Association of Transcription Factor YY1 with the High Molecular Weight Notch Complex Suppresses the Transactivation Activity of Notch

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Abstract

Notch receptors are evolutionarily conserved from Drosophila to human and play important roles in cell fate decisions. After ligand binding, Notch receptors are cleaved to release their intracellular domains. The intracellular domains, the activated form of Notch receptors, are then translocated into the nucleus where they interact with other transcriptional machinery to regulate the expression of cellular genes. To dissect the molecular mechanisms of Notch signaling, the cellular targets that interact with Notch1 receptor intracellular domain (N1IC) were screened. In this study, we found that endogenous transcription factor Ying Yang 1 (YY1) was associated with exogenous N1IC in human K562 erythroleukemic cells. The ankyrin (ANK) domain of N1IC and zinc finger domains of YY1 were essential for the association of N1IC and YY1 according to the pull-down assay of glutathione S-transferase fusion proteins. Furthermore, both YY1 and N1IC were present in a large complex of the nucleus to suppress the luciferase reporter activity transactivated by Notch signaling. The transcription factor YY1 indirectly regulated the transcriptional activity of the wild-type CBF1-response elements via the direct interaction of N1IC and CBF1. We also demonstrated the association between endogenous N1IC and intrinsic YY1 in human acute T-cell lymphoblastic leukemia cell lines. Taken together, these results indicate that transcription factor YY1 may modulate Notch signaling via association with the high molecular weight Notch complex.