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The Expression of Water Channels AQP1 and AQP2 in a Large Series of ADPKD Kidneys

Dear Sir,

We read with interest the paper by Hayashi et al. [1] reporting the expression of AQP2 and AQP3 in cyst-lining epithelial cells from ADPKD kidneys. The authors suggest that about 30% of the cysts in ADPKD are derived from collecting-duct cells and that these cells remain well differentiated in terms of AQP expression. However, these conclusions are limited by the small number of ADPKD kidneys ($n = 2$) studied and by the fact that both AQP2 and AQP3 are located in the same cells – the principal cells of the collecting duct.

Recently, we have investigated the expression of AQP1 (also called CHIP28), the constitutively active water channel, and that of AQP2 (or AQP-CD) in a large series of early- and end-stage ADPKD kidneys ($n = 21$), using Western blot analysis and immunohistochemistry [2]. Early-stage ADPKD kidneys contained morphologically normal tubules as well as cysts, while end-stage kidneys contained only cysts amid an expanded interstitium. Our data show that the classical distribution of AQP1 (apical and basolateral membrane of the proximal tubule and descending thin limbs of Henle's loop epithelial cells) and AQP2 (apical membrane area of the collecting-duct principal cells) is maintained in the early stages of ADPKD. The single exception was that AQP1 was mostly located in the apical membrane region of slightly expanded proximal tubules. In end-stage ADPKD, two thirds of the cysts expressed either AQP1 or AQP2, but these two water channels were never colocalized in the same cyst. We performed a quantitative

analysis in 4 ADPKD kidneys (991 randomly selected cysts were examined) to evaluate AQP1 and AQP2 immunolabeling as a function of the size of cysts. This analysis showed that total water channel expression decreased with increasing cyst size, in relation with a significant, size-related decrease in AQP1 expression, whereas the percentage of AQP2-positive cysts did not alter significantly. Consequently, the ratio of AQP2- to AQP1-positive cysts increased significantly with cyst enlargement. The expression of AQP1 and AQP2 in ADPKD was confirmed by Western blot analysis, which also showed a decrease in AQP expression associated with the degree of cystic progression in ADPKD.

In conclusion, our data confirm and extend those presented by Hayashi et al. [1]. From the quantification of AQP1 and AQP2 immunoreactivity in a total of 991 ADPKD cysts, we confirm that a mean of 33% of cysts stained for AQP2, while a mean of 30% of cysts stained for AQP1. Expression of AQP1 and AQP2 are mutually exclusive, even in end-stage ADPKD, when fine morphological discrimination of tubular origin is lost. The fact that one third of the cysts express neither AQP1 nor AQP2 might imply that these cysts originate from nephron segments that do not express these channels, e.g. the ascending limb of Henle's loop, and the connecting and distal convoluted tubules. Thus, aquaporins 1–3 appear to belong to a group of proteins (such as GP330 or vinculin) [3] that retain their differential expression even into end-stage ADPKD.

References

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