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

**Prof. Wolf-Karsten Hofmann**
*University Hospital Mannheim, Germany*

## Abstract

**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.