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618.ACUTE LYMPHOBLASTIC LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Pre-Clinical Developmental Hematopoiesis Demonstrates the Heterogeneity of KMT2A-Rearranged Infant Acute Lymphoblastic Leukemic Populations

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KMT2A-rearranged (KMT2A-r) infant acute lymphoblastic leukemia (ALL) has a poor prognosis with increased risk of relapse when diagnosed at younger ages. Understanding the origin of these leukemic cells is crucial to comprehend disease development and prognosis differences. The unclear delineation of the identity of early blood populations in humans is a challenge in defining the cell type(s) driving this infant ALL. Recent pre-clinical studies revealed that definitive hematopoietic stem cells (HSCs) have minimal contribution to embryonic hematopoiesis, while independently arising embryonic hematopoietic progenitors (HPCs) that possess more limited self-renewal and/or multilineage differentiation capacities, are both necessary and sufficient to sustain the developing embryo. Here, we aim to leverage pre-clinical knowledge on the markers that distinguish HSCs from HPCs to investigate the potential contribution of HPCs in driving prenatal and infant leukemias. We defined transcriptional signatures from developmental HSC and HPC populations using thirteen single cell RNA sequencing (scRNA-seq) datasets from zebrafish, eight datasets generated by our research group and five from independent published studies. We then employed a neural network approach to define the orthologous cell type signatures most likely correlating with human healthy and blast cells from publicly available data of 18 KMT2A-r infant ALL patients. In accordance with previous literature, HSC and lymphomyeloid progenitor signatures are both highly represented in the leukemic blast populations. Additionally, we found subpopulation differences in gene expression within leukemic blasts cells including lymphoid progenitor, granulocytic, and T cell signatures, possibly suggesting heterogeneity in either their cell type of origin or developmental differentiation potential. Our findings support the ability to use orthologous scRNA-seq to decipher new understanding on the role of HSCs and HPCs in hematological malignances affecting infants and children.

Disclosures No relevant conflicts of interest to declare.

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