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A PPAR gamma agonist methyl honokiol induces apoptosis through triggering intrinsic apoptosis pathway and inhibiting PI3K/Akt survival pathway in SiHa human cervical cancer cells

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4-O-methylhonokiol (MH), a bioactive compound derived from Magnolia officinalis, is known to possess several bioactivities such as anti-tumor or anti angiogenesis effects in prostate, colon and ovarian cancer cells. However, the precise anti-cancer effect of MH in cervical cancer cells has not been studied yet. In this study, we demonstrated that MH induced apoptosis in SiHa cervical cancer cells by enhancing PPARγ activation followed by inhibiting PI3K/Akt survival pathway and inducing mitochondrial-dependent apoptosis pathway. The tumor suppressors were modulated by MH in SiHa human cervical cancer cells: ppRB were down-regulated while CDK inhibitor p21, p53/pp53, and pRb were enhanced. MH up-regulated PPAR-γ and PTEN expression levels while Akt/Akt phosphorlylation levels were decreased in MH-induced apoptotic process, supporting that MH is a PPAR-γ activator. Additionally, the expression of anti-apoptotic factor Bcl-2 was decreased whereas a well known apoptotic factor Bax was increased, thereby releasing cytochrome c into cytosol in MH-treated cervical cancer cells. Furthermore, MH treatment led to the activation of caspases-3/-9 and proteolytic cleavage of PARP. The expression level of extrinsic death receptor Fas (CD95) was not altered by MH treatment. Taken together, MH, activates PPAR-γ/PTEN expressions, induces apoptosis via suppressing AKT/PI3K survival pathway, cell cycle arrest at sub-G1 phase and mitochondria-emanated intrinsic pathways in SiHa human cervical cancer cells. These findings suggest that MH can be used as a therapeutic agent for human cervical cancer.

Biography

Yong-Seok Song has completed his Bachelor's degree from Konkuk Univerity. Uder the tutelage of Professor Do Young Yoon. He is currently working on the modulating effect of a new isoform of IL-32 theta on adipogenesis and cancer towards a master and PhD's degree.

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