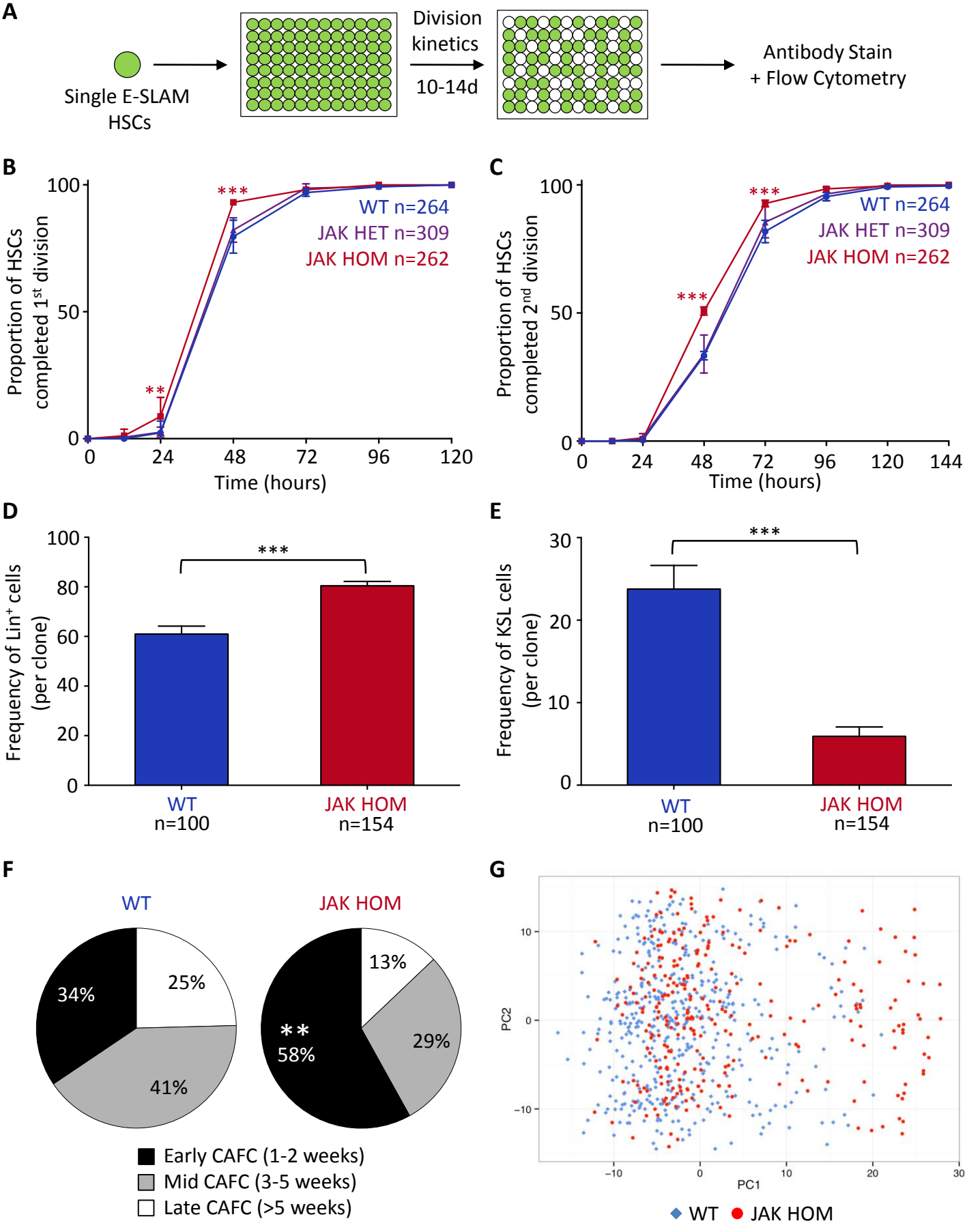
