cDNA cloning of kidney proximal tubule Na^+-dependent glutamate transporters and the appraisal of their roles in Na^+-reabsorption

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Summary

Na^+-coupled organic solute transport plays important roles in the reabsorption of Na^+ from proximal tubules in kidney. For the understanding of the mechanisms of the coupling of Na^+ transport and organic solute transport, the mechanisms of regulation of function, and the actual contribution of the Na^+-coupled organic solute transport to Na^+ reabsorption, it is necessary to reveal molecular nature of Na^+-dependent organic solute transport systems. In this study, we have focused on Na^+-dependent glutamate transport systems which are responsible for the Na^+-coupled reabsorption of glutamate and aspartate from proximal tubule.

We screened mouse kidney cDNA library using rabbit intestine high-affinity glutamate transporter EAAC1 cDNA as a probe and isolated an EAAC1 cDNA to confirm that EAAC1 is an isoform of glutamate transporter which is expressed in kidney. The tubular distribution of expression of EAAC1 in proximal tubules was determined with *in situ* hybridization to be localized mainly in S2 and S3 segments. This was inconsistent with the results from micropuncture experiments which showed that more than 90% of glutamate disappeared from tubular fluid at S1 segment, suggesting the existence of additional glutamate transporter isoforms in S1 segment.

In order to clone a S1 segment glutamate transporter, we performed RT-PCR. The novel PCR product obtained from mouse testis (and kidney) was used to isolate full length cDNA. The cDNA from mouse testis encoded a novel Na^+-dependent neutral amino acid transporter (SNAT1). SNAT1 was shown to be expressed also in kidney. SNAT1 has a structure related to glutamate transporters and exhibited low level of glutamate transport. It has to be determined whether SNAT1 is a S1 segment glutamate transporter or other unknown transporters exist in S1 segment.