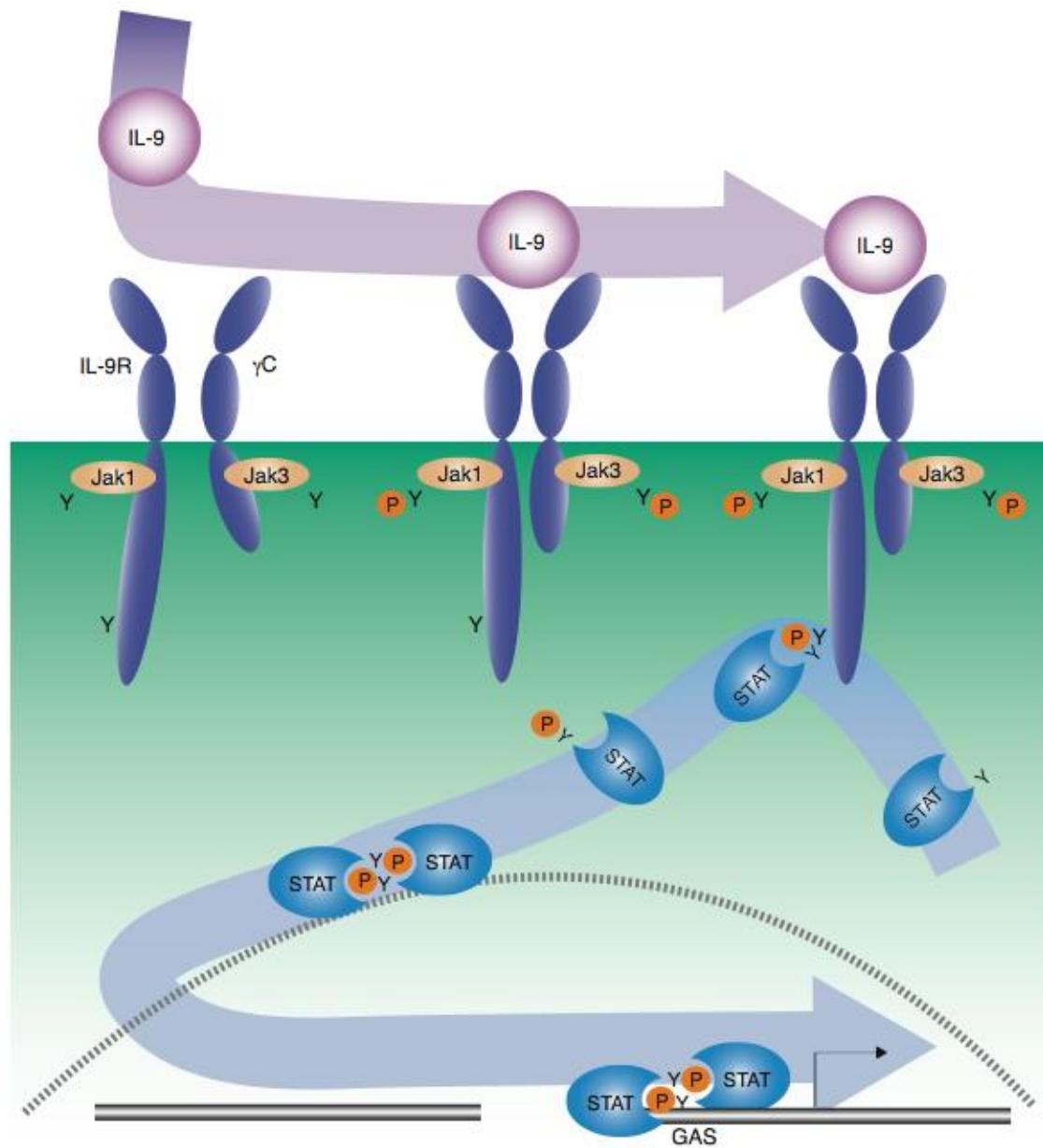
JAK mutations resistant to ATP-competitive JAK inhibitors

