Philadelphia chromosome-like acute lymphoblastic leukemia

Philadelphia chromosome-like acute lymphoblastic leukemia (Ph-like ALL) is a subtype of acute lymphoblastic leukemia (ALL) that is characterized by the presence of genetic abnormalities similar to those found in Philadelphia chromosome-positive ALL (Ph-positive ALL), but without the typical Philadelphia chromosome (Ph) translocation.

Ph-like ALL is caused by a variety of genetic abnormalities that result in the activation of genes that are normally not expressed in normal lymphoid cells. This abnormal gene expression can lead to uncontrolled cell growth and the development of leukemia.

Ph-like ALL is more common in children and young adults and is associated with a poor prognosis. However, recent advances in targeted therapies, including tyrosine kinase inhibitors (TKIs), have shown promise in the treatment of Ph-like ALL.

Diagnosis of Ph-like ALL is made through genetic testing and bone marrow biopsy. Treatment may include chemotherapy, radiation therapy, and stem cell transplantation, in addition to targeted therapies such as TKIs. Prognosis depends on factors such as age, white blood cell count, and response to treatment.

Incomplete understanding of the heterogeneity within the tumor cells presents a major challenge for the diagnosis and therapy of Ph-like ALL.

Zhang et al. exhibited a comprehensive cell atlas of one Ph-like ALL patient with a novel TPR-PDGFRB fusion gene at diagnosis and relapse by using single-cell RNA sequencing (scRNA-seq). Twelve heterogeneous B-cell clusters, four with strong MKI67 expression indicating highly proliferating B cells, were identified. A relapse-enriched B-cell subset associated with poor prognosis was discovered, implicating the transcriptomic evolution during disease progression. Integrative single-cell analysis was performed on Ph-like ALL and Ph+ ALL patients, and revealed Ph-like specific B-cell subpopulations and shared malignant B cells characterized by the ectopic expression of the inhibitory receptor CLEC2D. Collectively, scRNA-seq of Ph-like ALL with a novel TPR-PDGFRB fusion gene provides valuable insights into the underlying heterogeneity associated with disease progression and offers useful information for the development of immunotherapeutic techniques in the future [1)]

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Zhang X, Hou Z, Huang D, Wang F, Gao B, Zhang C, Zhou D, Lou J, Wang H, Gao Y, Kang Z, Lu Y, Liu Q, Yan J. Single-cell heterogeneity and dynamic evolution of Ph-like acute lymphoblastic leukemia patient with novel TPR-PDGFRB fusion gene. Exp Hematol Oncol. 2023 Feb 17;12(1):19. doi: 10.1186/s40164-023-00380-8. PMID: 36797781.