

Molecular Mechanisms of Renal Urate Transport: Urate Transportsome

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Recent molecular identification of urate transport proteins provides a basis for understanding molecular mechanisms of renal urate handling and interesting targets for the development of drugs to modify urate flux (Anzai et al., *Curr Rheumatol Rep*, 2005). The urate transporter URAT1 (*SLC22A12*), identified by our group, is expressed in the apical membrane of proximal tubular cells and is thought to play a central role in renal urate reabsorption (Enomoto et al., *Nature*, 2002). URAT1 interacts with a variety of therapeutic drugs and pharmacological reagents. Because URAT1 controls the blood urate level, it is important to clarify the regulatory mechanisms of URAT1. Particularly, URAT1 possesses a PDZ motif, known for protein-protein interaction modules, at its C-terminus. By yeast two-hybrid library screening, we identified that URAT1 interacts multivalent PDZ domain-containing protein PDZK1 via its C-terminal PDZ motif (Anzai et al., *J Biol Chem*, 2004). As coexpression of PDZK1 and URAT1 in HEK293 cells increased urate transport by URAT1 1.4-fold, PDZK1 is thought to regulate URAT1 transport activity via PDZ interaction. To date, several proteins related to renal urate transport have been found to interact with PDZ proteins at the apical membrane. These results indicate that the urate transport molecular complex (Urate Transportsome) is formed through apical PDZ network and it may contribute to the renal urate handling as a functional unit (Anzai et al., *Curr Opin Nephrol Hypertens*, 2005).