exploited for other related malignancies (e.g. AML), of which glucocorticoids remain largely inefficacious.

Summary/Conclusion: Our results collectively indicate that CD9 negativity was definitively linked to glucocorticoid resistance, which could be partially reversed by CD9 reactivation through a NR3C1-independent mechanism. Comprehensive understanding of the interaction between CD9 and glucocorticoid susceptibility could lead to improved therapeutic strategies for resistant pediatric B-ALL. The findings could also be exploited for other related malignancies (e.g. AML), of which glucocorticoids remain largely inefficacious.

**PF168 KINASE AND CYTOKINE RECEPTOR SIGNALING PATHWAY ACTIVATING ALTERATIONS IN UNIFORMLY TREATED B-ALL**

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**Background:** Recent B-acute lymphoblastic leukemia (B-ALL) studies revealed a new subgroup of patients with ABL-class and JAK-STAT fusions, which can be targeted using small-molecule inhibitors (Roberts et al., 2017). Positivity for ABL-class or JAK-STAT fusions was associated with positive post-induction minimal residual disease (MRD) (Pui et al., 2017) and inferior outcome (Boer et al., 2017) but most studies were conducted in non-uniformly treated patient populations.

**Aims:** To identify kinase and cytokine receptor pathway activating alterations and determine their clinical significance in uniformly treated B-ALL.

**Methods:** The study includes 160 B-ABL-negative B-ALL (122 pediatric, 38 adults ≥18 y/o) patients treated according to MRD-driven pediatric-adult NOPOHALL-2008 protocol. 101 B-ALL cases (including high hyperdiploids and low hyperdiploids) without canonical B-ALL aberrations were selected for targeted RNA-Sequencing (RNA-Seq). Sequencing was performed using TruSight Pan-Cancer sequencing panel (Illumina Inc., CA). FISH analysis was used to identify CRLF2-IGH gene rearrangements.

**Results:** Of 101 B-ALL patients (75 pediatric, 26 adults), N-RAS and FISH analysis identified three (3%) cases with ABL-class (ABL1-ETV6, ABL2-ZC3HAV1, PDGFRB-EB1) fusions and four (4%) cases with JAK-STAT fusions (JAK2-BCR, n = 1; CRLF2-IGH, n = 3). Five of seven ABL-class and JAK-STAT mutually exclusive fusions were detected in adults, with remaining ten (9.9%) gene fusions were identified in the pediatric group, of which five cases had PAX5 gene and three had ZNF184 gene rearrangements.

Gene mutation analysis detected Ras pathway mutations in a total of 48 (47.5%) cases: NRAS (n = 21), KRAS (n = 17), PTPN11 (n = 7). Other JAK-STAT and FLT3-TKD gene mutations were present in 10 (9.9%) and 8 (7.9%) cases, respectively. Thirty-seven (36.6%) patients harbored other gene variants (n = 23) or had no recurrent gene variants/fusions (n = 14) detected by RNA-Seq.

ABL-class and JAK-STAT fusions were more frequent among adults than pediatric patients (19.2% vs. 2.7%) while ABL-class fusions were exclusive to adults (p = 0.032). The prognostic analysis was restricted to the adult group. More adult patients with ABL-class or JAK-STAT fusions had positive post-induction day 29 MRD values compared to negative patients (p < 0.001) and were more frequently assigned to NOPOH-2008 high-risk groups or had induction failure (80% vs 30.3%, p = 0.035). 75th percentile event-free (EFS) and overall survival (OS) were 5 vs. 3.5 (p = 0.008) and 15 vs. 37 (p = 0.07) months in ABL-class or JAK-STAT fusion positive vs. negative adult groups, respectively.

In multivariate analysis, the positivity for ABL-class or JAK-STAT fusions was an independent risk factor for worse EFS (p = 0.032) but not for OS (p = 0.24).

**Summary/Conclusion:** Overall, ABL-class and JAK-STAT fusions were infrequent and were more often detectable in adults compared to children. Adult patients with ABL-class or JAK-STAT fusions had higher post-induction MRD values and were more frequently assigned to high-risk disease groups or had induction failure resulting in lower event-free survival.
PF171 DIFFERENTIAL EXPRESSION PATTERNS OF SPECIFIC LONG NONCODING RNAs AND COMPETING ENDOGENOUS RNA NETWORK IN ACUTE LYMPHOCYTE LEUKEMIA

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Background: Increasing evidence has demonstrated that long non-coding RNAs (lncRNAs) play an important role in the competitive endogenous RNA (ceRNA) networks in that they regulate protein-coding gene expression by sponging microRNAs (miRNAs). However, the roles of specific lncRNA and its related competing endogenous RNAs (ceRNA) network in acute lymphocyte leukemia (ALL) are not fully understood.

Aims: The aims of this study were to use RNA expression profiles to perform bioinformatics analysis of RNA-seq data from cases of ALL from the Cancer Genome Atlas (TCGA), the Kyoto Encyclopedia of Genes and Genomes (KEGG), and the Gene Ontology (GO) database to construct a ceRNA network of miRNAs, IncRNAs, and lncRNAs.

Methods: All patient datasets were obtained from TCGA database. IncRNA and mRNA expression files included leukemia and corresponding normal samples were also downloaded from TCGA portal. An EdgeR (empirical analysis of digital gene expression data) R package was used to identify the RNAseq data of acute lymphoblastic leukemia. Only the differential expression genes (DEGs) with adj.Pval < 0.05 and log2 fold change (FC) ≥ 2 were considered as significant. Based on bioinformatics generated from mircode, starBase, and mirTarBase, we constructed an IncRNA-miRNA-mRNA network (ceRNA network) in ALL. Database for annotation, visualization, and integrated discovery (DAVID), was used for GO analysis to understand the functions of targeted genes in terms of biological process (BP), cellular component (CC) and molecular function (MF). In addition, KEGG and an R Package, clusterProfiler, was distinguished pathway enrichment of each targeted gene. Cutoff value was set as P value < 0.05.

Results: We found 755 differentially expressed IncRNAs and 6131 differentially expressed genes (DEGs). The functional enrichment indicated that the DEGs mainly regulated the pathways of programmed cell death, cell cycle, apoptosis and so on. Through integrated IncRNA-mRNA and miRNA-mRNA pairs, the ceRNA network was constructed. The resulting ceRNA network included 395 mRNAs, 135 IncRNAs and 31 miRNAs. 18 out of the 135 IncRNAs (RP11-497G19.2, LOC339535, LA16c-32F2.1, AK127310, XLOC_006664, RPI1-16A4.1, RPI1-698.3, LOC100507254, KB-1183DS.14, LOC100506305, RPI1-87C12.5, WASR1, RPI3-523C21.1, RPI1-32F22.2, AC02454.1, LOC286367, LOC286367, RPI3-523C21.2) were identified and found to be associated with the complete remission rate of ALL patients (P < 0.05)