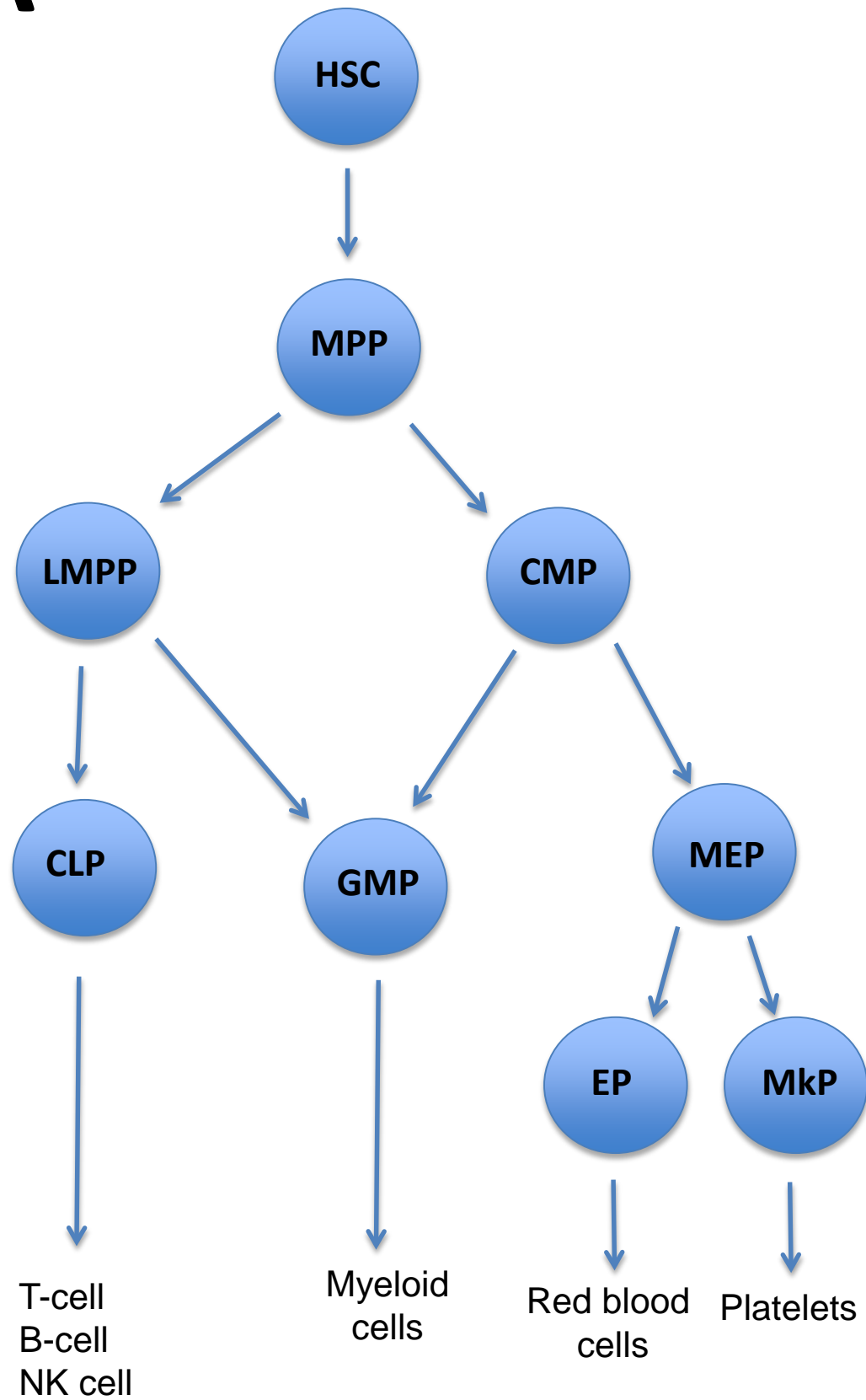


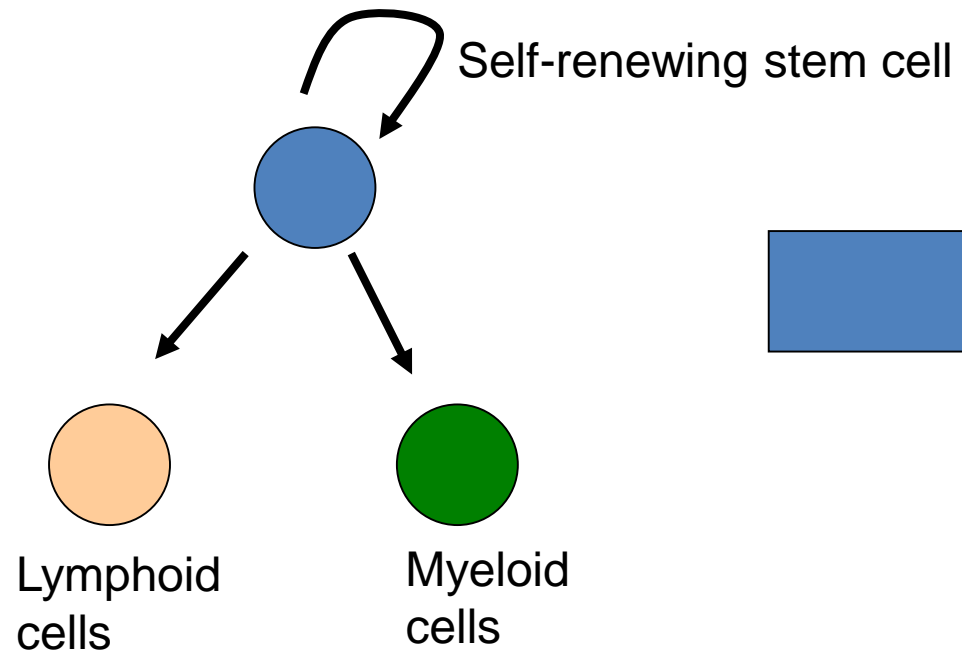
A**B**

Stem and progenitors	HSC	MPP	LMPP/CLP	CMP
Key receptors	MPL	MPL	IL7R FLT3	MPL GMCSF IL3R GCSF
Impacting Mutation	JAK2V617F Mutant CALR MPLW515L	JAK2V617F Mutant CALR MPLW515L	None	JAK2V617F Mutant CALR MPLW515L
Progenitors and precursors	GMP	MEP	EP	MkP
Key receptors	GMCSF IL3R GCSF	IL3R EPOR MPL	EPOR	MPL
