Mechanistic computational modeling of blood stem cell dynamics in health and disease

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Stem cells play a crucial role in tissue maintenance, regeneration and cancer. The hematopoietic (blood forming) system is a paradigmatic example to study these phenomena. Hematopoiesis (blood cell formation) is hierarchically organized and maintained by hematopoietic stem cells (HSCs). In a multi-step process HSCs give rise to different types of increasingly specialized cells which eventually produce mature blood cells. Furthermore, during a process referred to as self-renewal, HSCs can give rise to HSCs which enables them to maintain or even expand their population throughout the life span of an organism. We combine mechanistic computational models with experimental and patient data to obtain insights into clinically relevant questions. The models are build on the level of cell populations and account for nonlinear feedback regulations. We apply them to better understand clinical interventions such as bone marrow transplantation and progression of malignant diseases such as acute myeloid leukemia, one of the most aggressive cancers. We focus on the following questions:

* How do kinetic cell properties (division rate, self-renewal probability) change during regenerative pressure?
* Which cell properties confer competitive advantages to leukemic cells?
* Which mechanisms drive clonal selection, therapy resistance and relapse?
* What is the role of systemic and micro-environmental feedbacks during leukemia progression?
* How can computational models contribute to prognostication and personalized medicine?