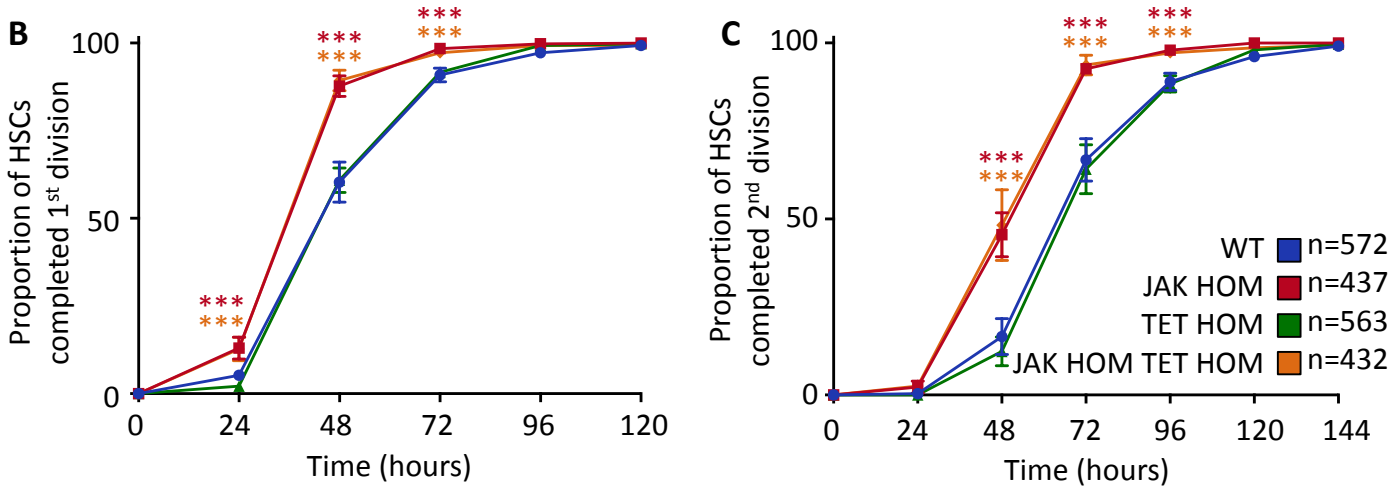