L. Knoops

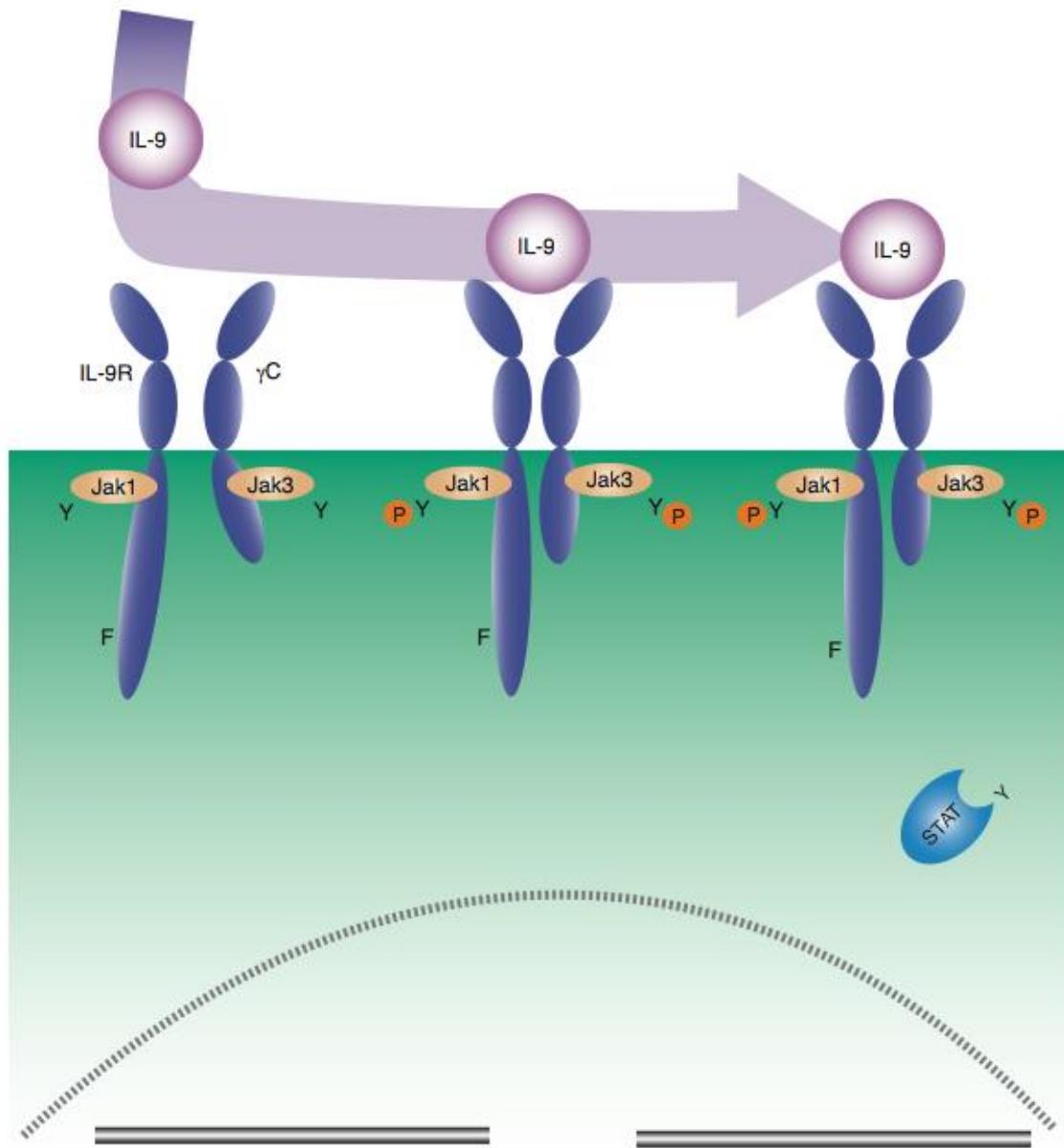


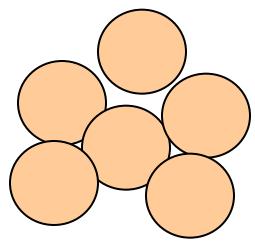
CLINIQUES UNIVERSITAIRES SAINT-LUC

IL-9 R signal transduction

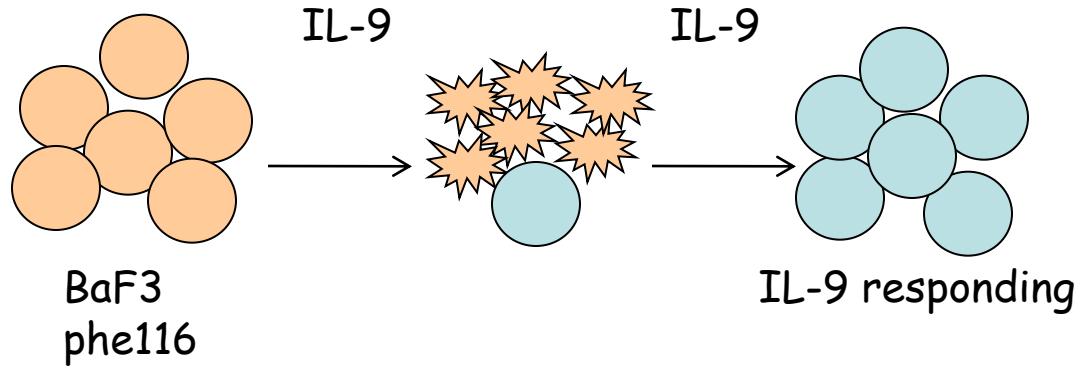


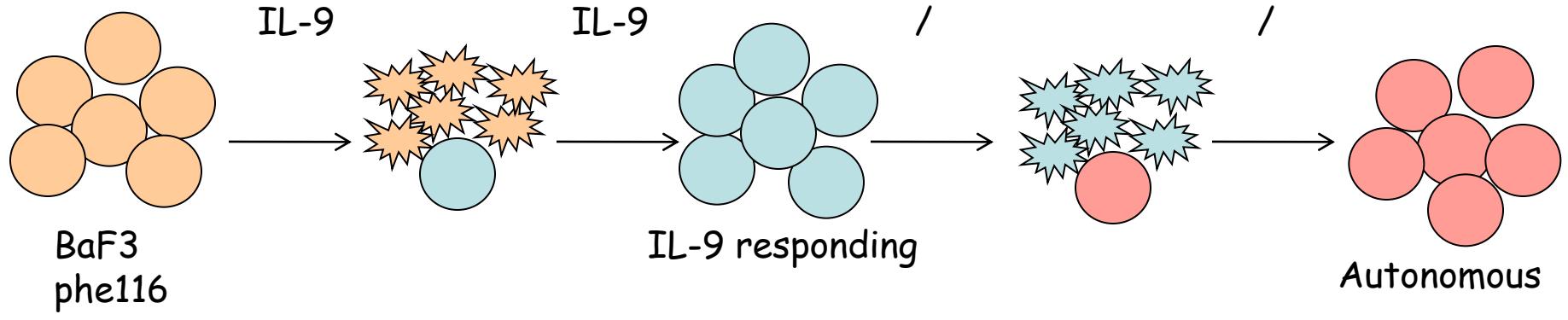
IL-9 R phe116 receptor



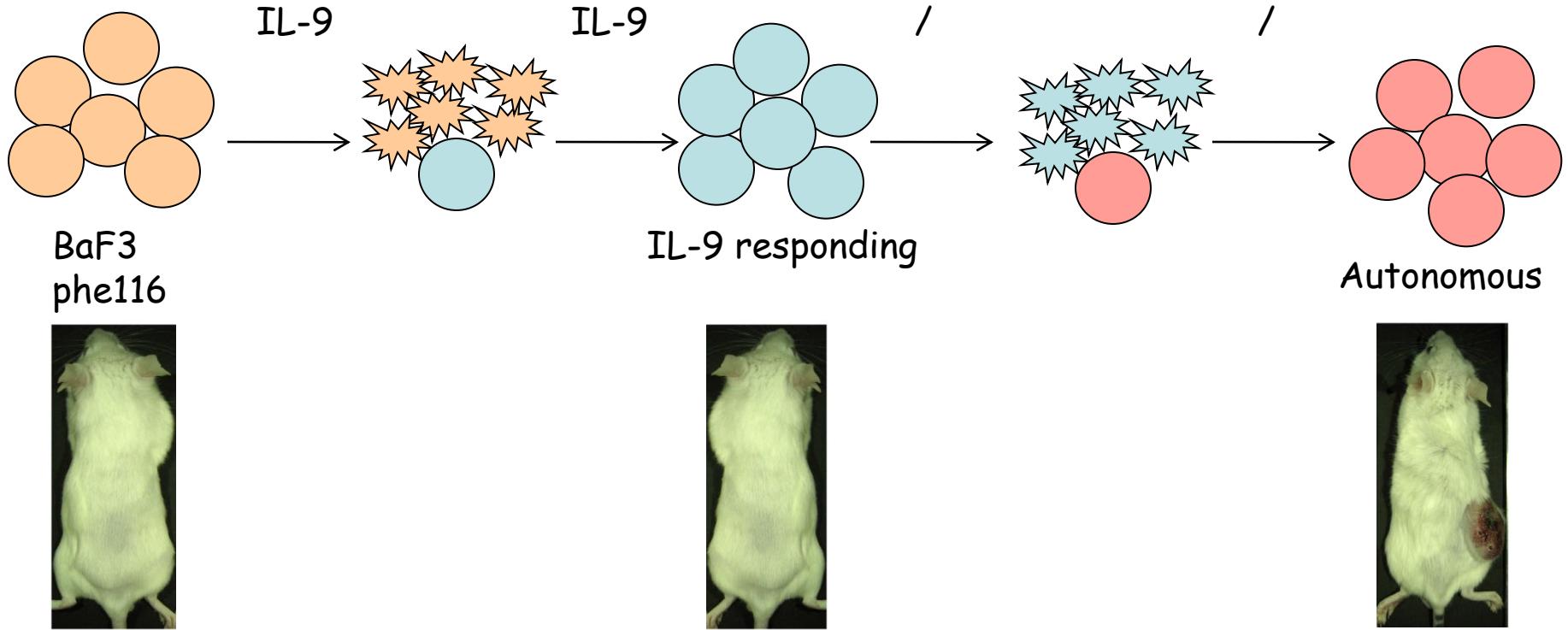


BaF₃
phe116

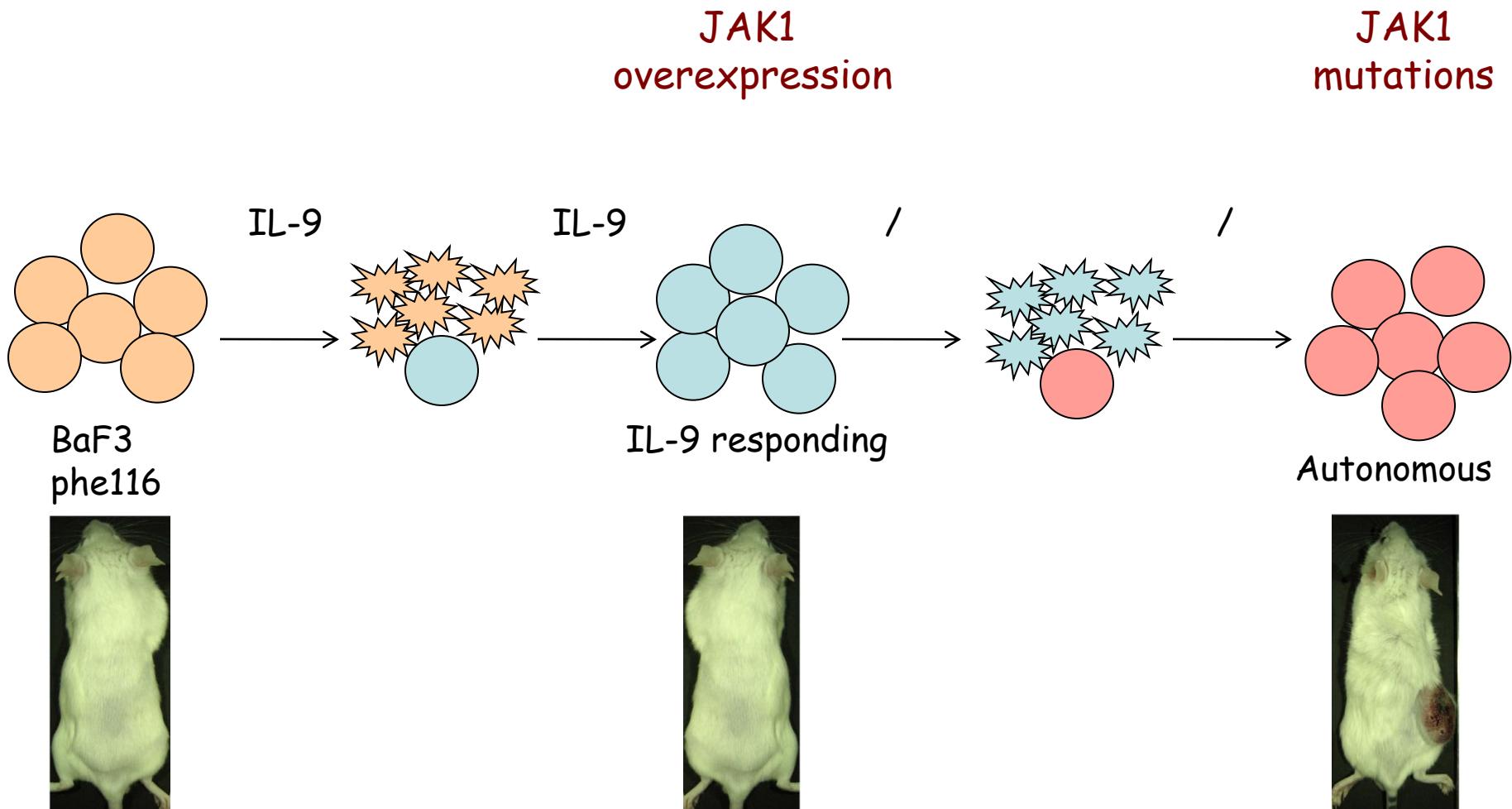




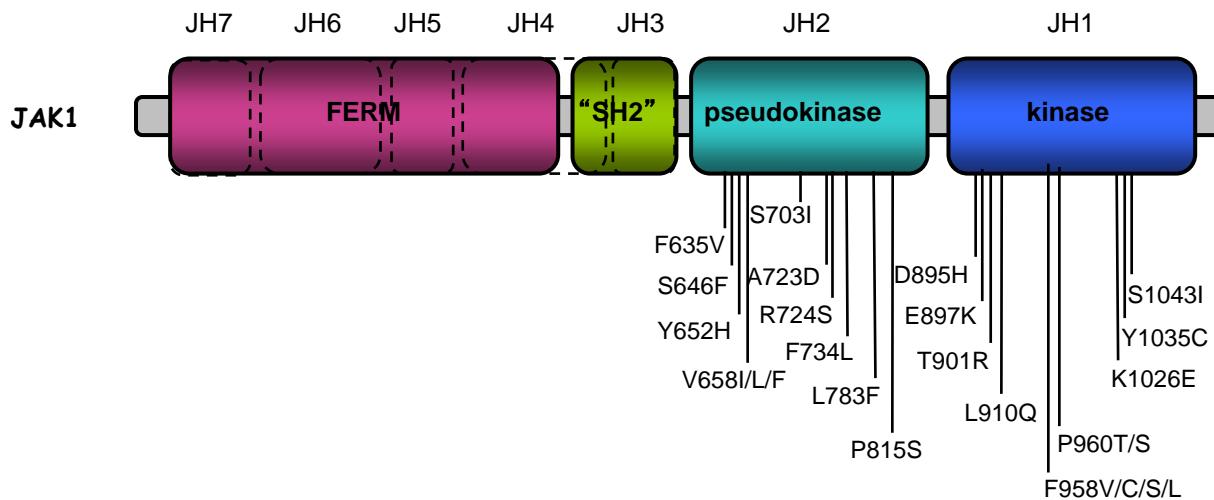
