Expression of splice variants of the transcription factor ONECUT2 in Hodgkin lymphoma cells

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Introduction

We identified a new splice variant of the transcription factor ONECUT2 in a cDNA library from chemo-resistant L-1236 Hodgkin lymphoma cells. ONECUT2 was already described to play an important role as transcriptional regulator in other tumor entities. However, the existence and function of ONECUT2s, as far as we know, is not known by now. This new splice variant uses an alternative second exon compared to the reference sequence. In ONECUT2s, the sequence encoding the HOX domain is lost whereas the CUT domain is preserved. We compared the effects of ONECUT2 and ONECUT2s on gene expression in transfected cells.

Methods

Expression of ONECUT2 and ONECTUT2s was assessed by quantitative real-time polymerase chain reaction (qRT-PCR) and RNA-seq. ONECUT2 variants were cloned into eukaryotic expression plasmids. Differential gene expression in transfected cells was analyzed by RNA-seq and DNA microarray analysis. Immunofluorescence staining was used to locate the protein product of ONECUT2 in overexpressing cells.

Results

We found high expression of ONECUT2 and ONECUT2s in HL cell lines as well as in normal liver. Interestingly, overexpressed ONECUT2 was located predominantly in the cytoplasm and not in the nucleus. ONECUT2 and ONECUT2s transgenic cells showed differential expression of several genes. A higher number of genes were downregulated by both ONECUT2 variants. Interestingly, most genes upregulated by ONECUT2 remain unchanged in ONECUT2s transgenic cells.

Conclusion

The data suggests that ONECUT2 as well as ONECUT2s play important roles in the gene regulation of HL cells. ONECUT2s has only limited capacity for upregulation of target gene expression which might be explained by the missing HOX domain.