What can single-cell profiling tell us about blood cancers?

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In some types of cancer, the same genetic alteration can result in drastically different disease phenotypes in different patients. For example, myeloproliferative neoplasm (MPN), arises when a hematopoietic stem cell (HSC) acquires a somatic driver mutation. The mutated HSC thereby gains a proliferative advantage over the other HSCs and gives rise to a disproportionately large population of differentiated blood cells that carry the same mutation. Intriguingly, the same somatic point mutation in the *JAK2* gene can give rise to an increase in the number of red blood cells, an increase in the number of platelets, or scarring of the bone marrow tissue, in different patients. This disconnect between genotype and phenotype is partly because the same mutation can have different consequences depending on the identity of the stem cell in which the mutation first occurs and the extent to which the population of mutated stem cells subsequently expands in each patient. Different HSCs –even within the same patient– can exhibit very different proliferation and differentiation dynamics. In addition, the dynamics of the expansion of the cancer stem cell population is potentially strongly stochastic; the population grows and shrinks from random fluctuations. I will discuss our recent efforts to understand this complex disease using emerging single-cell technologies and quantitative modeling.

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