White Blood Cell Dynamics in Health and Disease - Insights from Mathematical Modeling

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Abstract: White blood cells (leukocytes) are required for immune defense. Their production is a tightly regulated process during which pluripotent hematopoietic stem cells (HSC) give rise to increasingly committed precursors which finally differentiate into leukocytes. The production of white blood cells has to be adapted to internal and external conditions such as blood loss, infections or chemotherapy. Recent experiments have uncovered the complexity of the regulatory mechanisms involved in these processes. We propose a combination of clinical data and quantitative mathematical modeling to study human leukocyte formation in different clinically relevant contexts. For that purpose we consider three scenarios (i) severe infection, (ii) bone marrow transplantation, and (iii) leukemia (blood cancer). All three conditions are linked to perturbations of regulatory feedback mechanisms. Based on multi-compartmental models formulated in the frameworks of ordinary differential equations, transport equations, and integro-differential equations we will address the following questions:

- How do HSC self-renewal and proliferation change if the demand for mature leukocytes increases? Which feedback mechanisms are required to explain clinical observations?
- How heterogeneous are HSC between individual patients? Are these differences clinically relevant?
- How do leukemic cells out-compete healthy blood cell formation? How do they respond to regulatory signals? Can we reduce the load of malignant cells by stimulating healthy blood cell formation?

Mathematical modeling is a powerful tool to rigorously analyze complex systems and to study how changes at the single cell level affect the organism. Our models help to reveal clinically relevant regulations of key HSC parameters such as proliferation and self-renewal and their impact on blood cell dynamics.

The talk is based on joint work with Anna Marciniak-Czochra (Institute of Applied Mathematics, Heidelberg University) and Anthony D. Ho (Heidelberg University Hospital, Department of Hematology and Oncology).

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