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Exploring lncRNA-mRNA signatures in induction therapy failure pediatric acute myeloid leukemia compared with primary tumors

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Long non-coding RNAs (lncRNAs) play a role in the pathogenesis of acute myeloid leukemia (AML) by affecting gene expression, including in pediatric AML. Deregulation of lncRNAs patterns has the potential to regulate tumor drug resistance and sustaining of leukemic stem cells. Here we investigated the expression patterns of lncRNAs and mRNAs in induction failure tumors compared to primary tumors, using TARGET-AML project data. We examined the molecular pathways for differentially expressed lncRNAs and mRNAs (using GO and LncPath) and constructed lncRNA-mRNA coexpression networks.

GO analysis showed that the most significantly enriched GO terms in upregulated genes were «Lymphocyte differentiation» (ontology: biological process), «Interleukin-2 receptor complex», «Interleukin-18 receptor complex» (ontology: cellular component) and « Interleukin-18 receptor activity» (ontology: molecular function). Downregulated genes were associated with such GO terms as «RDNA heterochromatin assembly», (ontology: BP), «Nucleosome», «DNA packaging complex» (ontology: CC) and «IgE binding», «Lipid antigen binding» (ontology: MF).

The lncRNA-mRNA co-expression networks were visualized using Cytoscape v.3.9.0. Figure 2 shows two networks of upregulated genes. Network A includes lncRNA AC007278.2 as a hub gene linked to 12 mRNAs and 5 lncRNAs; network B includes lncRNA LINC00472 as a hub gene linked to 1 mRNA and 1 lncRNA. Figure 3 shows the co-expression networks of downregulated genes with two hub lncRNAs LAMP5-AS1 and LINC00477 associated with 9 mRNAs and 1 lncRNA.

The lncRNA-mRNA landscape of induction failure tumors compared to primary tumors in pediatric AML is extremely inconsistent. In both upregulated networks and downregulated co-expression networks, there are parallel processes associated with the effects of therapy and mechanisms of drug resistance and immune system escape. Most of the genes involved in the interaction networks are nonspecific for a particular tumor type; intriguingly, some of them are associated with invasion processes that are not typical for hematological malignancies. Detailed studies of the resulting interactions using other pediatric AML datasets are needed to better understanding the current results.