The activated Notch1 receptor cooperates with alpha-enolase and MBP-1 in modulating c-myc activity

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Abstract

The Notch signal pathway plays multifaceted roles to promote or suppress tumorigenesis. The Notch1 receptor intracellular domain (N1IC), the activated form of the Notch1 receptor, activates the c-myc proto-oncogene. The complex of N1IC and transcription factor YY1 binds to the human c-myc promoter to enhance c-myc expression in a CBF1-independent manner. Here we demonstrated that N1IC interacted with the c-Myc-regulating proteins -enolase and c-myc promoter binding protein 1 (MBP-1). Both -enolase and MBP-1 suppressed the N1IC-enhanced activity of the c-myc promoter in a CBF1-independent manner. The YY1 response element in front of the P2 c-myc promoter was essential and sufficient for the modulation of c-myc by N1IC and -enolase or MBP-1. Furthermore, N1IC, YY1, and -enolase or MBP-1 but not CBF1 bound to the c-myc promoter through associating with the YY1 response element. Hemin-induced erythroid differentiation was suppressed by N1IC in K562 cells. This suppression was relieved by the expression of -enolase and MBP-1. In addition, both -enolase and MBP-1 suppressed the N1IC-enhanced colony-forming ability through c-myc. These results indicate that the activated Notch1 receptor and -enolase or MBP-1 cooperate in controlling c-myc expression through binding the YY1 response element of the c-myc promoter to regulate tumorigenesis.