

Prostacyclin protects renal tubular cells from gentamicin-induced apoptosis via peroxisome proliferator-activated receptor-alpha-dependent pathway

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摘要

Abstract

To study the protective effect of prostacyclin (PGI₂) we increased PGI₂ production by infected NRK-52E cells with an adenovirus carrying cyclooxygenase-1 and prostacyclin synthase. PGI₂ overexpression protected these cells from gentamicin-induced apoptosis by reducing cleaved caspase-3 and caspase-9, cytochrome c, and decreasing generation of reactive oxygen species. Expression of the nuclear receptor of PGI₂, peroxisome proliferator-activated receptor-alpha (PPARalpha), was reduced during gentamicin treatment of the cells, while its overexpression significantly inhibited gentamicin-induced apoptosis and the amount of cleaved caspase-3. Transformation with PPARalpha short interfering RNA abolished the protective effect of PGI₂ overproduction in gentamicin-treated cells. The PPARalpha activator docosahexaenoic acid given to gentamicin-treated mice significantly reduced the number of apoptotic cells in renal cortex, but this protective effect was not seen in PPARalpha knockout mice. Our study suggests that increased endogenous PGI₂ production protects renal tubular cells from gentamicin-induced apoptosis through a PPARalpha-signaling pathway.