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# Twist2 Is a Key Regulator of Cell Proliferation in Acute Lymphoblastic Leukaemia

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**Abstract :** Background: Acute lymphoblastic leukaemia (ALL) is the most frequent type of childhood malignancy, accounting for 25% of all cases. TWIST2, a basic helix-loop-helix transcription factor, has been implicated in ALL development. Prior studies found that TWIST2 undergoes epigenetic silencing in more than 50% cases of ALL through promoter hypermethylation and suggested that re-expression of TWIST2 may inhibit cell growth/survival of leukaemia cell lines. TWIST2 has also been implicated as a regulator of NF-kappaB activity, which is constitutively active in leukaemia. Here, we use a lentiviral transductions system to confirm the importance of TWIST2 in controlling leukaemia cell growth and to investigate whether this is achieved through altered regulation of NF-kappaB activity. Method: Re-expression of TWIST2 in leukaemia cell lines was achieved using lentiviral-based transduction. The lentiviral vector also expresses enhanced green fluorescent protein (eGFP), allowing transduced cells to be tracked using flow cytometry. Analysis of apoptosis and cell proliferation were done using annexinV and VPD450 staining, respectively. Result and Discussion: TWIST2-expressing cells were rapidly depleted from a mixed population in ALL cell lines (NALM6 and Reh), indicating that TWIST2 inhibited cell growth/survival of ALL cells. In contrast, myeloid cell lines (HL60 and K562) were comparatively insensitive to TWIST2 re-expression. Analysis of apoptosis and cell proliferation found no significant induction of apoptosis, but did find a rapid induction of proliferation arrest in TWIST2-expressing Reh and NALM6 cells. Initial experiment with NF-kappaB inhibitor demonstrated that inhibition of NF-kappaB has similar impact on cell proliferation in the ALL cell lines, suggesting that TWITST2 may induce cell proliferation arrest through inhibition of NF-kappaB. Conclusion: The results of this study suggest that epigenetic inactivation of TWIST2 in primary ALL leads to increased proliferation, potentially by altering the regulation of NF-kappaB.

**Keywords :** leukaemia, acute lymphoblastic leukaemia, NF-kappaB, TWIST2, lentivirus
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