Kurztitel: Dissecting the role of the polycomb –like protein PHF19/PCL3 in acute myeloid leukemia (AML)

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Background

Overexpression of homeobox genes is one of the molecular hallmarks of human acute myeloid leukemia (AML). So far it is largely unknown which mechanisms induce deregulated homeobox expression in AML. Expression of homeobox genes is controlled by the so called 'Polycomb repressor complex' (PRC). The PRC2-associated polycomb-like proteins PHF1 and PHF19 act as epigenetic modifiers facilitating histone H3 lysine 36 trimethylation (H3K36me3) and H3K27me3 thereby mediating silencing of homeobox genes such as Hoxa5 and Meis1, both associated with human acute myeloid leukemia. In this project it will be tested whether PHF19 is downregulated in human AML, characterized by aberrant upregulaton of homeobox genes, thereby contributing to the establishment of aberrant overexpresson of leukemogenic homeobox genes in this disease. Furthermore, it will be evaluated whether this gene plays an essential role in epigenetically modifying the chromatin structure within the leukemic hierarchy, from leukemic stem cells to their differentiated downstream progeny.