ABSTRACT

THESIS: TAL1 and the atypical NF-κB heterodimer p65/c-Rel in T-cell acute lymphoblastic leukemia

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T-ALL accounts for 15% of childhood leukemias and approximately 60% of patients overexpress TAL1. TAL1/SCL encodes a transcription factor that regulates hematopoiesis by dimerizing with additional transcription factors including E12, E47, and GATA-1. TAL1 has also been found to repress expression of NF-κB1, potentially promoting formation of an NF-κB p65/c-Rel heterodimer that encourages cell survival by up-regulating IAPs and IκB. However, the correlation between TAL1 and p65/c-Rel expression and their effects on downstream targets like IKK, IκB, and other anti-apoptotic proteins is poorly understood. Jurkat cells, expressing TAL1, were treated with TNFα and/or etoposide to induce apoptosis and experiments were performed to assess the expression of proteins of interest. Caspase-8 activity assays were also performed to help delineate the apoptotic signal present in these cells. Determining if interactions between TAL1, NF-κB, and other downstream targets help promote apoptotic resistance will further research into better, more targeted treatments for T-ALL.