Low protein diet prevents the progression of renal injury via attenuating mTOR/p70S6K pathway in rats with chronic renal failure

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Low protein diet (LPD) is one of important therapeutic approaches in patients with chronic renal failure (CRF). However, the mechanism of LPD for preventing the progression of CRF remains unclear. It has been shown that the mammalian target of rapamycin (mTOR)/p70S6kinase pathway is activated by such nutrients as amino acids, and the excessive activation of mTOR promotes accumulation of matrix proteins in several tissues including the kidney. In this study, we examined the effect of LPD on the content of phosphorylated p70S6kinase in renal cortex of 5/6 nephroctomized CRF rats. The results indicated that the phosphorylated p70S6kinase in renal cortex was significantly higher in CRF rats treated with normal protein diet (NPD) than that of sham operated rats in week 8 (NPD-CRF vs Sham; 283 ± 111%, $p<0.05$). On the other hand, LPD attenuated the phosphorylated p70S6K level in renal cortex from CRF rats (LPD-CRF vs Sham; 115 ± 33%, NS). Moreover, the progression of CRF was significantly ameliorated by LPD when compared with NPD. LPD improved in proteinuria, glomerular and tubulointestinal matrix accumulation, overexpression of transforming growth factor-beta1. Taken together, there is a possibility that LPD prevents the progression of renal injury via attenuating the activation of mTOR/p70S8K pathway in CRF rats.

Next step of this project is to examine whether mTOR inhibitor, rapamycin, can prevent the progression of renal injury in CRF model. Rapamycin has been applied to reduce the proliferation of both vascular endothelial and smooth muscle and the protein accumulation after the percutaneous transluminal angioplasty in patients with coronary artery diseases. If rapamycin can prevent the progression of CRF in our study, co-administration of LPD and rapamycin might become an effective approach for patients with CRF.