S46-3 The roles of a novel PG transporter in the local clearance and metabolism of PGE2 in renal cortex

◯Ryo HATANO[1], Shushi NAGAMORI[1], Yoshikatsu KANAI[1]

[1]Osaka Univ Grad. Sch. of Med.

PGE_2 is one of the important lipid mediators in the regulation of renin release and the tubule-glomerular feedback in the kidney. PGE_2 is mainly synthesized in macula densa cells of distal tubules in response to the decrease of tubular electrolyte concentration. PGE_2 secreted from the macula densa transduces the signals to the juxtaglomerular apparatus for renin release and dilatation of afferent arterioles via its receptors. After acting on the receptors, PGE_2 is required to be removed from the extracellular space to keep the sensitivity of the receptors. However, the mechanisms of prostaglandin clearance have not been elucidated despite the proposed involvement of the carrier-mediated uptake of PGE_2 across the plasma membrane followed by enzymatic oxidation in cytoplasm.

In the present study, as a candidate for PGE_2 clearance transporter in renal cortex, we have found a novel PG transporter specifically expressed in kidney. We designated it as OAT-PG (prostaglandin specific organic anion transporter) that belongs to SLC22 family. Importantly, OAT-PG has been found on the basolateral membrane of proximal tubules, where it colocalizes with 15-hydroxyprostaglandin dehydrogenase (15-PGDH), the rate-limiting enzyme of prostaglandin metabolism. Furthermore we have found the defected PGE_2 local clearance in OAT-PG knockout mice. In the lecture, a new concept for local PGE_2 clearance in renal cortex will be proposed.