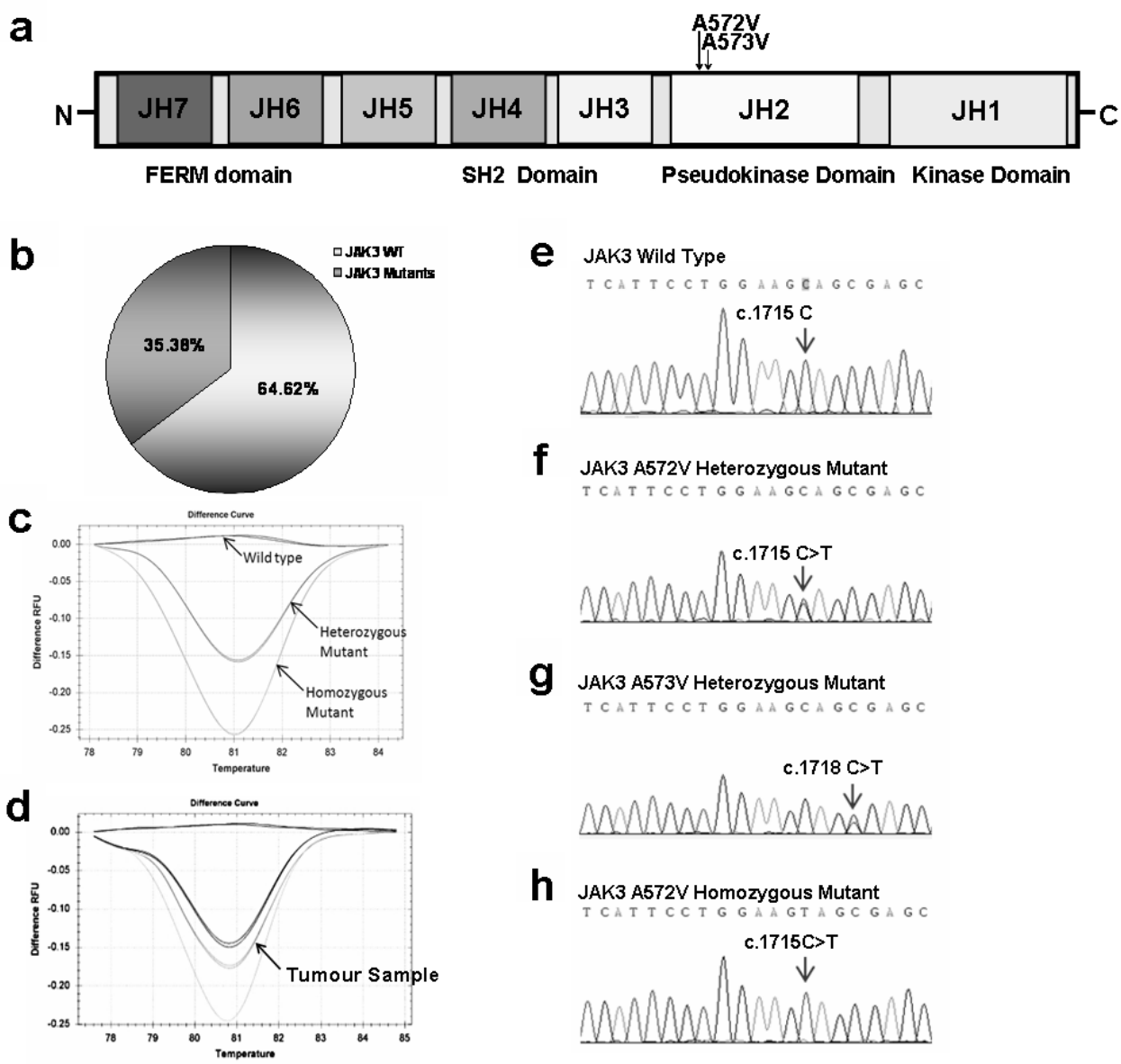
a
A572V
A573V
N
JH7
JH6
JH5
JH4
JH3
JH2
JH1
C
FERM domain
SH2 Domain
Pseudokinase Domain
Kinase Domain
b
JAK3 WT
JAK3 Mutants
35.38%
64.62%
c
Difference Curve
Wild type
Heterozygous Mutant
Homozygous Mutant
Difference RFU
Temperature
d
Difference Curve
Tumour Sample
Difference RFU
Temperature
e
JAK3 Wild Type
c.1715 C
f
JAK3 A572V Heterozygous Mutant
c.1715 C>T
g
JAK3 A573V Heterozygous Mutant
c.1718 C>T
h
JAK3 A572V Homozygous Mutant
c.1715C>T

