GLOMERULAR DISEASE

Parietal epithelial cell tight junctions prevent protein escape

The formation of tight junctions by parietal epithelial cells (PECs) creates a barrier that confines proteins to the Bowman's space, say the researchers of a new study. Disruption of these tight junctions increases the permeability of this barrier and, according to the study authors, may result in periglomerular inflammation. As lead researcher Stuart Shankland explains, "our findings show that in the normal situation, PEC tight junctions and the Bowman's basement membrane form a barrier to direct urine from the glomerulus to the tubular system. In the disease state, PECs and their tight junctions are destroyed, allowing proteins to escape into the extraglomerular compartment and resulting in the recruitment of inflammatory cells".

Previous studies have shown that cultured PECs express several tight junction proteins. These findings led the researchers of the current study to investigate whether these tight junctions form a functional barrier.

The researchers first examined the expression of tight junctions in the mouse kidney *in vivo*. Ultrastructural analysis of PECs by immunohistochemical analysis revealed tight junctions at the apical side of PECs in healthy mice. However, in mice with anti-glomerular basement membrane (GBM) nephritis, these tight junctions were disrupted when PECs detached from the underlying Bowman's basement membrane.

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To investigate the function of the tight junction barrier, the researchers used labeled tracers that were small enough to pass through the podocyte slit diaphragm under normal conditions. Two different tracers were used—ovalbumin and dextran, conjugated to Texas red. In healthy mice, the tracers were detected in the glomerular capillary loops and in the urinary space but not in the extraglomerular space. By contrast, in mice with anti-GBM nephritis, tracers localized to the extraglomerular space. The researchers say their findings suggest an important role for PECs in preventing protein from passing into the glomerular space. They hypothesize that PEC injury leads to abnormal morphology and function of the tight junction proteins, resulting in increased barrier permeability and the passing of proteins into the extraglomerular space, which initiates an inflammatory response.

Shankland says that his research team is currently pursuing studies to further elucidate the function of PECs. At present, they are investigating other disease models and hope to determine the mechanisms that underlie altered barrier function in disease states.

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Original article Ohse, T. *et al*. A new function for parietal epithelial cells: a second glomerular barrier. *Am J. Physiol. Renal Physiol*. **297**, F1566–F1574 (2009)