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당뇨 조건 하에서 족세포의 비후가 세포사멸에 선행한다

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Podocyte Hypertrophy Precedes Apoptosis Under Experimental Diabetic Conditions

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Podocyte hypertrophy and apoptosis are two hallmarks of diabetic glomeruli, but the sequence in which these processes occur remains a matter of debate. Here we investigated the effects of inhibiting hypertrophy on apoptosis, and vice versa, in both podocytes and glomeruli, under diabetic conditions. Hypertrophy and apoptosis were inhibited using an EGFR inhibitor (PKI 166) and a pan-caspase inhibitor (zAsp-DCB), respectively. We observed significant increases in the protein expression of p27, p21, phospho-eukaryotic elongation factor 4E-binding protein 1, and phospho-p70 S6 ribosomal protein kinase, in both cultured podocytes exposed to high-glucose (HG) medium, and streptozotocin-induced diabetes mellitus (DM) rat glomeruli. These increases were significantly inhibited by PKI 166, but not by zAsp-DCB. In addition, the amount of protein per cell, the relative cell size, and the glomerular volume were all significantly increased under diabetic conditions, and these changes were also blocked by treatment with PKI 166, but not zAsp-DCB. Increased protein expression of active fragments of caspase-3 and cleaved poly (ADP-ribose) polymerase, together with increased Bax/Bcl-2 ratios, were also observed in HG-stimulated podocytes and DM glomeruli. Treatment with either zAsp-DCB or PKI 166 resulted in a significant attenuation of these effects. Both PKI 166 and zAsp-DCB also inhibited the increase in number of apoptotic cells, as assessed by Hoechst 33342 staining and TUNEL assay. Furthermore, both the EGFR inhibitor and the pan-caspase inhibitor significantly reduced albuminuria in DM rats. In conclusion, under diabetic conditions, inhibition of podocyte hypertrophy results in attenuated apoptosis, whereas blocking apoptosis has no effect on podocyte hypertrophy, suggesting that podocyte hypertrophy precedes apoptosis.

Key Words: 당뇨병성 신병증, 족세포, 세포 비후, 세포 사멸
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