In vitro model of tumorigenesis



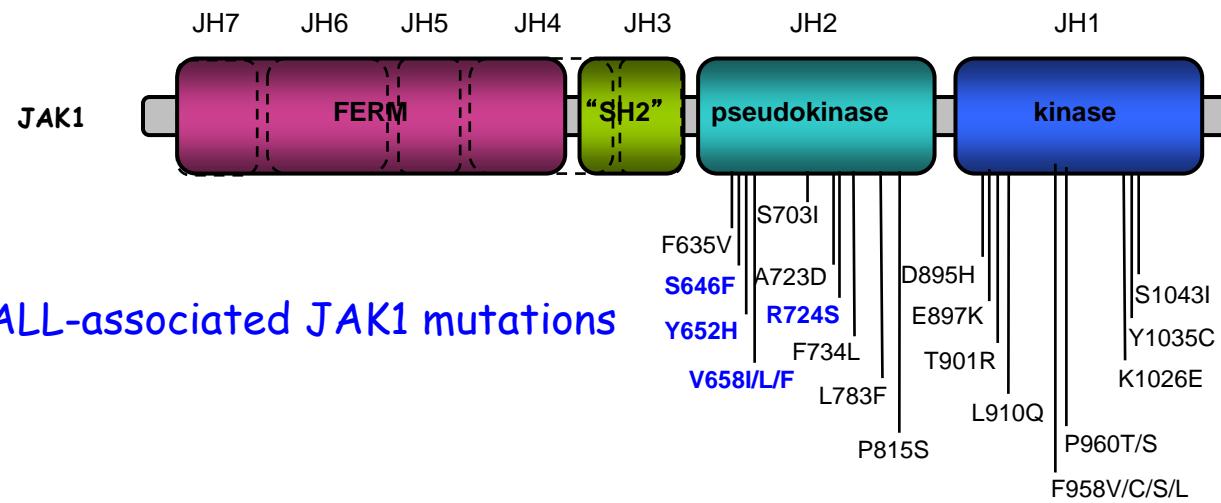
In vitro model of tumorigenesis



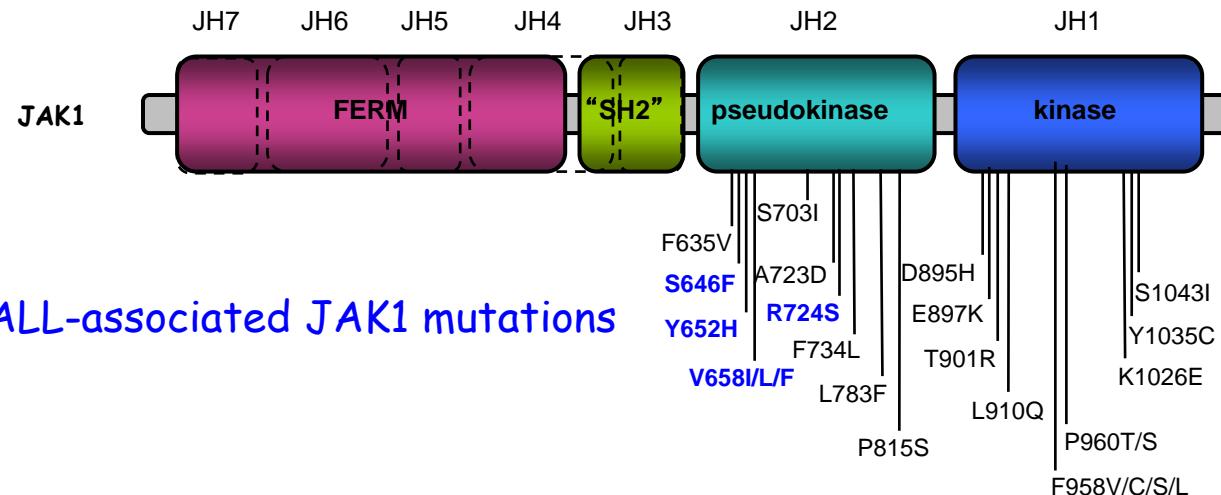
JAK1 activating mutations



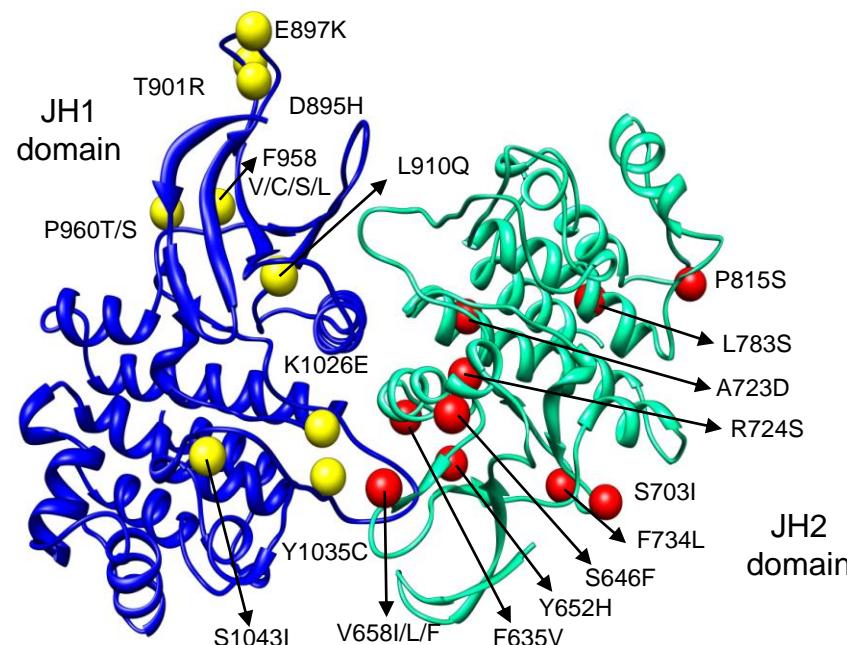
JAK1 activating mutations



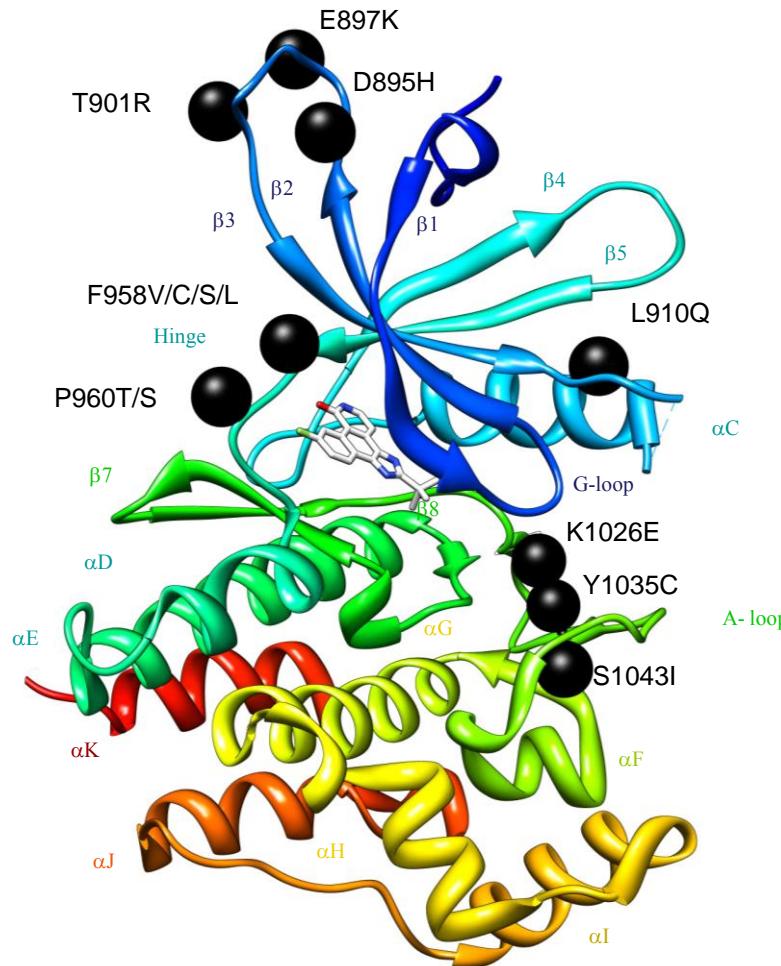
JAK1 activating mutations



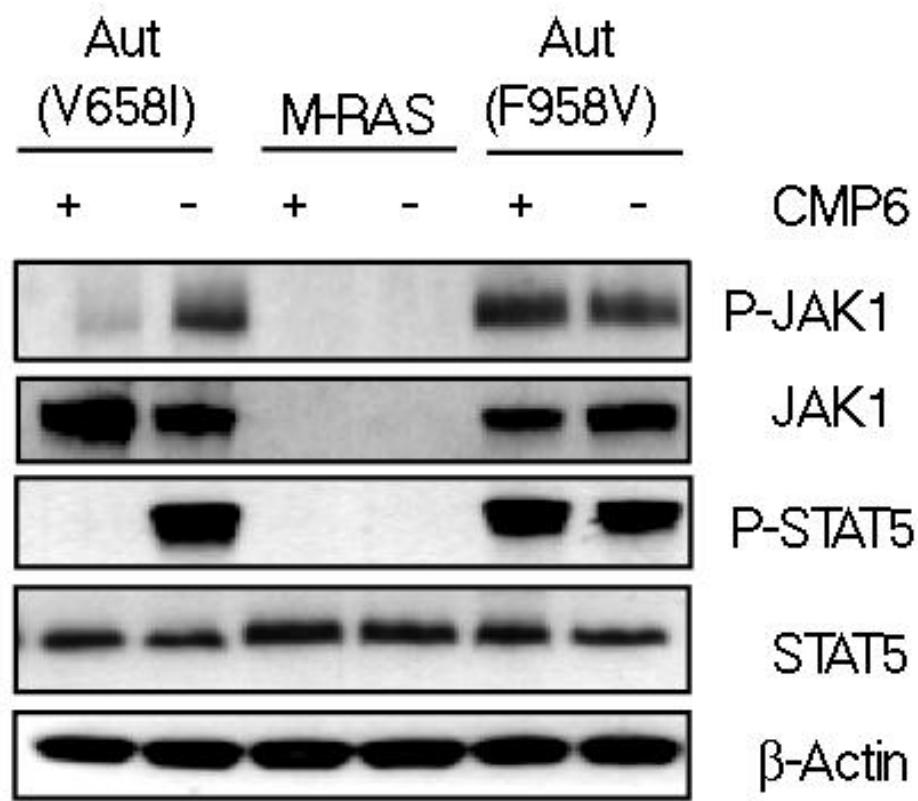
ALL-associated JAK1 mutations

