Mathematical modeling of heterogeneity and clonal selection in acute leukemias, Anna Marciniak-Czochra, Interdisciplinary Center for Scientific Computing (IWR), Institute of Applied Mathematics, University of Heidelberg, Germany

Abstract

Motivated by clonal selection observed in acute leukemias (AML and ALL), we propose a range of mathematical models describing evolution of a multiclonal and hierarchical cell population. The models are applied to study the role of self-renewal properties, growth kinetics and regulatory feedbacks during disease development and relapse. Effects of different time and space scales are investigated. It is shown how resulting nonlinear and nonlocal terms may lead to a selection process and ultimately to therapy resistance. Model results imply that enhanced self-renewal of cancer stem cells may be the key mechanism in the clonal selection process, while heterogeneity in the progenitor cell population does not play such a role in cancer evolution. Model-based interpretation of clinical data allows estimating parameters that cannot be measured directly. This may have clinical implications for future treatment Mathematical modeling of heterogeneity and clonal selection in acute leukemias

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