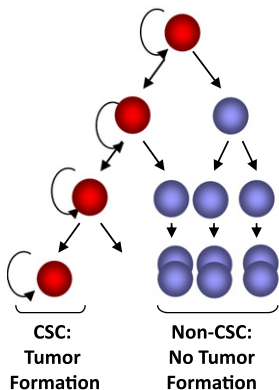


CSC model I



CSC model II

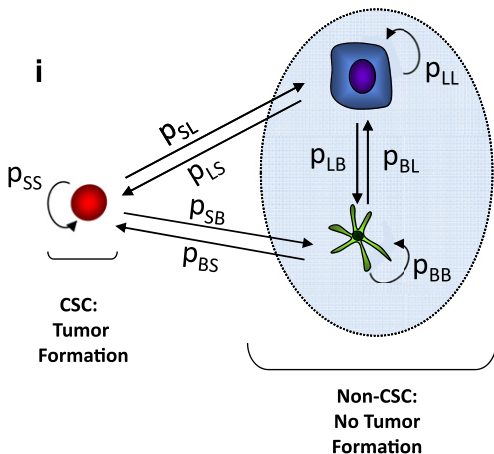


Figure 5. Two Distinct Models of Cancer Cell Populations

In the existing paradigm (model I), CSCs give rise to non-CSCs but not vice versa, resulting in a hierarchical cell-lineage structure reflective of normal tissue biology. We propose an alternative scenario (model II) in which there is bidirectional interconversion between CSC and non-CSC states. The rates of transition between cell states, which vary across distinct cancer cell populations, can be computed with the Markov modeling approach described in the main text and [Experimental Procedures](#).

ii