Figure 1

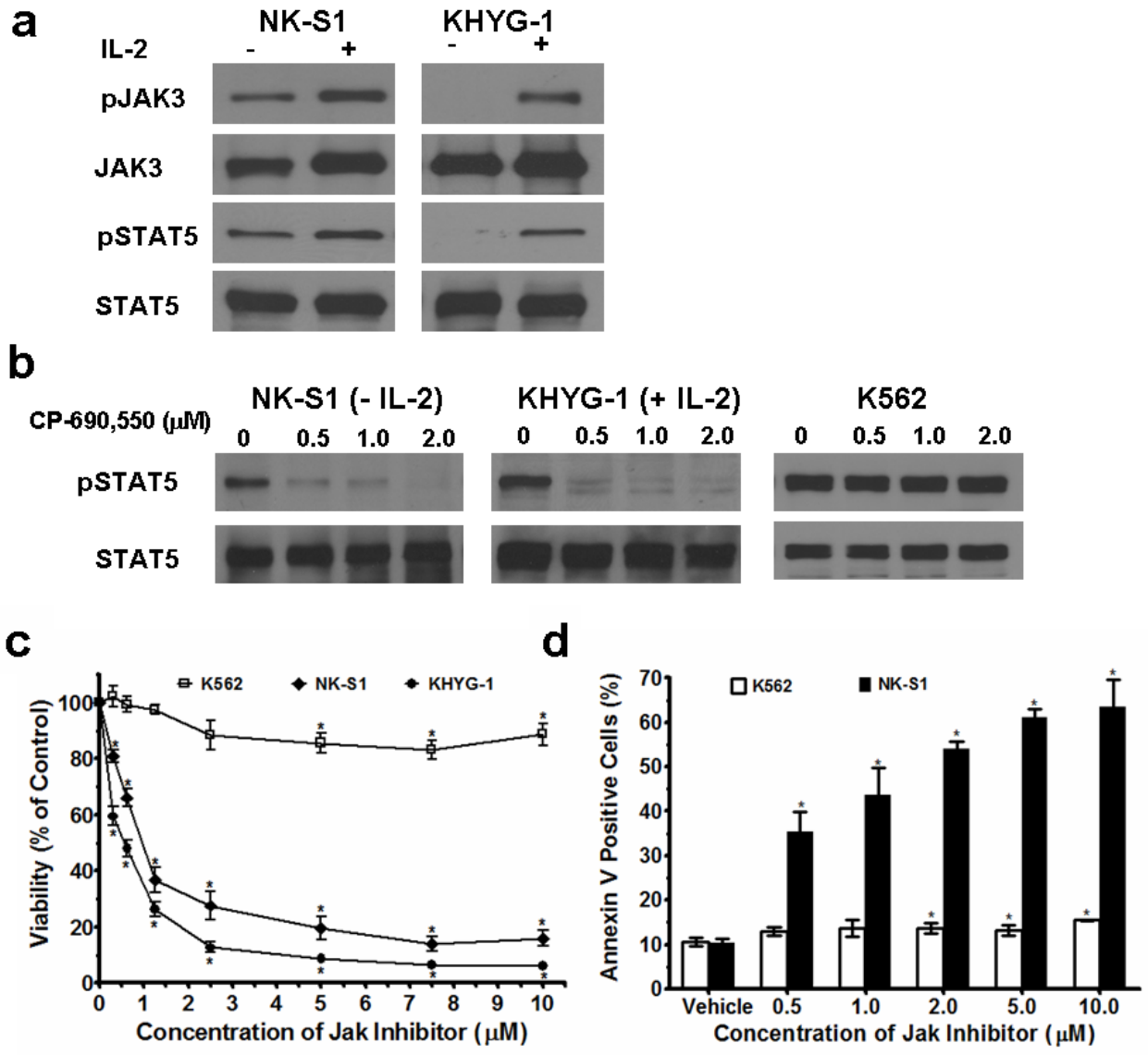
a
NK-S1
KHYG-1
IL-2
- + - +
pJAK3
JAK3
pSTAT5
STAT5
b
CP-690,550 (μM)
NK-S1 (- IL-2)
KHYG-1 (+ IL-2)
K562
0 0.5 1.0 2.0
pSTAT5
STAT5
c
K562
NK-S1
KHYG-1
Viability (% of Control)
Concentration of Jak Inhibitor (μM)
d
K562
NK-S1
Annexin V Positive Cells (%)
Vehicle 0.5 1.0 2.0 5.0 10.0
Concentration of Jak Inhibitor (μM)

