IL-5 inhibits apoptosis by up-regulation of c-myc expression in human hematopoietic cells

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Abstract

Interleukin-5 (IL-5) induction of c-Myc expression is associated with IL-5 inhibition of apoptosis in hematopoietic cells. In this study, TFalpha1 and TFalpha8 cells with stable overexpression of IL-5 receptor alpha (IL-5Ralpha) subunit in TF-1 cells, a human hematopoietic progenitor cell line which expressed low levels of IL-5Ralpha, were used to explored how IL-5 up-regulate c-Myc and the role of c-Myc in IL-5 signaling. First, we demonstrate that IL-5 induced c-Myc RNA and protein expressions, as well as activated Janus kinases (JAK1 and JAK2) and signal transducer and activator of transcription-5b (STAT5b). JAK inhibitor AG490 and c-Myc inhibitor 10058-F4, both, reduced IL-5-mediated cell proliferation in a dose- and time-dependent manner. Both, AG490 and 10058-F4, also reduced IL-5-mediated anti-apoptotic activity. Furthermore, AG490 inhibited IL-5-mediated c-Myc induction and promoter activity. We further examined the role of JAK1 and JAK2 in the induction of c-Myc expression using the CDJAK fusion proteins, which consisted of a CD16 extracellular domain, a CD7 transmembrane domain, and either JAK1 (CDJAK1) or JAK2 (CDJAK2) as intracellular domains. Simultaneous activation of JAK1 and JAK2 by anti-CD16 antibody crosslinking of CDJAK1 and CDJAK2 could induced c-Myc expression and promoter activity; AG490 inhibited CDJAK1 and CDJAK2-mediated effects. These results suggest that IL-5 induces cell proliferation and anti-apoptosis through the JAK/c-Myc pathway, and that JAK1 and JAK2 activation participate in IL-5-induced up-regulation of c-Myc.