Impacting Mutation	JAK2V617F	JAK2V617F Mutant CALR MPLW515L	JAK2V617F	JAK2V617F Mutant CALR MPLW515L

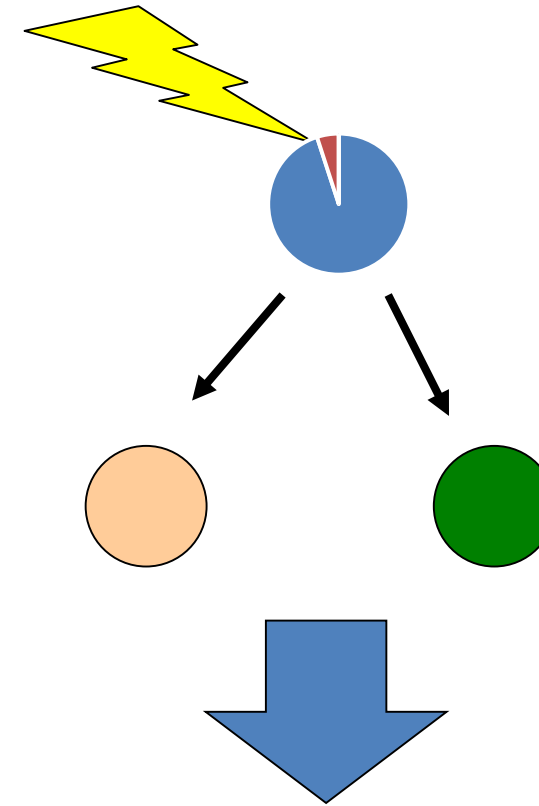
HSC = hematopoietic stem cell
 MPP = multipotent progenitor
 LMPP = lymphoid primed multipotent progenitor
 CMP = common myeloid progenitor
 Pre-MEP = megakaryocyte erythroid progenitor
 GMP = granulocyte macrophage progenitor
 MkP = megakaryocyte precursor
 EP = erythroid precursor
 CLP = common lymphoid progenitor