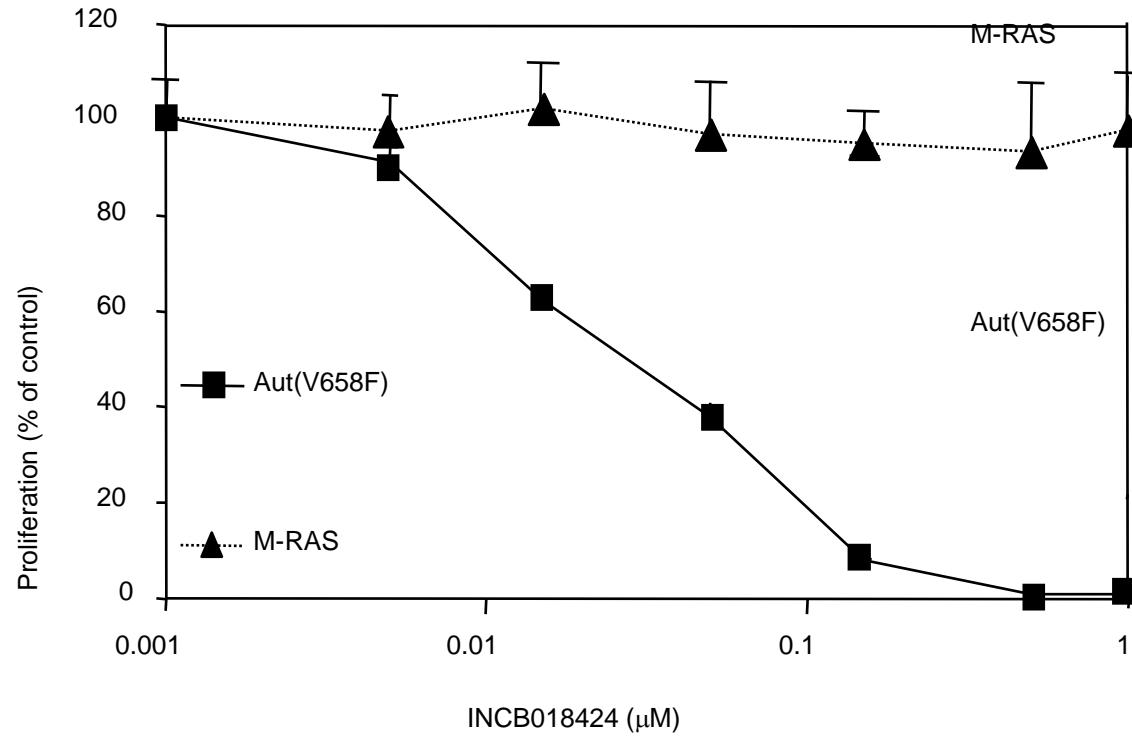


JAK1 activating mutations : kinase domain

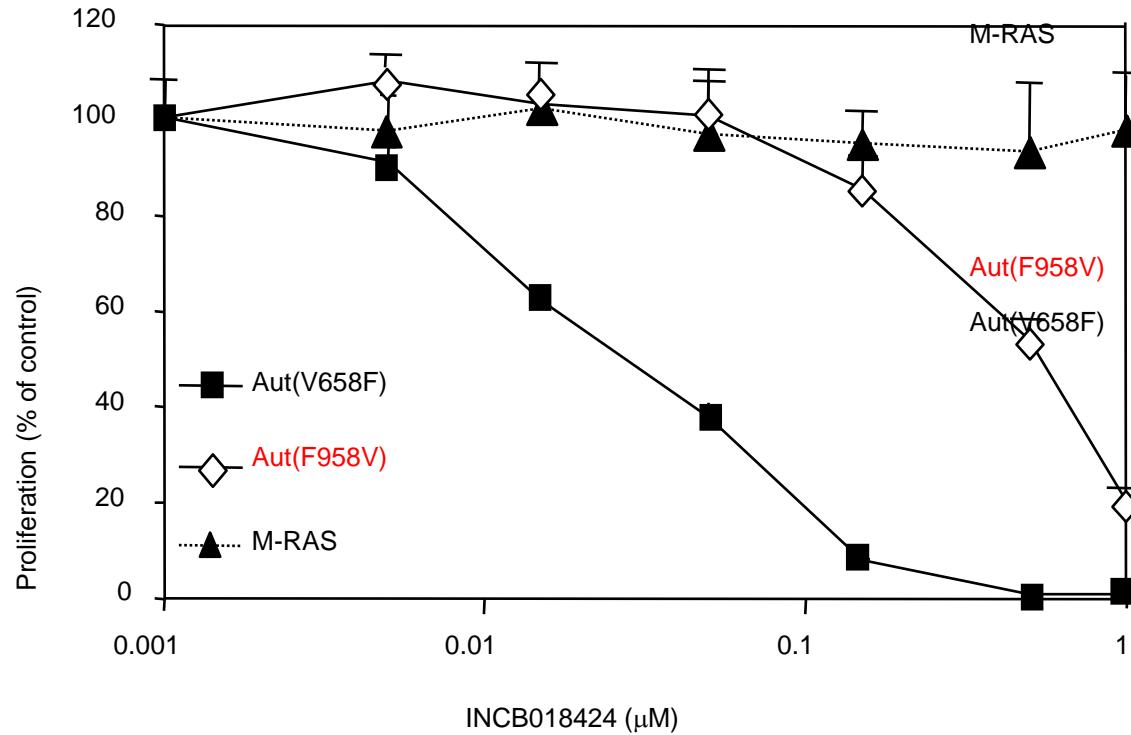


JAK1 F958V is resistant to JAK inhibitor I





JAK1 F958V is resistant to INC424



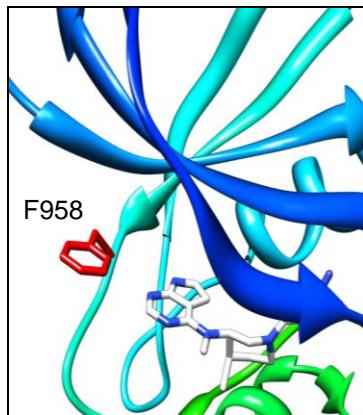
JAK1 and ABL1 hinge regions

P960T/ S
F958V/ C/ S/ L (JAK i nhi bi t or s)

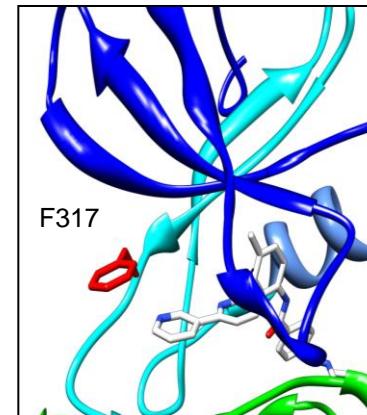
JAK1	925	KLI MEFLPSGSLKEYLPK-NKN	973
	:... : :.. :..	
ABL1	312	YII TEFMTYGNLLDYL RECNRQ	333
		T315I / A/ S (I mat i ni b)	
		E316D	
		F317L/ I	
		M318A	
		G321V	

JAK1 and ABL1 hinge regions

P960T/ S
F958V/ C/ S/ L (JAK i nhi bi t or s)
JAK1 925 KLI**M**EFLPSGSLKEYL**PK-NKN** 973
.:|.|.|:...|:|..||..|:..|:..|:
ABL1 312 YII**TEFMTYGNLLDYL**RECNRQ 333
T315I / A/ S (I mat i ni b)
E316D
F317L/ I
M318A
G321V



