β-catenin and TCFs/LEF signaling discordantly regulate IL-6 expression in astrocytes

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Video Byte

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Abstract

Inflammation in the brain is a hallmark of many neurodegenerative diseases, including Alzheimer's and Huntington's disease. One of the key orchestrators of neuroinflammation is IL-6, a cytokine secreted by brain-resident cells called astrocytes. While low levels of IL-6 support neurons and synapses in the brain, higher levels of IL-6 are produced in response to injury or infection, triggering a series of proinflammatory signaling cascades. Unfortunately, how astrocytes regulate IL-6 expression remains unclear. A recent study evaluated signaling pathways involved in IL-6 gene regulation, including β-catenin, TCFs/LEF, C/EBP, and NF-κB. Using human astrocytes, researchers silenced or overexpressed the signaling proteins and measured IL-6 levels. They found that TCF/LEF induces IL-6 in the presence of ATF2, while β-catenin inhibits IL-6 by interacting with TCF/LEF. Interestingly, neither of these signaling pathways is known to regulate IL-6 in other cell types. The discovery of this novel mechanism of IL-6 control in astrocytes may help to inform brain-specific treatment targets for neuroinflammation providing new hope for those struggling with neuroinflammatory and neurodegenerative diseases.