

## Gene expression profiling of differentiating hematopoietic stem cells identifies transcriptional dysregulation in haematological malignancies

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**Objective:** The development of haematological malignancies is suggested to follow a multistep pathogenesis and is characterized by accumulation of molecular defects of the hematopoietic stem/progenitor cells resulting in aberrant differentiation and proliferation.

**Methods:** To detect alterations within the transcriptional program in myelodysplastic syndrome (MDS) derived CD34+ cells during lineage-specific differentiation, we performed serial gene expression analysis of in vitro differentiated erythro-, granulo- and megakaryopoietic cells using oligonucleotide microarrays (HG-U133, Affymetrix, Santa Clara, CA). Disease-specific data were compared to data from differentiating stem cells from healthy individuals. For selected genes, expression data were confirmed using real-time PCR.

**Results:** First we could describe a complete lineage-specific transcriptional program of normal CD34+ cells during lineage-specific in-vitro differentiation. Furthermore, in MDS we identified genes with altered expression during lineage-specific differentiation in either low or high risk MDS cells compared to the expression patterns of continuously up- or down-regulated genes from the normal transcriptional program of hematopoiesis. In cluster analyses we could show that MDS samples have a distinct expression pattern of a set of selected genes compared to normal cells that allows to predict the affiliation of a sample to one group. Furthermore, this study gives an overview of genes that are differentially expressed in MDS cells compared to normal hematopoiesis.

**Conclusion:** Our data provide the first comprehensive transcriptional analysis of differentiating human CD34+ cells derived from MDS patients compared to normal individuals. It gives new insights to understand the alteration of differentiation and proliferation of MDS stem cells.

### Biography

Wolf-Karsten Hofmann has been Professor of Medicine and Head of the Department of Haematology and Oncology, University Hospital Mannheim, Germany, since May 2009. He received his medical degree in 1994 from the University of Jena, Germany. Until 2003, Professor Hofmann was a resident in the Department of Haematology and Oncology at the University of Frankfurt am Main, Germany. During that time, he was also board certified in internal medicine (2002) and haematology and oncology (2003), and completed a 2-year post-doctorate fellowship in the Department of Haematology and Oncology at the University of California – Los Angeles, CA, USA. From 2004 to 2009, he had the position of full professor of medicine at the Department of Haematology and Oncology, University Hospital Benjamin Franklin, Berlin, Germany. Professor Hofmann has focused his scientific activities on translational research projects, utilizing highthroughput molecular techniques for the genomic analysis of primary tumour cells from patients with haematological malignancies, in particular patients with myelodysplastic syndromes (MDS) and acute lymphoblastic leukaemia (ALL). His research group was the first to describe the complete transcriptional program of differentiating haemopoietic stem cells. He has been the Principal Investigator for a number of national and international clinical trials.