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BASIC RESEARCH

Prorenin receptor is needed for podocyte function

Two studies published recently in the *Journal of the American Society of Nephrology* report on the necessity of the prorenin receptor for the structure, function and survival of the podocyte.

Previous studies have shown that podocyte damage is a key factor in proteinuric glomerular diseases and that the loss of podocytes is predictive of disease progression. The prorenin receptor (PRR) is highly expressed in the kidney, particularly in podocytes, but its role in podocyte function is not understood.

> "...podocyte-specific PRR-knockout mice died of renal failure..."

Fabian Riediger and co-workers in Germany generated homozygous podocyte-specific PRR-knockout mice and found that these mice died prematurely, 2–3 weeks after birth. They found that, within 2 weeks of birth, the mice had developed nephrotic syndrome, decreased serum albumin levels, and increased levels of serum creatinine, serum urea, and serum cholesterol. The researchers also noted that albuminuria was present in these mice by day 2 after birth. Electron microscopy findings revealed foot process effacement in podocytes of PRR-knockout mice after 14 days, abnormalities in the actin cytoskeleton, and cell death. Riediger *et al.* report that the alterations in the actin cytoskeleton occurred as a result of impaired vacuolar acidification and that PRR deletion led to impaired autophagy. The authors state that the PRR is essential for podocyte survival by maintaining the protein turnover machinery. "We propose a new model of podocyte survival and protection, where the PRR affects intravesicular acidification and protects cells against disturbed protein degradation or protein turnover due to impaired autophagy," they say. "We suggest that PRR deficiency leads to intensified ER [endoplasmic reticulum] stress, massive accumulation of unprocessed proteins, and finally, podocyte death."

Another study, authored by Yoichi Oshima *et al.*, reports that the PRR is essential for the maintenance of normal podocyte structure and function. These researchers found that podocyte-specific PRR-knockout mice died of renal failure and severe proteinuria within 4 weeks of birth. They showed that foot process effacement was present in the podocytes of these mice and that the slit-diaphragm proteins nephrin and podocin had reduced expression and abnormal localization. Using *in vitro* studies, the reseachers also showed that loss of the PRR affected the function of the vacuolar H^+-ATPase, leading to impaired intracellular acidification and abnormal structure and function of the podocyte. The authors say that their findings demonstrate that the PRR is essential for filtration barrier function and for trafficking and degradation systems in murine podocytes. "The regulation of slit-diaphragm proteins, the membrane trafficking/degradation system by the PRR, and the clinical relevance of the PRR in human podocytopathy require further investigation in future studies," they state.

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Original articles Riediger, F. *et al.* Prorenin receptor is essential for podocyte autophagy and survival. *J. Am. Soc. Nephrol.* doi:10.1681/ASN.2011020200 | Oshima, Y. *et al.* Prorenin receptor is essential for normal podocyte structure and function. *J. Am. Soc. Nephrol.* doi:10.1681/ASN.2011020202