Figure 1

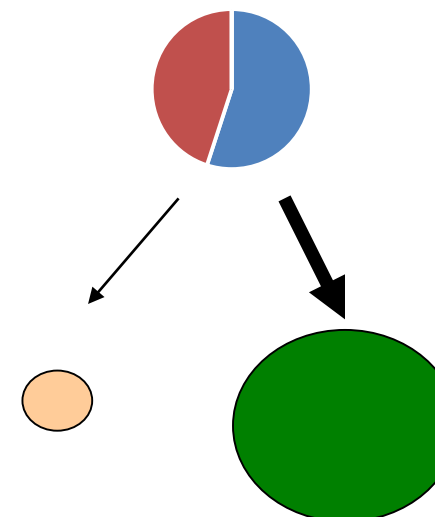
1. Normal hematopoiesis



2. MPN-associated **Mutation** in a single HSC



3. MPN Stem Cell
Selective advantage over normal HSC
Myeloid lineage bias and **myeloproliferation**:



4. Cell-extrinsic impact of MPN clone promotes a **self-reinforcing malignant niche** that favors MPN stem cells over normal HSC

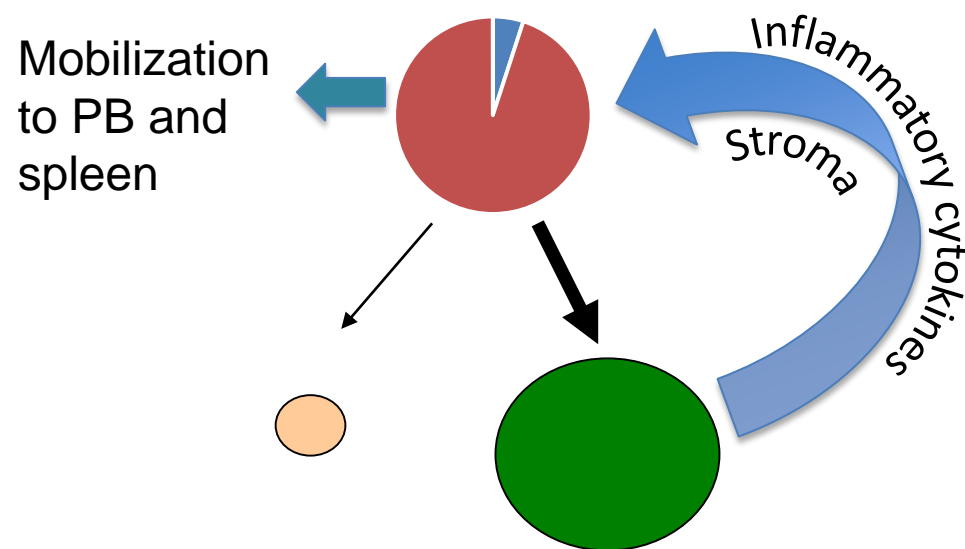


Figure 2

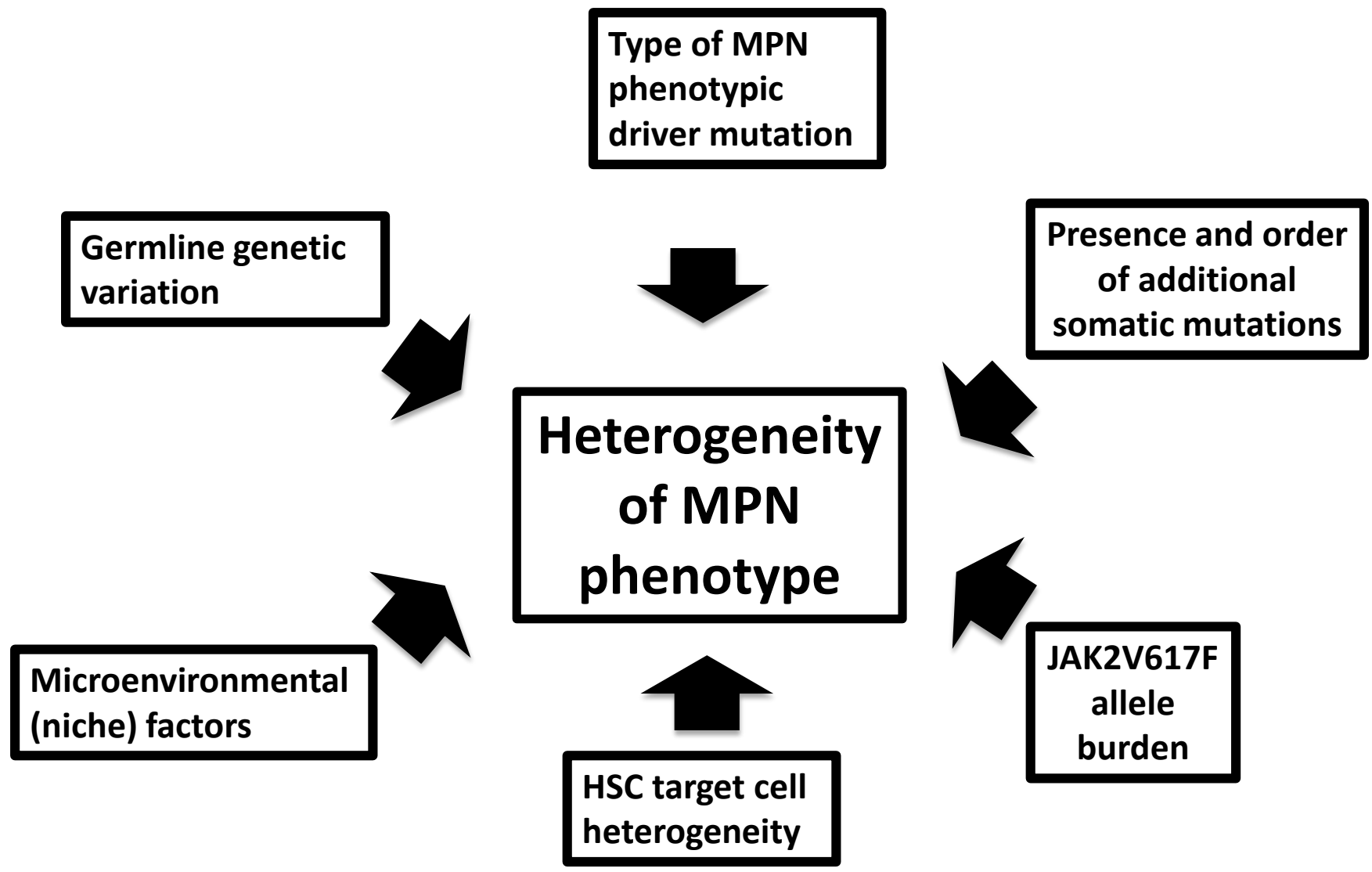


Figure 3

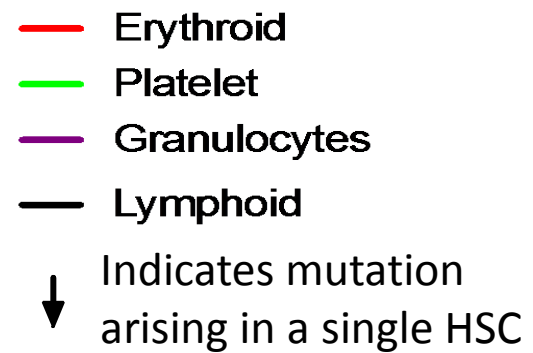
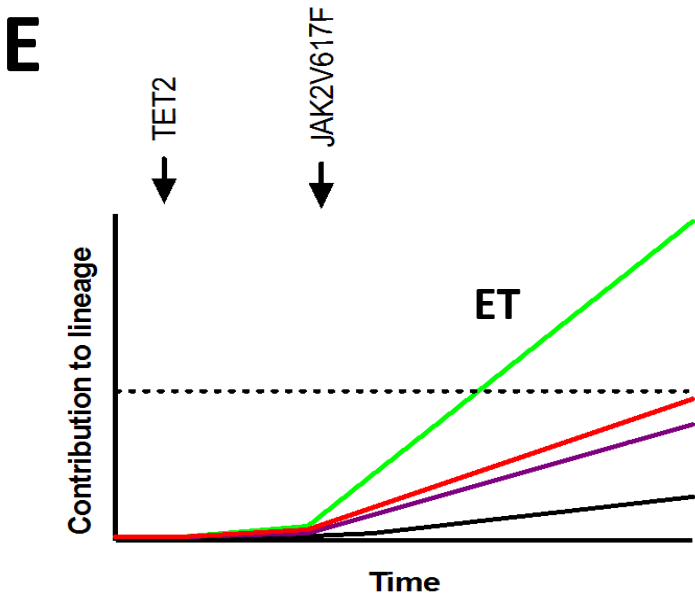
