REGIONAL CENTRE FOR BIOTECHNOLOGY
Journal Club

"STAT3 mediates oncogenic addiction to TEL-AML1 in t(12;21) acute lymphoblastic leukemia"
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Seminar room, ATPC building

Abstract

The t(12;21)(p13;q22) translocation is the most common chromosomal abnormality in pediatric leukemia. Although this rearrangement involves 2 well-characterized transcription factors, TEL and AML1, the molecular pathways affected by the result of the translocation remain largely unknown. Also in light of recent studies showing genetic and functional heterogeneities in cells responsible for cancer clone maintenance and propagation, targeting a single common deregulated pathway may be critical for the success of novel therapies. Here we describe a novel signaling pathway that is essential for oncogenic addiction in TEL-AML1 leukemia. Our data indicate a direct role for TEL-AML1, via increasing the activity of RAC1, in regulating the phosphorylation of signal transducer and activator of transcription 3 (STAT3), which results in transcriptional induction of MYC. We demonstrate that human leukemic cell lines carrying this translocation are highly sensitive to treatment with S3I-201, a specific STAT3 inhibitor, and, more interestingly, that primary human leukemic samples are also responsive to the drug in the same concentration range. Thus, STAT3 inhibition represents a promising possible therapeutic strategy for the treatment of TEL-AML1 leukemia.