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Calpain에 의한 Polycystin-1의 분해에 따른 신호전달계의 변화

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Calpain-Mediated Polycystin-1 Cleavage Induces Altering of Signaling Pathways

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Autosomal dominant polycystic kidney disease (ADPKD), characterized by the growth of renal cysts and progressive renal failure, is a common genetic disorder. ADPKD is caused by mutations in either PKD1 gene or PKD2 gene, which encode the transmembrane proteins called polycystin-1 and polycystin-2, respectively. In this study, we investigated the functions of normal polycystin-1 to understand pathological phenomena in ADPKD, in which polycystin-1 loses its function or has abnormal functions. Polycystin-1 undergoes several different cleavages, each of which generates fragments that may participate in specific signaling processes. Using a PEST FIND program and in vitro degradation reactions, we found that polycystin-1 contains a PEST domain in intracellular C-terminus and that calcium-dependent proteases, μ-calpain and m-calpain cleaved PEST sequences at C-terminus of polycystin-1. Further, the function of polycystin-1 was also addressed by using the full-length polcystin-1 protein transfected cell lines, and it was found that full-length polycystin-1 inhibited cell proliferation via activation of JAK2 leading to inhibition of activation of ERK whereas the truncation was found to enhance proliferation probably through modulation of intracellular calcium concentration status. This instability of polycystin-1 by calcium dependent proteases may be one of the pathogenesis in ADPKD.

Key Words: 우성다낭신, 폴리시스틴-1, 칼페인
ADPKD, Polycystin-1, Calpain