A
Single E-SLAM HSCs
Division kinetics
10-14d
Antibody Stain + Flow Cytometry
B
Proportion of HSCs completed 1st division
Time (hours)
WT n=264
JAK HET n=309
JAK HOM n=262
C
Proportion of HSCs completed 2nd division
Time (hours)
WT n=264
JAK HET n=309
JAK HOM n=262
D
Frequency of Lin+ cells (per clone)
WT n=100
JAK HOM n=154
E
Frequency of KSL cells (per clone)
WT n=100
JAK HOM n=154
F
WT
JAK HOM
34%
25%
41%
13%
58%
29%
Early CAFC (1-2 weeks)
Mid CAFC (3-5 weeks)
Late CAFC (>5 weeks)
G
PC1
PC2
WT
JAK HOM

Figure 1

A

		JAK2 (Li et al, 2014)	TET2 (Ko et al, 2011)
WT		+/+	+/+
JAK HOM		V617F/V617F	+/+
TET HOM		+/+	-/-
JAK HOM TET HOM		V617F/V617F	-/-



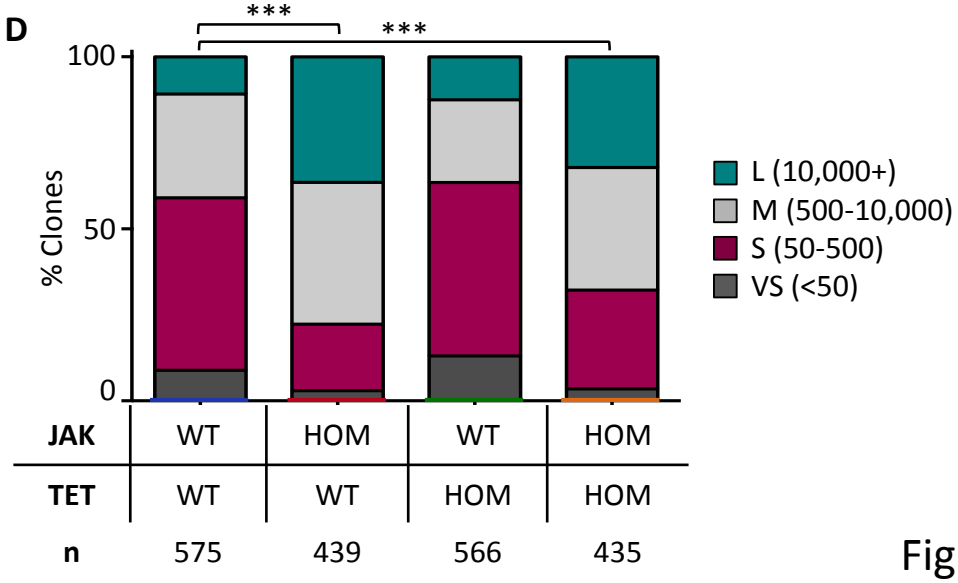
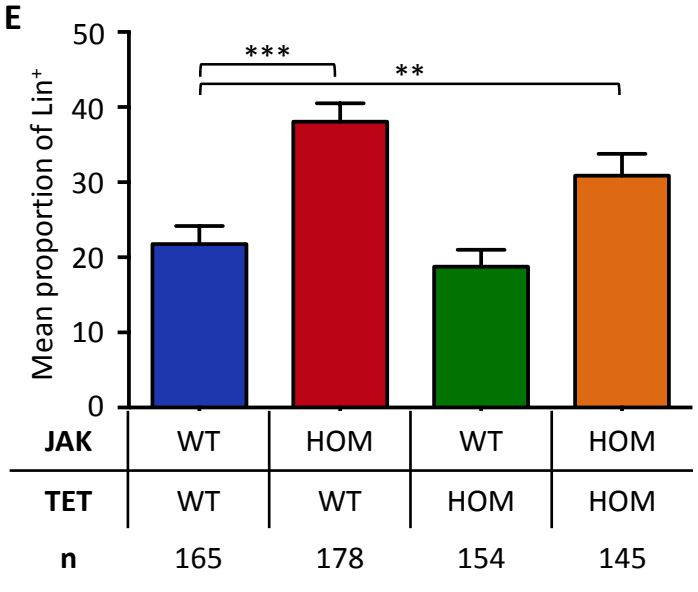
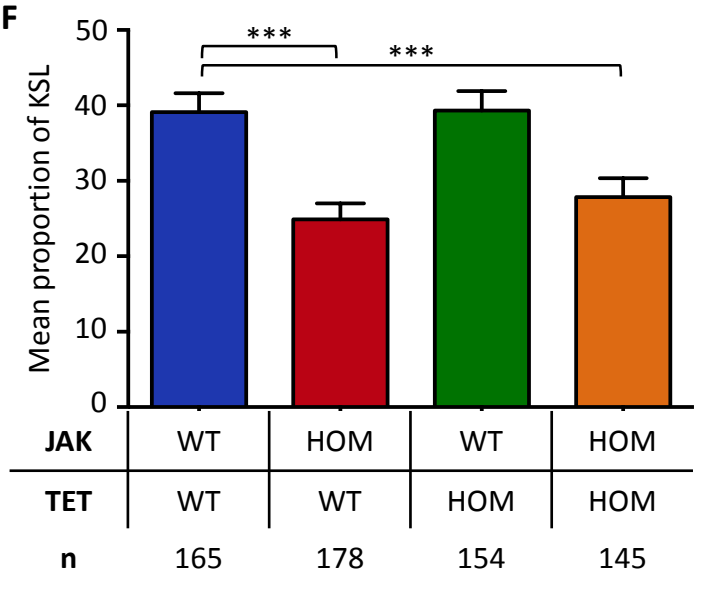


