NACK and INT coordinately activate Notch-mediated transcription in tumorigenesis

Elena Shersher
Mohini Lahiry
Annamil Alvarez-Trotta
Giulia Diluvio
David Robbins
Ramin Shiekhattar
Anthony J. Capobianco

Video Byte

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Abstract

Transcriptional regulation is an important and complex process whose dysregulation can lead to disease. For example, aberrant activation of signaling involving the transcriptional activator Notch drives many processes in tumor formation. However, the exact mechanism by which Notch regulates transcription remains unclear. To find out more, researchers recently used various protein biochemistry and molecular biology approaches to analyze the composition and functions of the Notch supercomplex. They found that the INT complex is part of the Notch transcriptional supercomplex and works together with NACK to activate Notch-mediated transcription. Specifically, NACK is needed for recruitment of the transcribing enzyme RNAPII to Notch-dependent gene promoters, while the INT complex is needed for phosphorylation of RNAPII at serine 5, which induces transcription. The study also revealed that INT subunits were overexpressed in esophageal adenocarcinoma cells, while silencing of the subunit INTS11 caused cell cycle arrest, cell growth arrest, and cell death in esophageal adenocarcinoma cells, indicating that INT helps cancer cells proliferate. Although additional research is needed, the findings identify INT as a new co-factor in Notch-mediated transcription that coordinates with NACK to activate Notch target genes and promote cancer cell proliferation.