

Ingenuity[®] Science Spotlight:

Articles featured in the Ingenuity Science Spotlight represent some of the best and most diverse examples of how IPA[®] has contributed to research across multiple platforms, research areas, and research goals.



New insights into MLL gene rearranged acute leukemias using gene expression profiling: shared pathways, lineage commitment, and partner genes.

A Kohlmann, C. Schoch, M. Dugas, S Schnittger, W. Hiddemann, W. Kern, and T. Haferlach . *Leukemia* (2005) 19, 953-964.

<http://www.ncbi.nlm.nih.gov/pubmed/15815718?dopt=Abstract>

In acute leukemia, the myeloid/lymphoid or mixed-lineage leukemia (MLL) gene, located at chromosomal band 11q23, is a recurrent target of chromosome translocation. The MLL fusion proteins play roles in signal transduction or transcriptional regulation during the oncogenic process. MLL gene rearrangements occur in both subtypes of leukemia, ALL (acute lymphoblastic leukemia) and AML (acute myeloid leukemia).

This study investigated global expression patterns and common target genes of ALL and AML leukemia subtypes, the MLL chimeric fusion genes, and how these fusion proteins affect the cellular properties of both myeloid and lymphoblastic lineages.

A series of 363 adult acute leukemia specimens were analyzed using the Affymetrix7 GeneChip7 U133 array sets. Although expression profiling indicated distinct expression signatures from two subtypes of leukemia, it could not clearly demonstrate an association between the differentially expressed genes and six partner genes that are known to interact with the MLL gene.

IPA helped identify molecular pathways and biological networks associated with leukemia. A biological network (Figure 3 in this paper) distinguished the t(11q23)/MLL from other acute leukemia subtypes. A group of up- or down-regulated common target genes associated with t(11q23)/MLL leukemia was specified. A network also identified genes expressed differently in ALL with t(11q23)/MLL compared to AML with t(11q23)/MLL, as displayed in Figure 5 in the paper. ALL and AML subtypes were segregated according to the lineages, lymphoblastic or myeloid, respectively. Signature genes were identified in ALL and AML subtypes from the pathways. PAX5, an early B-cell lineage commitment factor, restricts developmental progression of lymphoid progenitors to the B-cell pathway. An essential B-cell regulator, EBF, functions in early B cell lymphopoiesis. Novel functional networks helped to better understand these two acute leukemia subtypes, including the identification of therapeutic targets.