Figure 2





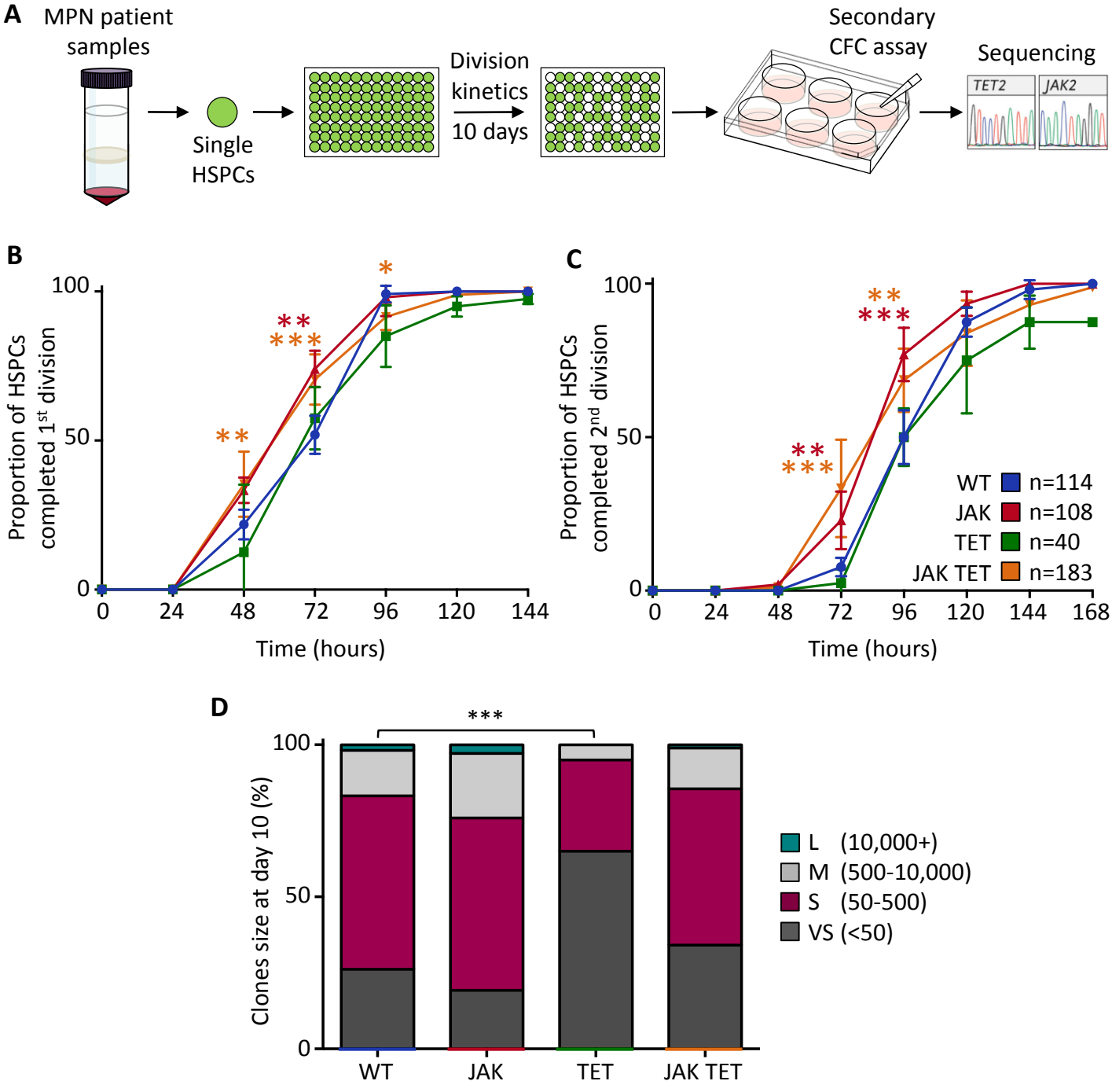

A
MPN patient samples
Single HSPCs
Division kinetics
10 days
Secondary CFC assay
Sequencing
TET2
JAK2
B
Proportion of HSPCs completed 1st division
Time (hours)
C
Proportion of HSPCs completed 2nd division
Time (hours)
WT n=114
JAK n=108
TET n=40
JAK TET n=183
D
Clones size at day 10 (%)
L (10,000+)
M (500-10,000)
S (50-500)
VS (<50)
WT
JAK
TET
JAK TET

