

Low protein diet attenuates the progression of renal disease by suppressing mTOR/S6k pathway in rats with chronic renal failure

Sakae Ohkawa² and Hiromichi Kumagai^{1,2}

¹*Global COE Program, ²Department of Clinical Nutrition,*

Graduate School of Nutritional and Environmental Sciences, University of Shizuoka

Recently, it has been shown that the mammalian target of rapamycin (mTOR)/p70S6kinase (S6k) pathway plays a significant role in the progression of renal hypertrophy and renal dysfunction in some experimental models with chronic renal failure. mTOR is a central regulator of cell growth and is regulated by a large number of signals including nutrients such as amino acids. In this study, we tested whether dietary protein can regulate renal mTOR phosphorylation and attenuate the progression of chronic renal failure (CRF).

The results indicated that the S6k, a down stream of mTOR, was significantly activated in renal cortex of 5/6 nephrectomized CRF rats treated with normal protein diet (23% casein; CRF-NPD) when compared with control rats (non nephrectomy, 23% casein diet; CONT). Low protein diet (8% casein; CRF-LPD) or rapamycin (1.0mg/kg/day, 23% casein; CRF-RAP), a specific inhibitor of mTOR, blocked excessive activation of S6k in CRF rats. Moreover, the progression of chronic renal disease was significantly ameliorated in CRF-LPD and CRF-RAP when compared with CRF-NPD. LPD or rapamycin administration improved in proteinuria, glomerular matrix accumulation, and overexpression of transforming growth factor-beta1.

In conclusion, we showed LPD attenuated the excessive activation of mTOR/S6 pathway, and this effect might be a reason for renoprotective effects of LPD in chronic renal disease.