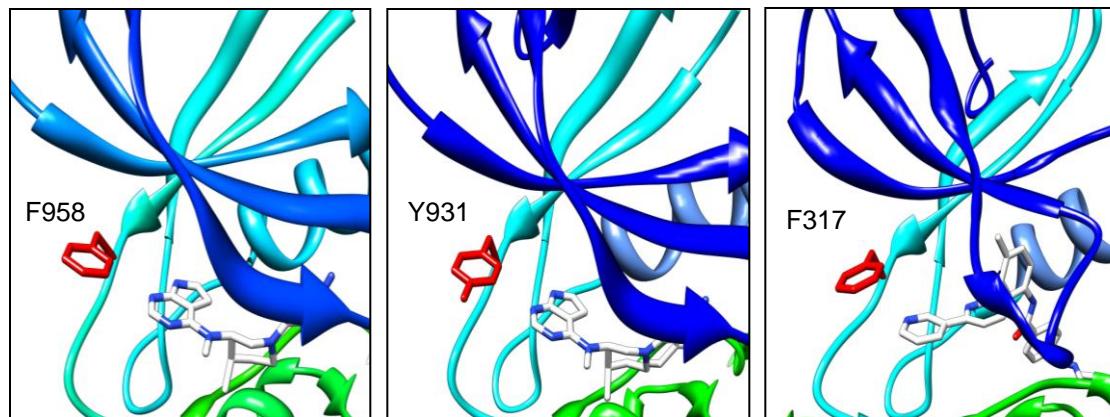
JAK1, CP-690,500
(PDB 3EYG)



ABL1, Imatinib
(PDB 2HYY)

JAK1 and ABL1 hinge regions

P960T/ S
F958V/ C/ S/ L (JAK i nhi bi t or s)
JAK1 925 KLI**M**EFLPSGSLKEYL**PK-NKN** 973
.:|.|.|:...|:|..||..|:..|:..|:
ABL1 312 YII**TEFMTYGNLLDYL**RECNRQ 333
T315I / A/ S (I mat i ni b)
E316D
F317L/ I
M318A
G321V

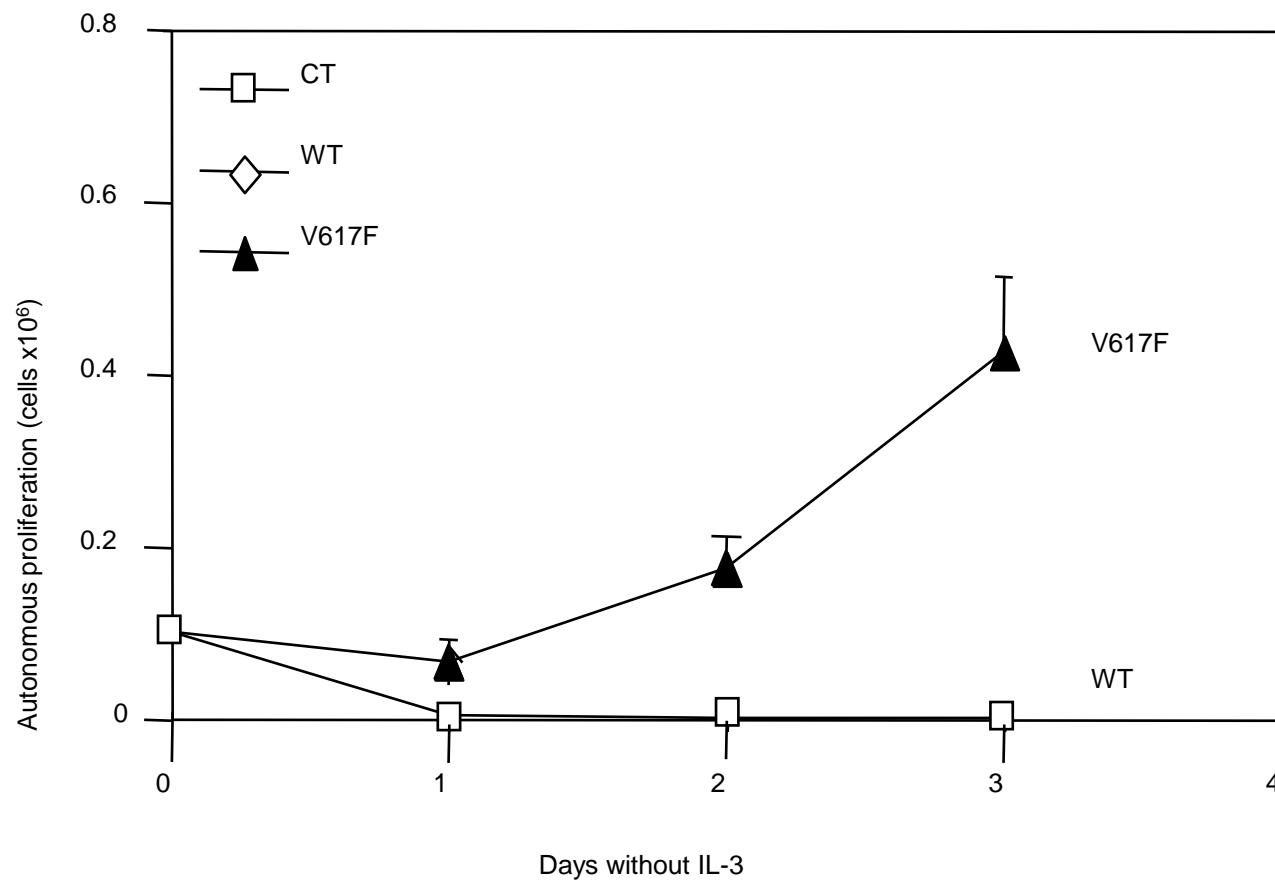


JAK1, CP-690,500
(PDB 3EYG)

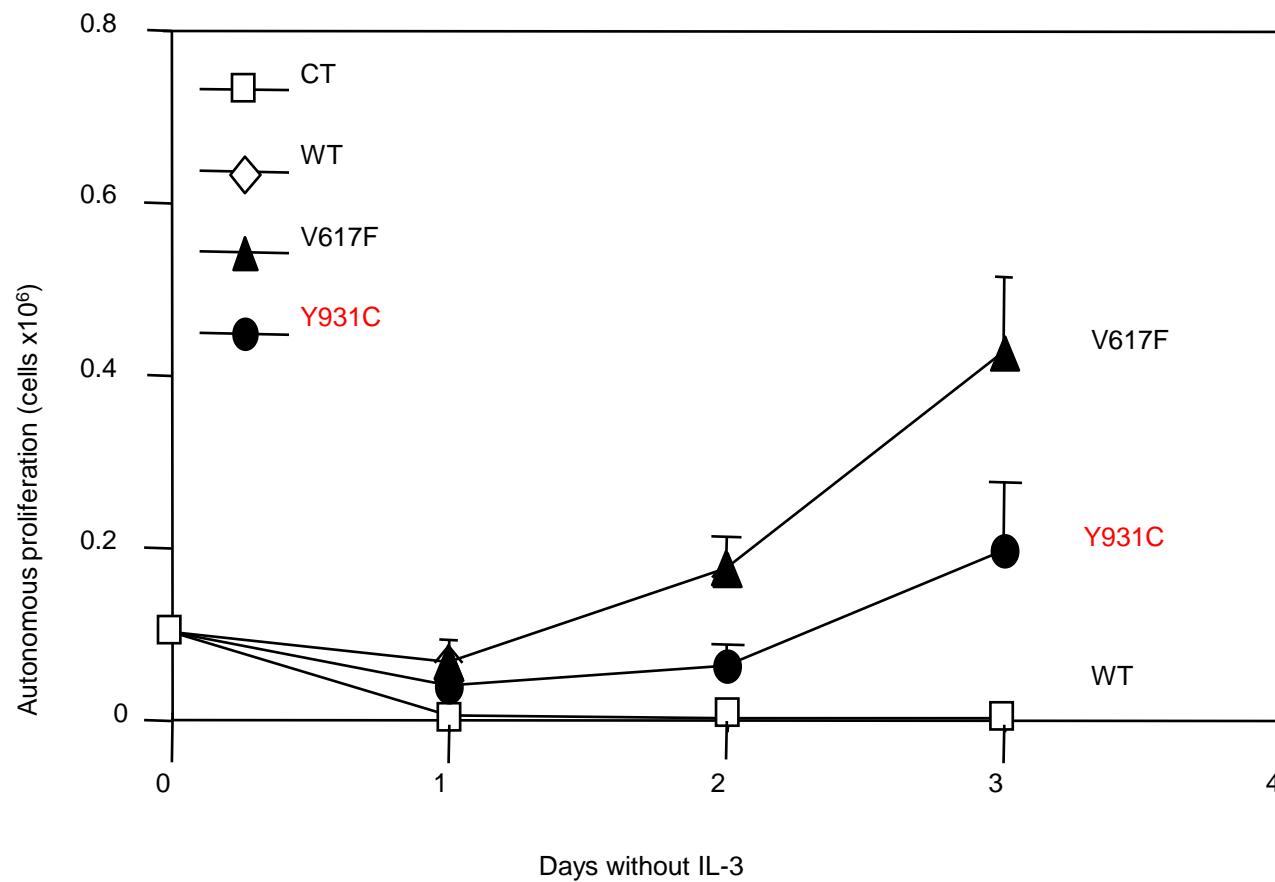
JAK2, CP-690,500
(PDB 3FUP)

