

Modelling of childhood acute lymphoblastic leukemia in zebrafish

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Acute lymphoblastic leukemia (ALL) represents the most prevalent type of cancer in children, with its complexity and variation in genetic backgrounds demanding sophisticated models for in-depth study. We have developed a novel zebrafish model for childhood ALL, focusing on the ETV6:RUNX1 gene fusion, a hallmark of approximately 25% of pediatric ALL cases. Utilizing CRISPR/Cas9 technology, the model incorporated this fusion alongside secondary mutations in *pax5* and *cdkn2a/b* genes, closely mirroring the disease's genetic underpinnings in humans. Results indicated an enlarged progenitor cell population, while leukemia development required additional genetic events, reflecting the disease's multistage progression. Importantly, RNA sequencing analyses revealed that the zebrafish model accurately recapitulated the transcriptional profile of human ALL, confirming its B-lineage origin and providing new insights into the leukemia's molecular drivers. This model not only deepens our understanding of ALL pathogenesis but also serves as a convenient platform for testing novel therapeutic interventions. Looking forward, the zebrafish model opens new avenues for dissecting the intricate molecular pathways involved in ALL pathogenesis and holds promise for the development of targeted therapies, potentially helping to improve treatment strategies for this childhood cancer.