Characterization of the Molecular Biology of Normal and Leukemic Hematopoiesis

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It is well accepted that leukemia originates from normal hematopoietic stem or progenitor cells which have acquired critical genetic alterations leading to uncontrolled self-renewal and impaired differentiation of the leukemic cells. The institute focuses on characterizing key molecular events which cause malignant transformation of normal hematopoietic stem cells into leukemic stem cells using a wide panel of different murine models that mimic human leukemias. Using murine bone marrow transplantation assays and retroviral gene transfer, we were able to identify several novel regulators of normal and leukemic stem cells, such as \textit{VENTX} or \textit{CDX2}. Furthermore, we could demonstrate that genetic alterations have to collaborate to induce acute myeloid leukemias (AML), such as the fusion gene \textit{AML1-ETO} and the \textit{FLT3} length mutation. In addition, we used murine leukemia models to profile leukemic stem cells and to identify differences between normal and leukemic stem cells, and could thus show that in acute myeloid leukemia characterized by...
Selected Publications:


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- Petropoulos K, Arseni N, Schessl C, Stadler CR, Rawat VP, Deshpande AJ, Bohlander SK, Hiddemann W, Quintanilla-Martinez L, Buske C (2008): The fusion gene CALM-AF10 the leukemic stem cell differs from its normal counterpart by the expression of the lymphoid-associated antigen B220. Currently, the group focuses on the relevance of lymphoid antigen expression in acute myeloid leukemias (J. Huang*, M. Feuring-Buske), the role of the LEF1 in human AML (K. Edmaier*, C. Buske), the identification of novel regulatory genes of leukemic stem cells (E. Gentner*, C. Buske), the function of the TET protein family in normal and malignant hematopoiesis (F. Mohr*, VPS Rawat), the role of non-coding RNAs in human leukemogenesis (S. Ihme, M. Mulaw), and the biology of NPM1 mutated leukemias (A. Muranyi, C. Buske). For this research program, the institute has access to state-of-the-art FACS technology as well as to next generation sequencing technology.

Leukemic subfractions isolated from patients with acute myeloid leukemia (AML) harbor leukemic stem cells and engraft into NSG mice.