Figure 3

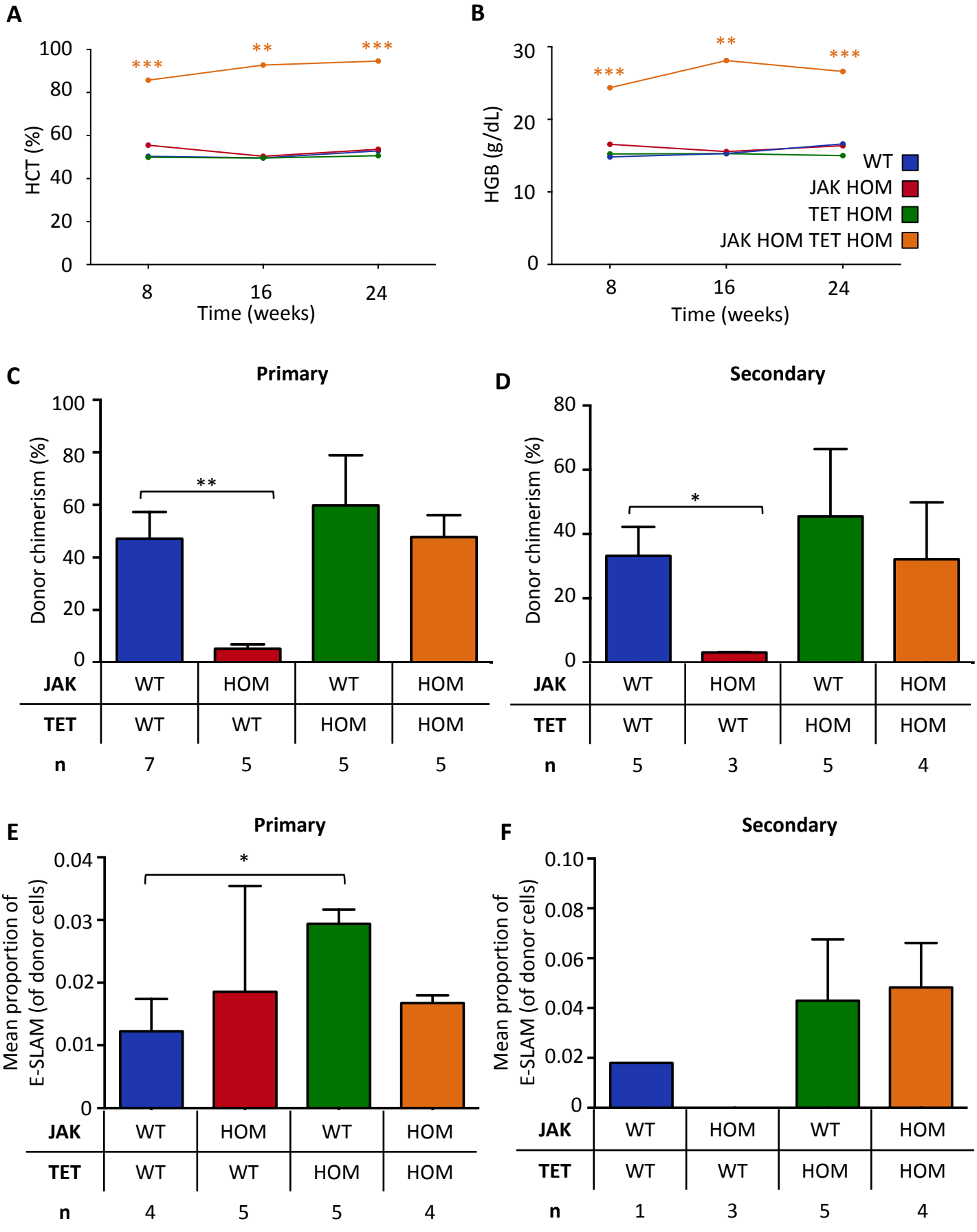

A
HCT (%)
Time (weeks)
B
HGB (g/dL)
Time (weeks)
WT
JAK HOM
TET HOM
JAK HOM TET HOM
C
Primary
Donor chimerism (%)
D
Secondary
Donor chimerism (%)
JAK
TET
n
E
Primary
Mean proportion of E-SLAM (of donor cells)
F
Secondary
Mean proportion of E-SLAM (of donor cells)

