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MEETING ABSTRACTS

GENISTEIN, A PHYTOESTROGEN IN SOYBEAN, INDUCES THE EXPRESSION OF ACETYLCHOLINESTERASE VIA G PROTEIN-COUPLED RECEPTOR 30 IN PC12 CELLS

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Several flavonoids have been identified to induce the expression of AChE in PC12 cells, e.g. daidzin, irisflorentin, cardamonin and genistein. Among them, genistein is the most robust inducer for AChE activity. Genistein, 4',5,7-trihydroxyisoflavone, is a major isoflavone in soybean, which is known as phytoestrogen having known benefit to brain functions. Being a common phytoestrogen, the possible role of genistein in the brain protection needs to be further explored. In PC12 cells, application of genistein significantly induced the expression of neurofilaments, markers for neuronal differentiation. In parallel, the expression of tetrameric form of proline-rich membrane anchor (PRiMA)-linked acetyl-cholinesterase (G4 AChE), a key enzyme to hydrolyze acetylcholine in cholinergic synapses, was induced in a dose-dependent manner: this induction included the associated protein PRiMA. Genistein-induced AChE expression was fully blocked by the pre-treatment of H89 (an inhibitor of protein kinase A) and G15 (a selective G protein-coupled receptor 30 (GPR30) antagonist), which suggested a direct involvement of a membrane-bound estrogen receptor-GPR30-in the cultures. In parallel, the estrogen-induced activation of GPR30 induced AChE expression in a dose-dependent manner. The genistein/estrogen-induced AChE expression was triggered by a cyclic AMP responding element (CRE) located on the *ACHE* gene promoter. The binding of this CRE site by cAMP response element-binding protein (CREB) induced ACHE gene transcription. We have shown for the first time the activation of GPR30 could be one way for estrogen or flavonoids, possessing estrogenic properties, to enhance cholinergic functions in the brain, which could be a good candidate for possible treatment of neurodegenerative diseases.

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