The CBF1-independent Notch1 signal pathway activates human c-myc expression partially via transcription factor YY1

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Abstract

Transcription factor Ying Yang 1 (YY1) indirectly regulates the C promoter-binding factor 1 (CBF1)-dependent Notch1 signaling via direct interaction with the Notch1 receptor intracellular domain (N1IC) on CBF1-response elements. To evaluate the possibility that the N1IC might modulate the gene expression of YY1 target genes through associating with YY1 on the YY1-response elements, we herein investigated the effect of Notch1 signaling on the expression of YY1 target genes. We found that the N1IC bound to the double-stranded oligonucleotides of YY1-response element to activate luciferase activity of the reporter gene with YY1-response elements through a CBF1-independent manner. Furthermore, the N1IC also bound to the promoter of human c-myc oncogene, a YY1 target gene, to elevate c-myc expression via a CBF1-independent pathway. The activation of reporter genes with YY1-response elements or human c-myc promoter by N1IC depended on the formation of N1IC–YY1-associated complex. To delineate the role of the Notch signal pathway in tumorigenesis, K562 cell lines expressing the N1IC were established. Compared with control cells, the proliferation and the tumor growth of N1IC-expressing K562 cells were suppressed. Taken together, these results suggest that the N1IC enhances the human c-myc promoter activity that is partially modulated by YY1 through a CBF1-independent pathway. However, the enhancement of c-myc expression by N1IC is insufficient to promote the tumor growth of K562 cells.