Figure 2

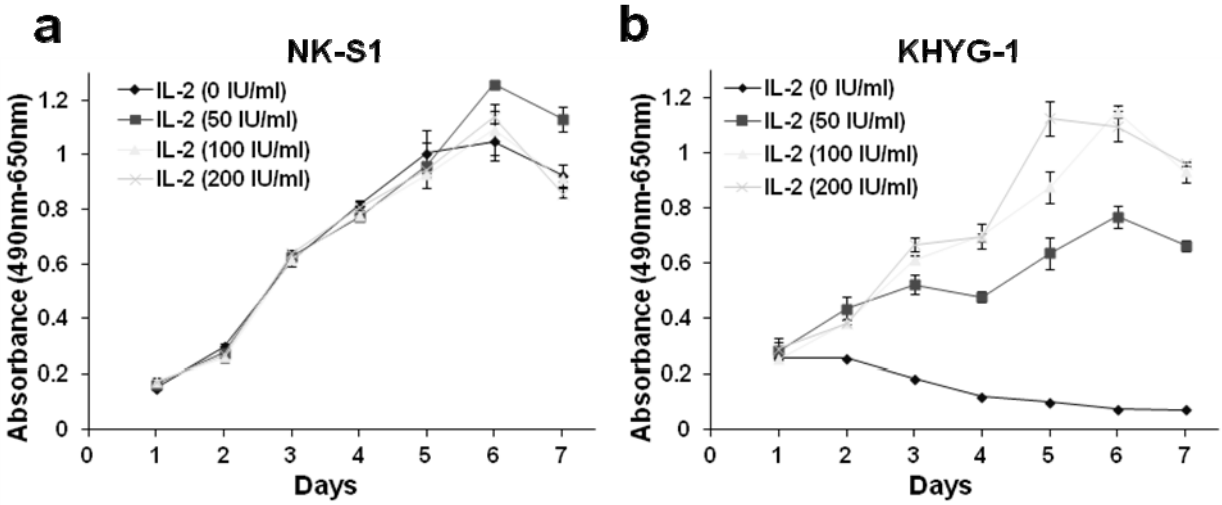
a
NK-S1
IL-2 (0 IU/ml)
IL-2 (50 IU/ml)
IL-2 (100 IU/ml)
IL-2 (200 IU/ml)
Absorbance (490nm-650nm)
Days
b
KHYG-1
IL-2 (0 IU/ml)
IL-2 (50 IU/ml)
IL-2 (100 IU/ml)
IL-2 (200 IU/ml)
Absorbance (490nm-650nm)
Days

