a

Cell-of-origin model

Subtype A

Subtype B

Subtype C

Stem cell
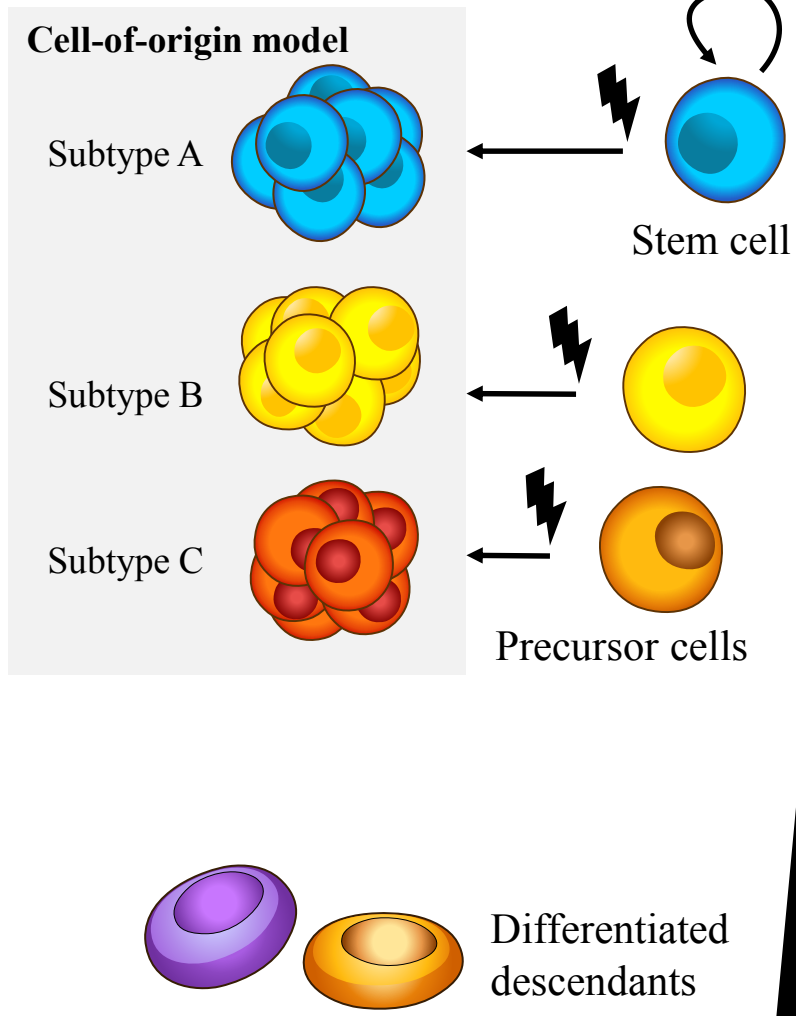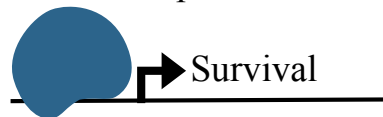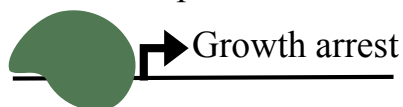
Precursor cells

Differentiated descendants

b

Lineage survival

lineage-associated transcription factors

Survival

Lineage differentiation

differentiation-associated transcription factors

Growth arrest

Tumor initiation

"Conditioned" genetic alterations

Tumor survival

lineage dependency and deregulation

Survival

Growth arrest

Tumor metastasis

adapted from Visvader (2011), Garraway and Sellers (2006)