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Ester alkaloids from *Cephalotaxus* interfere with the type I interferon pathway

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Inappropriate recognition of self-DNA contributes to interferonopathy and promotes autoimmune diseases like Systemic Lupus Erythematosus (SLE) and chronic polyarthritis. The cyclic GMP-AMP Synthase-Stimulator of Interferon Genes (cGAS-STING) pathway plays an important role in production of inflammatory cytokines. To identify potential suppressors of STING-Induced type I interferon (IFN) induction, 70% ethanol extracts of medicinal plants were screened for inhibitory activity against IFN-β promoter activation. As a result 70% ethanol extract of *Cephalotaxus koreana* specifically down-regulated STING-induced, but not *TBK1*- or *IRF3*-induced, IFN-β promoter activity. The compounds exerting inhibitory activity specifically against STING-mediated IFN-β promoter activation in 70% ethanol extract of *Cephalotaxus koreana* were identified as ester alkaloids, homoharringtonine and harringtonine. These two compounds inhibited 2'3'-cGAMP-induced IFN-stimulated gene expression and interaction between STING and *TBK1*. These suppressive effects were not observed with cephalotaxine devoid of the ester side-chain. Our data support the potential utility of homoharringtonine and harringtonine to treat STING-associated interferonopathy and autoimmune diseases.

Biography

Ga-Young Park is currently pursuing his graduation from the Department of Life Science at Gachon University, Republic of Korea.

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