Recent Progress in Renal Organic Anion Transporters

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Human transporter genes consist of SLC (Solute career) and ABC (ATP-binding cassette) series. SLC are divided into 46 families including 360 members, and ABC are 7 families with 47 members. In the kidney, numerous endogenous and exogenous compounds are taken up and eliminated through various transporters.

Organic anion transporters play important roles in maintenance of renal functions, because most wasted metabolites are anionic. Organic anion transporters (OAT) having 12 membrane spanning domains and belonging to SLC22 include OAT1, OAT2, OAT3, OAT4 and URAT1, all of which are strongly expressed in the human kidney. In general, these transporters recognize various anionic substrates with different chemical structures (multispecificity) except URAT1. OATs functions are regulated by age, sex, glycosylation, phosphorylation and binding proteins.

Recently, we identified Oat5 from rat kidneys which is expressed in the apical membrane of the proximal tubule (S2 and S3). Oat5 is an exchanger and transports estrone sulfate. Different from other members, succinate is a counter anion for Oat5. Since recently identified succinate receptor (GRP91) in the distal tubule (DT) causes hypertension, Oat 5 as a supplier of succinate may play a role in blood pressure control.

As a new member in SLC22, we could characterize an orphan transporter and named OAT-PG because this transporter can transport prostaglandins. OAT-PG is phylogenetically situated close to URAT1, and is highly expressed in the apical membrane of terminal thick ascending limb (TAL) and DT where cyclooxygenase (COX)-2 is localized. OAT-PG takes up radiolabeled PGD2, PGE1, PGE2, PGF2a in a high affinity fashion, of which Km values are 0.38, 0.16, 0.09 and 0.11 nM, respectively. Mode of OAT-PG transport is PGs/PGs exchanger. PGs synthesized in the glomerulus and vasa recta by COX-1, and/or in the TAL and DT by COX-2 may bind PG receptor(s), and regulate sodium transport different from renin-aldosterone system.

Identification of novel isoforms and novel transport substrates of OATs will lead to the further understanding of their roles in renal physiology, pathophysiology and pharmacology.