Figure 4

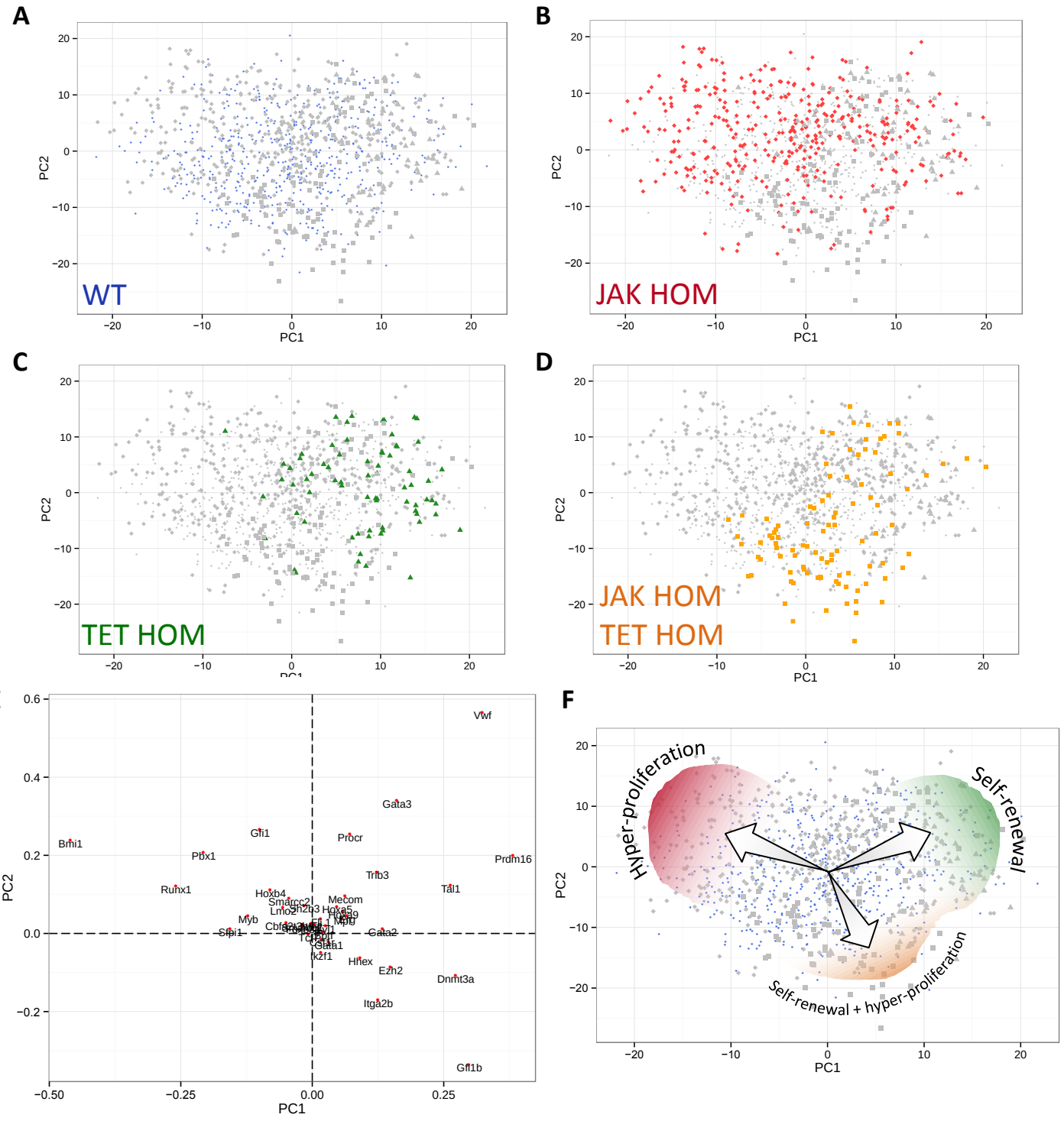

A
WT
B
JAK HOM
C
TET HOM
D
JAK HOM
TET HOM
E
Vwf
Gata3
Gfi1
Bmi1
Procr
Pbx1
Prdm16
Trib3
Runx1
Hoxb4
Tal1
Mecom
Myb
Gata2
Hhex
Ezh2
Dnmt3a
Itga2b
Gfi1b
F
Hyper-proliferation
Self-renewal
Self-renewal + hyper-proliferation
PC1
PC2

