Unraveling why children with Down syndrome have increased leukemia risk

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Children with Down syndrome (DS) have an increased risk of developing leukemia, in particular acute megakaryoblastic leukemia (AMKL) and acute lymphoblastic leukemia (ALL). Through their studies in a mouse model of DS, a team of researchers led by John Crispino, at Northwestern University, Chicago, has now identified a potential explanation as to why children with DS are at increased risk of AMKL. In doing so, they have also identified a candidate therapeutic target.

DS is a genetic condition in which a person has an extra copy of chromosome 21 (they have 3 copies rather than 2). It is not clear, however, which genes on chromosome 21 are responsible for the increased risk of developing leukemia observed in children with DS. Crispino and colleagues found that increased expression of the protein templated by the chromosome 21 gene Dyrk1a promotes AMKL in a mouse model of DS. Interestingly, an inhibitor of DYRK1A activity inhibited the in vitro growth of AMKL cells lines from individuals with DS. Crispino and colleagues therefore suggest that developing small-molecule inhibitors of DYRK1A activity may have therapeutic potential for DS-AMKL.

Shai Izraeli and Yehudit Birger, at Sheba Medical Center, Israel, second this idea in an accompanying commentary.

More information: Increased dosage of the chromosome 21 ortholog Dyrk1a promotes megakaryoblastic leukemia in a murine model of Down syndrome. View this article at: www.jci.org/articles/view/6045 … ebdcc7eb0722a8d27c0b

DYRK1A in Down Syndrome: an oncogene or tumor suppressor? View this article at: www.jci.org/articles/view/6237 … 3ae146d8c86858ca1679

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