

[P-21]

**15-DEOXY- Δ 12,14-PROSTAGLANDIN J2 DECREASED
ACTIVATION OF TRANSCRIPTION FACTOR NF- κ B BY
BETA-AMYLOID IN MUTANT PS-2 TRANSFECTED PC12
CELLS**

Jae Ho Oh¹, Jin Tae Hong², Yong Soon Kim¹, Youg Kyu Kim¹, Ki Sook Park¹, Chi Won Song¹, Hai Kwan Jung¹, Chang Won Park¹, Kyung Mi Jung¹,
Ki Hwa Yang¹ and Soo Youn Chung¹

¹National Institute of Toxicological Research, Korea Food and Drug Administration

²College of Pharmacy, Chungbuk National University

Mutations in the presenilin genes (PS-1 and PS-2) are linked to early onset familial Alzheimer's disease (AD), but its underlying cellular mechanisms have not been clear. 15-Deoxy- Δ 12,14-prostaglandin J2 (15-deoxy-PGJ2) is known as a naturally occurring ligand of the peroxisome proliferator-activated receptor- γ (PPAR- γ). In this study, we investigated whether N141I PS-2 mutation can be in a favor of production of beta-amyloid (A β), and thereby increase the induction of apoptosis. We also examined the expression of inflammatory mediators to test whether inflammation may be a causing factor of the induction of apoptosis, and also investigated whether or not 15-deoxy-PGJ2 inhibits apoptosis by A β in mutant N141I PS-2 transfected PC12 cells. A β prominently enhanced expression of caspase 3, caspase 9, p21 and transcription factor NF- κ B activation, however, did not induce PPAR- γ expression. We observed significant increase of A β production, the expression of genes involved in inflammation (TNF- α , COX-2, I κ B), and A β -induced apoptosis in PC12 cell transfected with mutant PS-2 compared to control PC12 cells. And 15-deoxy-PGJ2 increased cell proliferation rate and cell viability of mutant N141I PS-2 transfected PC12 cells that were decreased by toxicity of A β , and inhibited activation of transcription factor NF- κ B by A β on dose-dependent manners. These results demonstrate that PS-2 mutations may significantly contribute to the production of A β causing apoptosis through induction of inflammation, and 15-deoxy-PGJ2 could be suggested as a potent AD therapeutic drug through decrease the activation of NF- κ B signal pathway.

keyword : Apoptosis, Cell viability, Inflammation