Figure 5

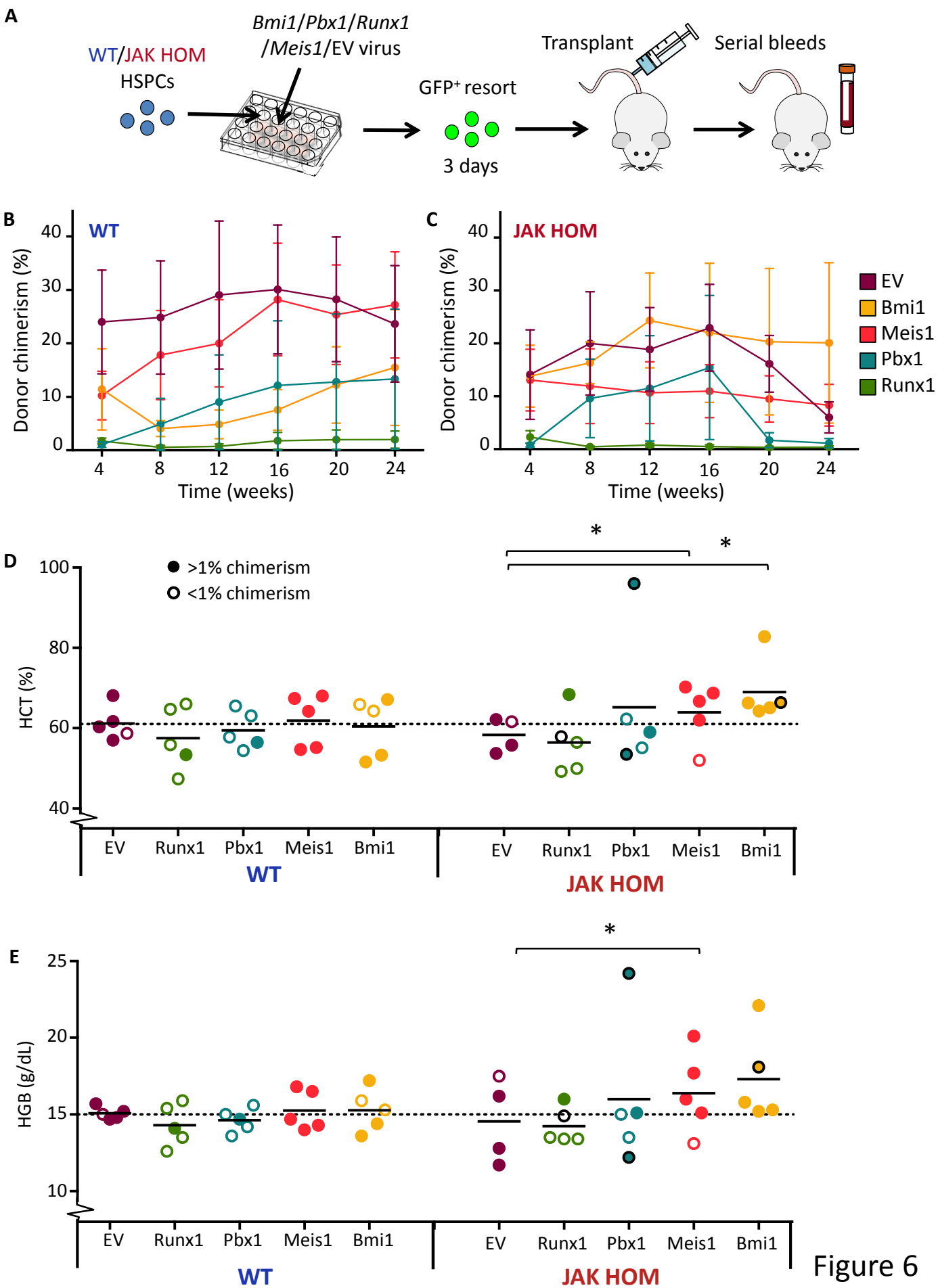

A
WT/JAK HOM
HSPCs
Bmi1/Pbx1/Runx1
/Meis1/EV virus
GFP+ resort
3 days
Transplant
Serial bleeds
B
WT
Donor chimerism (%)
Time (weeks)
C
JAK HOM
EV
Bmi1
Meis1
Pbx1
Runx1
D
>1% chimerism
<1% chimerism
HCT (%)
EV
Runx1
Pbx1
Meis1
Bmi1
WT
JAK HOM
E
HGB (g/dL)

Figure 6