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# STAT Transcription Factors in Tumor Development and Targeted Therapy of Malignancies

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Additional information is available at the end of the chapter

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## 1. Introduction

The signal transducers and activators of transcription, STAT proteins, were originally discovered in interferon (IFN)-regulated gene transcription in the early 1990's. Since then, a number of cytokines have been recognized to activate various STAT proteins. STATs constitute a family of seven transcription factors, STAT1 $\alpha/\beta$ , STAT2, STAT3 $\alpha/\beta$ , STAT4, STAT5A, STAT5B and STAT6, that transduce signals from a variety of extracellular stimuli initiated by different cytokine families that aside from interferons (interferon  $\alpha$ ,  $\beta$  and  $\gamma$ ) include gp130 cytokines, i.e., IL-6, IL-12, IL-23 and  $\gamma$ C cytokines that include IL-2, IL-15 and IL-21 [1].

Although structurally similar, the seven STAT family members possess diverse biological roles and are engaged in numerous processes from embryonic development, organogenesis, cell differentiation to regulation of immune processes. Awareness of their important role in regulation of cell proliferation, differentiation and survival has spurred interest in investigation of their activity in malignant transformation [2]. Evidence has now accumulated that confirms their role in pathogenesis of leukemias and numerous solid tumors [3] (Table1).

Aside from cytokine receptors, STATs are also activated by receptors for growth factors (family of tyrosine kinase receptors) that include receptors for epidermal growth factor - EGFR, platelet-derived growth factor - PDGF, hepatocyte growth factor - HGF and colony-stimulating factor 1- CSF-1 receptors that possess an intrinsic tyrosine kinase activity [4]. These receptors may activate STAT proteins either directly or indirectly by means of JAK kinase proteins. Also, free intracellular enzymes, i.e., non-receptor tyrosine kinases that include oncogenes *src* and *bcr-abl* activate various STATs [5].



































