Figure 3

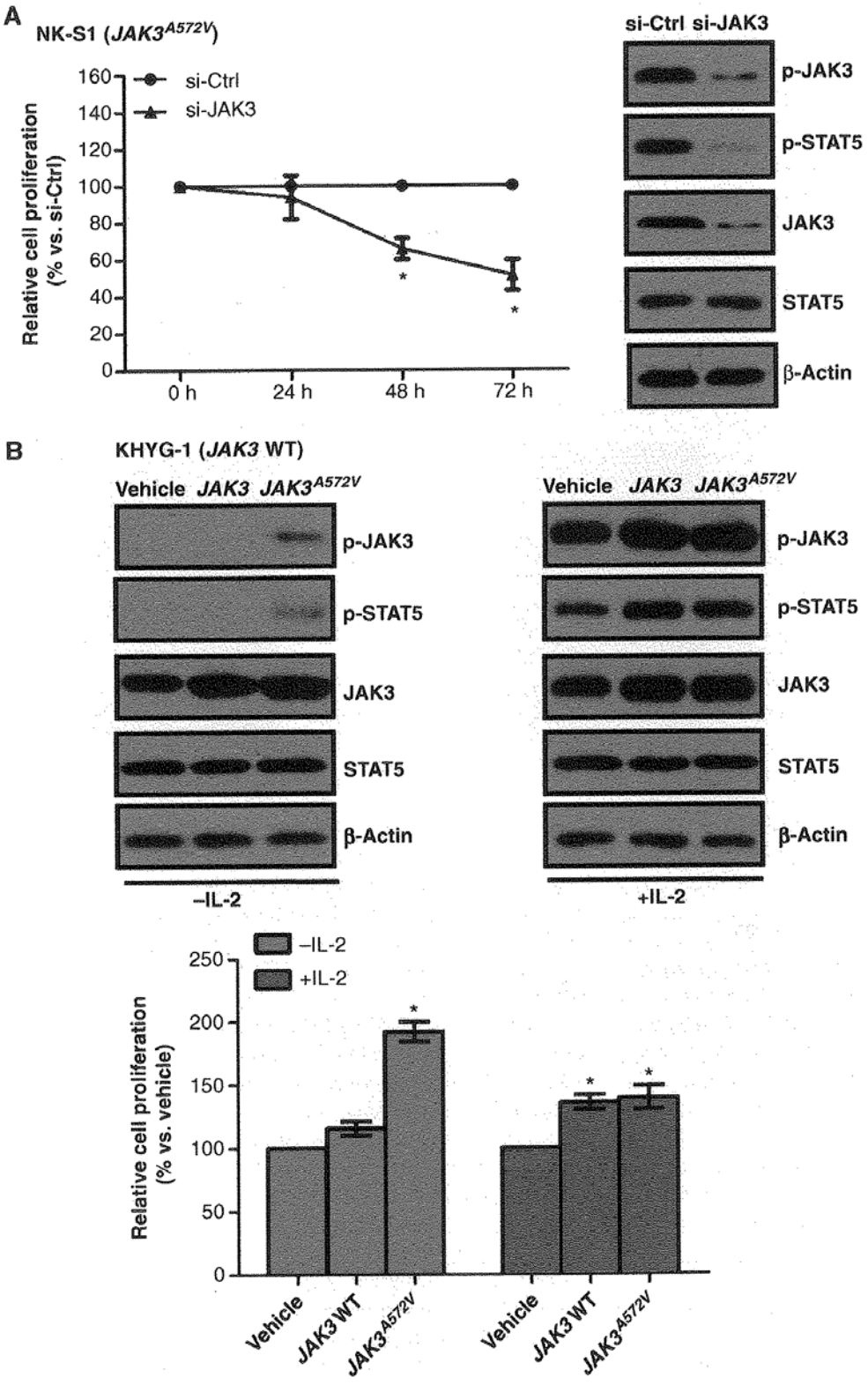
A
NK-S1 (JAK3A572V)
si-Ctrl
si-JAK3
Relative cell proliferation (% vs. si-Ctrl)
160
140
120
100
80
60
40
20
0
0 h
24 h
48 h
72 h
si-Ctrl si-JAK3
p-JAK3
p-STAT5
JAK3
STAT5
β-Actin
B
KHYG-1 (JAK3 WT)
Vehicle JAK3 JAK3A572V
p-JAK3
p-STAT5
JAK3
STAT5
β-Actin
–IL-2
Vehicle JAK3 JAK3A572V
p-JAK3
p-STAT5
JAK3
STAT5
β-Actin
+IL-2
–IL-2
+IL-2
Relative cell proliferation (% vs. vehicle)
250
200
150
100
50
0
Vehicle
JAK3WT
JAK3A572V
Vehicle
JAK3WT
JAK3A572V

Figure 4