Regulation of STING expression via the RIG-I dependent RNA sensing pathway

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The cytoplasmic pattern recognition receptor RIG-I is essential for recognizing RNA viruses with a 5' triphosphate (ppp) signature. Upon viral RNA recognition, RIG-I recruits adaptor protein MAVS to trigger the activation of IRF3 and NF-kB transcription factors through TBK1-IKK complexes, leading to the production of type I IFNs (α, β), pro-inflammatory cytokines, and antiviral factors. STING has been identified as an RIG-I signaling cofactor and a critical adaptor protein in a recently identified cGAS-mediated cytosolic DNA sensing pathway. In a recent functional study aiming to gain system-wide insight into downstream effector function of RIG-I, we identified STING among a plethora of differentially expressed genes induced by the RIG-I agonist 5’ppp RNA; in the present study, we further detail the mechanism of STING regulation. Our data shows that Sendai virus (SeV) infection induces STING expression at both the mRNA and protein levels in various cell types including A549, Huh7, PC3, and U87. Furthermore, by employing multiple RIG-I deficient or pathway-impaired cell lines, STING induction is shown to be dependent on functional RIG-I signaling. STING induction by the RIG-I agonist 5’ppp RNA was recognized as a delayed event resulting from an autocrine/paracrine mechanism. Indeed, co-treatment with TNFα and IFNα has a synergistic effect on the regulation of STING expression. Following SeV infection or TNFα-IFNα combined treatment, STING induction is partially decreased by siRelA or siIRF3; and is strongly diminished under combined siRelA and siIRF3 condition. Taken together, these observations demonstrate that STING expression is regulated via RIG-I signaling.

Biography

Rongtuan Lin is an Associate Professor in the Department of Medicine, McGill University and a Senior Investigator at the Lady Davis Institute for Medical Research. He received his PhD degree from Concordia University and completed Post-doctoral training at the Lady Davis Institute for Medical Research. He has authored more than 120 publications and has served on several grant review panels. He made important contributions in the fields of innate antiviral immunity.

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