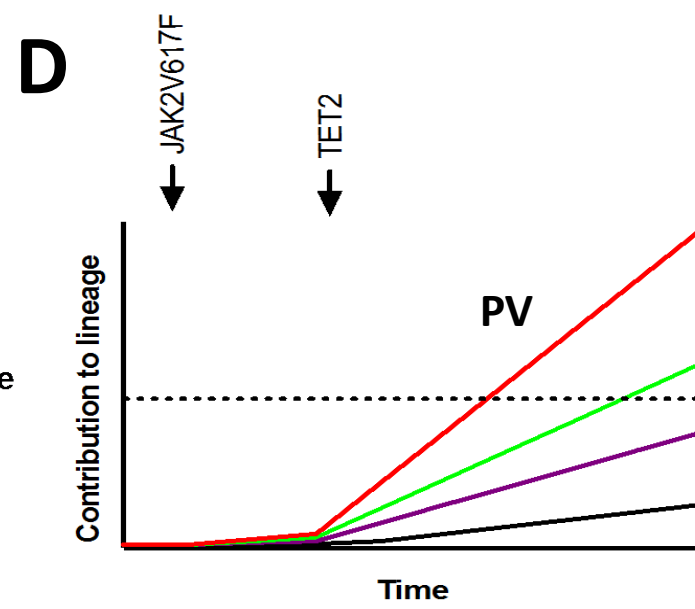
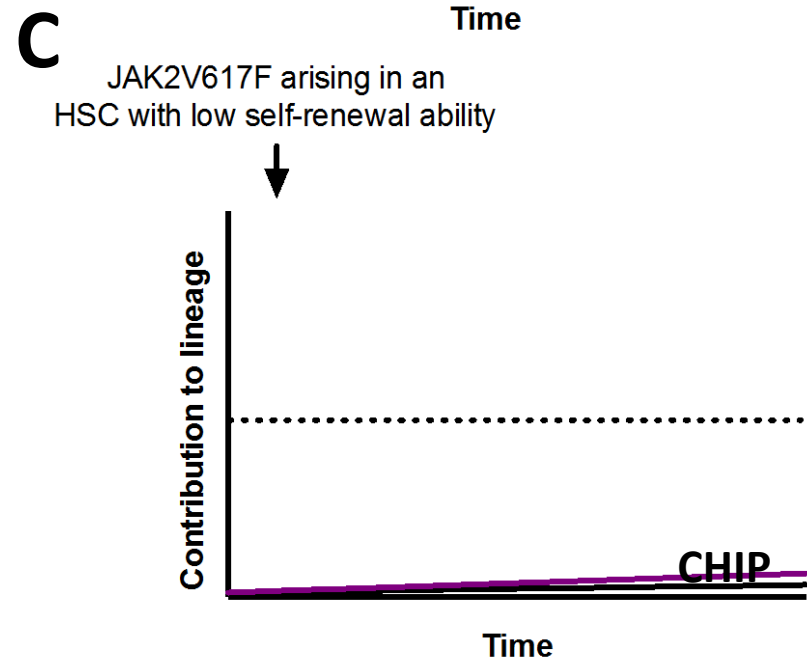
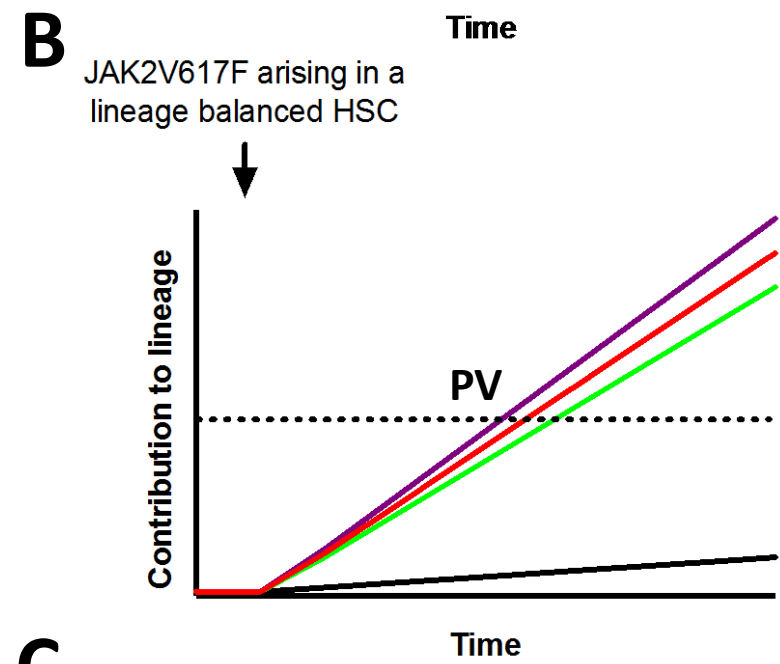
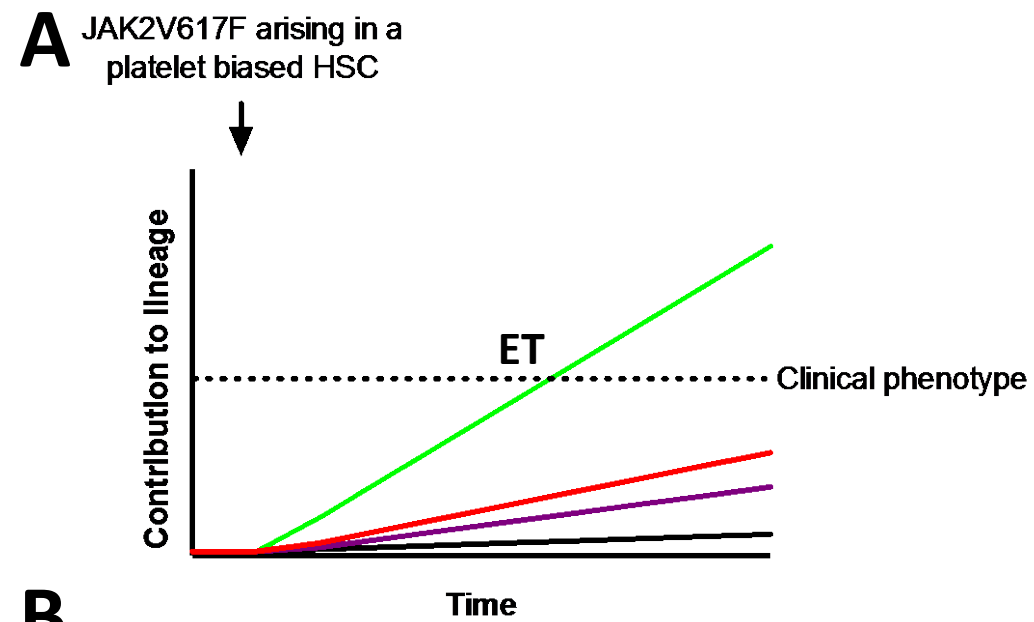


Figure 4