SODIUM-D-GLUCOSE TRANSPORT IN *SQUALUS ACANTHIAS* KIDNEY AND INTESTINE: FUNCTIONAL AND MOLECULAR DIFFERENCES

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In a variety of species it has been shown that D-glucose absorption in the kidney and intestine is mediated by sodium-D-glucose cotransport systems (SGLT). Interestingly, biodiversity of cellular functions does not require a large number of functionally different units; it can be managed by a limited number of closely related molecules like in the SGLT family. To date, there are two major members, SGLT1 and SGLT2. SGLT1 is characterized by a sodium to glucose stoichiometry of 2 Na^+ to 1 D-glucose and a high affinity to D-glucose and galactose whereas SGLT2 has a one to one stoichiometry and a relatively low affinity for the sugars.

In functional studies using isolated brush border membrane vesicles we have previously obtained evidence that the sodium-D-glucose cotransporter present in the shark kidney belongs to the SGLT2 type transporter (Kipp, H. et al. Am. J. Physiol. 273:R134-R142, 1997). Further support for this assumption was provided by the successful cloning of a SGLT2 type transporter from this tissue (Kinne, R.K.H. at. al. unpublished data). The current investigation is aimed to define the molecular nature of the transporter responsible for absorption of sugar in the intestine of the shark.

As a first step we studied the tissue distribution of the renal SGLT2 in the shark by isolating mRNA, transcribing it into cDNA and measuring the number of copies of SGLT2 using specific primers and real time PCR. About 2000 copies of SGLT2 per nanogram of cDNA were found in shark kidney mRNA whereas no significant signal could be detected in mRNA isolated from intestinal mucosal scrapings. In order to exclude an accidental degradation of the mRNA during its isolation we also tested the samples for the presence of ß-actin mRNA. Using the appropriate primer for this message significant high signals for ß-actin were obtained both in renal and intestinal samples.

Therefore, we turned again to functional studies using brush border membrane vesicles isolated from intestinal mucosal scrapings in order to define the intestinal D-glucose transporter protein by determining its apparent affinity for D-glucose and its relative inhibition by D-galactose and D-xylose. These experiments showed that the apparent K_m for D-glucose was about 70 times lower in the intestine than in the kidney (0.027 mM versus 1.9 mM) and the inhibition by D-galactose was 2.5 fold larger (73% versus 29% at 0.1 mM D-glucose and 5 mM D-galactose). There was also a significant difference in the inhibitory potency of xylose.

Taken together these results suggest that in the shark different transporters mediate the sodium dependent D-glucose absorption in kidney and intestine. In the kidney predominantly SGLT2 is involved whereas in the intestine - as in the skate (Althoff, Th. et al. unpublished data) and in many other species – a sodium-D-glucose cotransporter belonging to the SGLT1 type within the SGLT family facilitates the transport across the brush border membrane.