Conference abstract PO-41

Screening for Discovery of Novel Peroxisome Proliferator-Activated Receptor-alpha and -gamma Agonists and Nuclear Factor-κB Inhibitors by Luciferase Reporter Gene Assays

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Peroxisome proliferator-activated receptors (PPARs) are transcription factors that belong to the nuclear receptor super family and represent promising therapeutic targets for several inflammatory and metabolic disorders. Nuclear factor-κB (NF-κB) is also a well-known transcription factor that regulates genes involved in inflammation. Agonists of PPARs and inhibitors of NF-κB have been reported to be beneficial in combating inflammation-related diseases and metabolic syndrome. Methods for PPAR-alpha and -gamma agonists and NF-κB inhibitor screening were established in cell-based assays. For PPAR-alpha and -gamma agonist screening, HEK293 cells were transiently cotransfected with PPAR-alpha or -gamma as a receptor plasmid and PPAR response element coupled with luciferase (PPRE-Luc) as a reporter plasmid. Once PPARs are activated by agonists, luciferase is produced by the transfected cells. Enhanced Green Fluorescence Protein (EGFP) was also cotransfected in this assay as an internal control to normalize the transfection efficiency. Inhibitors of NF-κB were screened using stably transfected HEK293 cells. Upon TNF-α stimulation, NF-κB is activated in these cells and luciferase is produced, which could be blocked by NF-κB inhibitors. Six plants traditionally used as anti-inflammatory remedies, each extracted in 4 different ways, were tested to find plant sources of PPAR-alpha and -gamma agonists. Of the 24 extracts tested, just extracts from leaves of *Urtica dioca* were detected to activate PPAR-alpha and/or -gamma, as well as to inhibit NF-κB activation. The method developed can be simply and rapidly performed to detect PPAR agonists and NF-κB inhibitors in plant extracts and thus to identify novel natural compounds as candidates for the treatment of inflammation-related diseases and the metabolic syndrome.

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