ABL1, Imatinib
(PDB 2HYY)

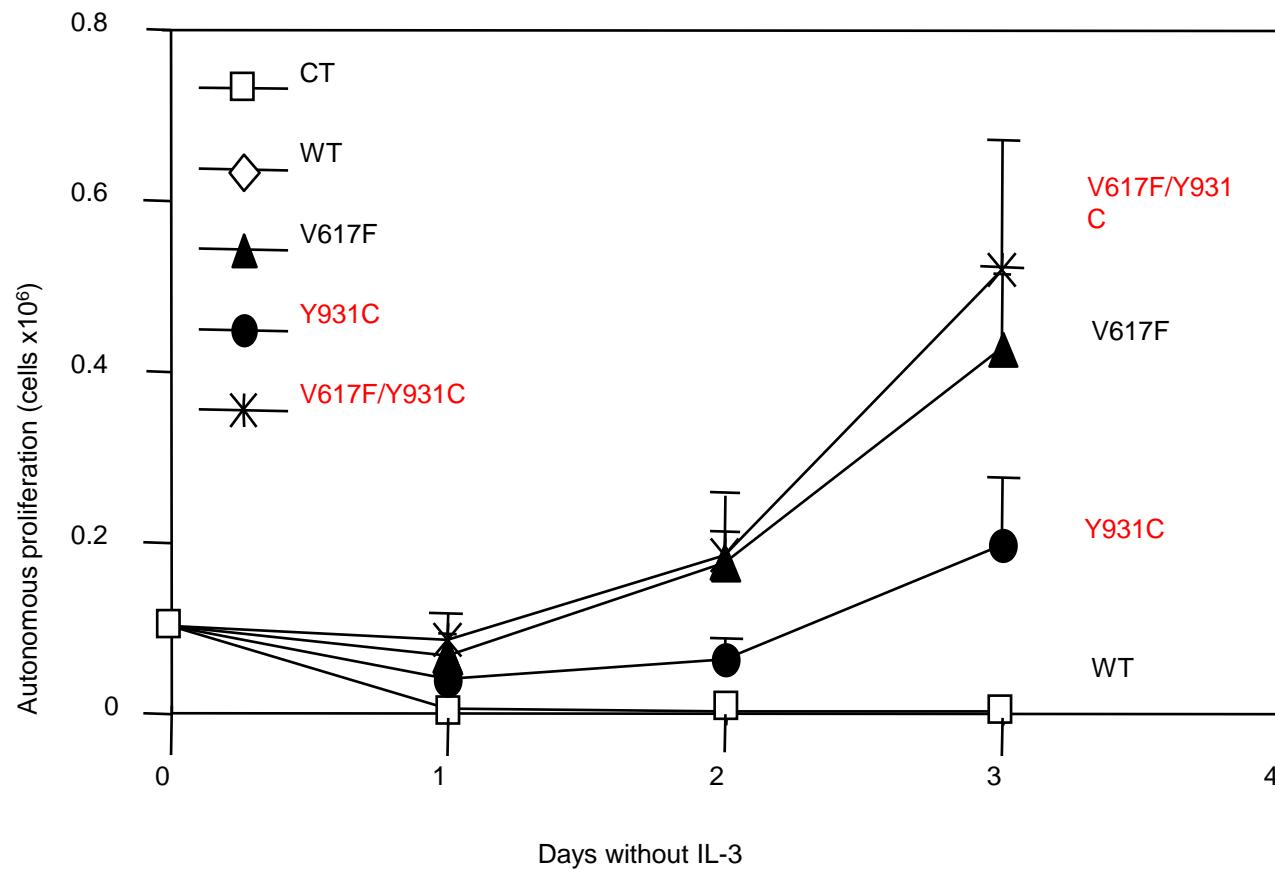
The JAK2 Y931C mutation - autonomous proliferation



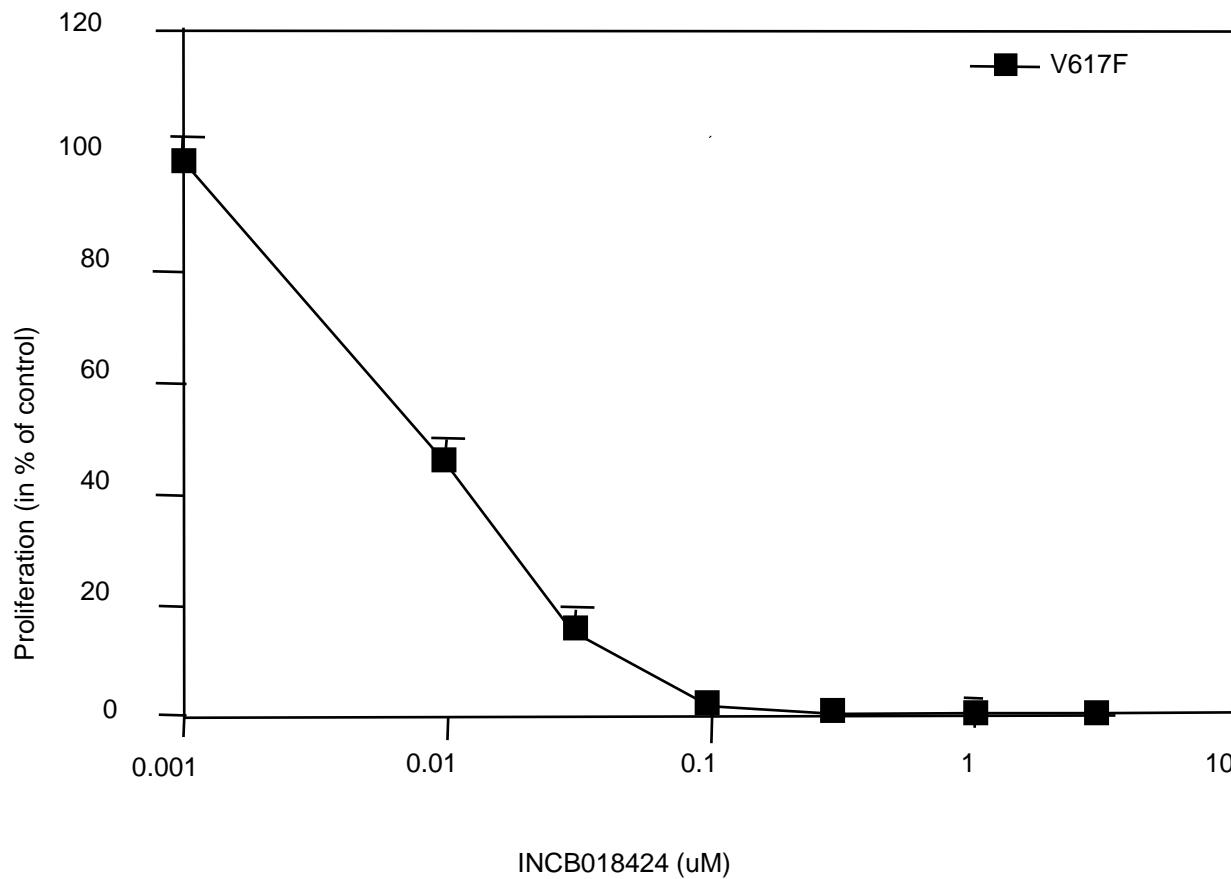
The JAK2 Y931C mutation - autonomous proliferation



