A Podocyte Receptor Tyrosine Phosphatase (GLEPP1). Characterization and Function

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Podocytes are key cells responsible for supporting the glomerular filtration barrier both physically and biochemically. The GLEPP1 receptor was identified, expression-cloned and sequenced in a search for podocyte-specific molecules that might regulate podocyte function. GLEPP1 is a 180 kDa glycoprotein that is located on the apical surface of podocyte foot processes. It functions as a tyrosine phosphatase. Knockout of GLEPP1 in the mouse results in short wide foot processes, reduced glomerular nephron content and increased expression of vimentin. There was no increase in albumin excretion in urine under normal conditions of renal mass and blood pressure. We hypothesize that GLEPP1 is a receptor that serves to elongate foot processes and thereby increase the paracellular filtration space between podocytes. No human counterpart of the GLEPP1 knockout mouse has yet been identified.

The Glomerular Podocyte, Glomerular Podocytopenia and Progression to Glomerulosclerosis

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Podocytes are highly specialized cells that function to support the glomerular filtration surface by a variety of mechanisms. Accumulating evidence suggests that podocyte depletion (podocytopenia) may be an important pathologic mechanism underlying glomerular diseases that progress to focal and global glomerulosclerosis. Podocytes may be lost from glomeruli by several mechanisms including by cell death and by detachment from the GBM under the influence of hypertension and other factors. Like neurons, podocytes have limited capacity to divide and thereby to replace lost cells. This hypothesis will be discussed with reference to podocyte biology, data from experimental models of glomerular injury and human biopsy material, as well as potential therapeutic strategies that might be used.