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## Elucidation of the Role of Aquaporins in the Regulation of the Osmolality of Gastrointestinal Contents

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### Summary

Aquaporins (AQPs) are a family of channel-forming membrane proteins that facilitate the transport of water and some low-molecular-weight solutes. They are suggested to be involved in the regulation of cellular osmolality and other important physiological activities. AQP11 is expressed in testis, liver, kidney, stomach, small intestine, etc.. We reported that *Aqp11*<sup>-/-</sup> mice were fatal due to uremia resulting from a polycystic kidney. Interestingly, vacuoles were formed before cyst development. The vacuoles were derived from the endoplasmic reticulum (ER), where AQP11 is normally expressed. These results suggested the importance of AQP11. But the physiological roles of AQP11 still remain unknown.

To elucidate the phenotypes in the organs, kidney, liver, stomach and jejunum, of 3-weeks-old *Aqp11*<sup>-/-</sup> mice, we investigated the tissue morphology, ER-stress-response, cell proliferation, and apoptosis using histochemical techniques. There were large histological differences in the kidney between *Aqp11*<sup>+/+</sup> mice and *Aqp11*<sup>-/-</sup> mice. In contrast, we could not find any histological difference in the liver, stomach and jejunum between *Aqp11*<sup>+/+</sup> mice and *Aqp11*<sup>-/-</sup> mice. This result suggested that the physiological roles of AQP11 were quite different between in the kidney and in the other organs.

We further analyzed the recently acquired gene expression profiles of the kidneys of 1-week-old *Aqp11*<sup>-/-</sup> mice, and found that, except for *Aqp11*, three aquaporins, *Aqp1*, *Aqp2*, and *Aqp3*, were significantly changed. *Aqp1* was down-regulated, and *Aqp2* and *Aqp3* were up-regulated. *In situ* hybridization analyses confirmed that the expression of *Aqp1* was down-regulated in the proximal tubules and that of *Aqp2* was up-regulated in the collecting ducts. The lack of *Aqp11*, which is expressed in proximal tubules only, influenced the expression of aquaporins in collecting ducts as well as in proximal tubules.