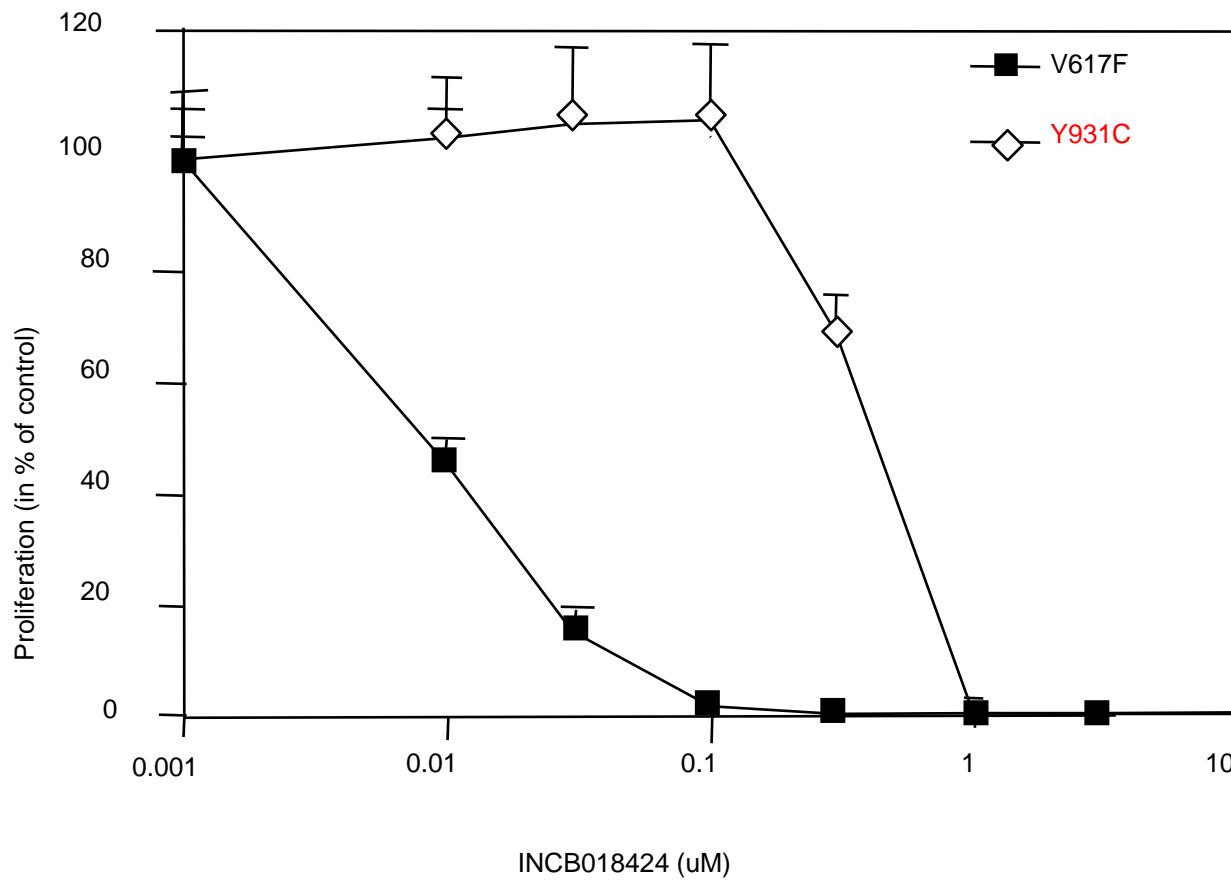
The JAK2 Y931C mutation - autonomous proliferation



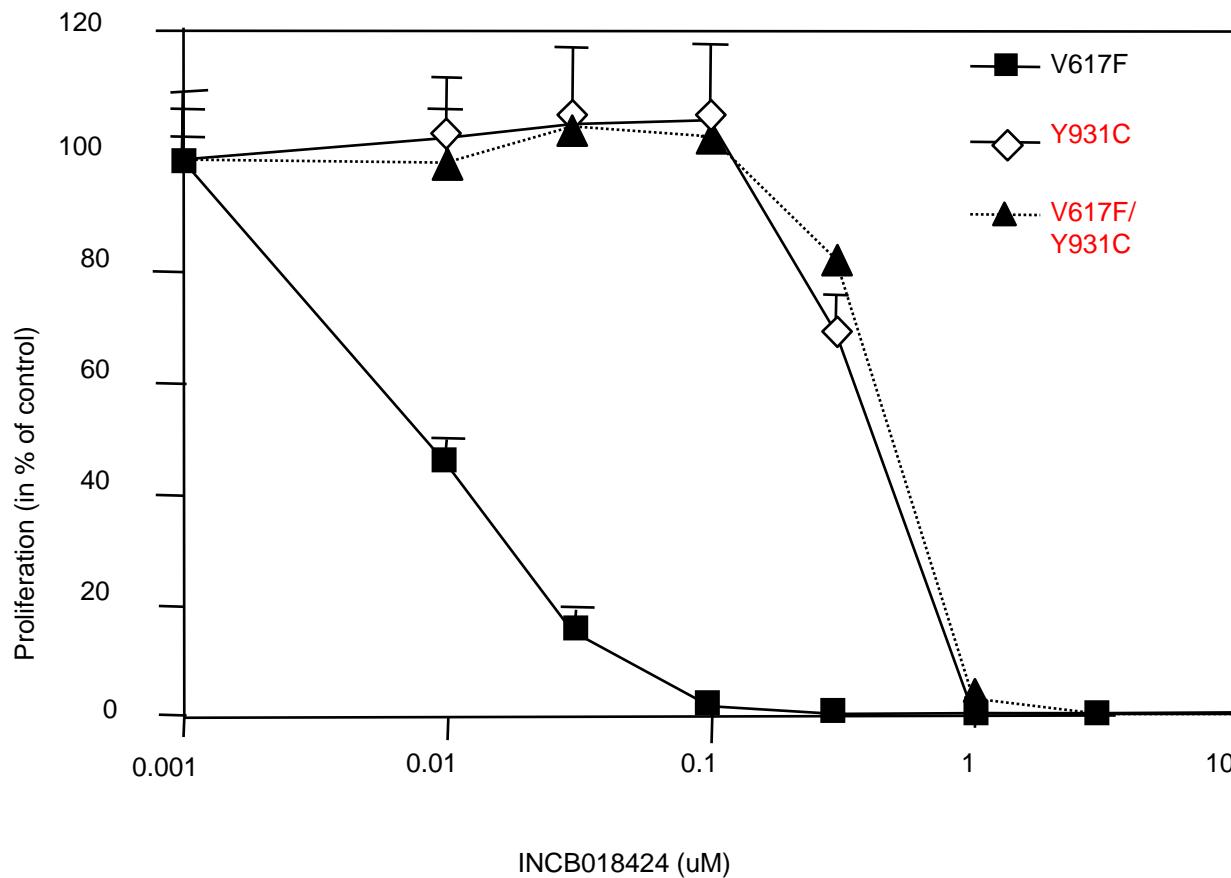
The JAK2 Y931C mutation - INC424 response



The JAK2 Y931C mutation - INC424 response



The JAK2 Y931C mutation - INC424 response



Laurent

Perrine

Emilie

Muriel

Tekla

Laure

Magali

Lorraine

Jean-Christophe
Jacques

Monique

Reece

Astrid

Isabelle(s)



+ SN Constantinescu