특별 강연 IV

Progressive Glomerular Disease: New Experimental Insights Into the Pathogenesis

Jürgen Floege

University Hospital, RWTH Aachen, Aachen, Germany

Glomerular disease including diabetic nephropathy and glomerulonephritides is the leading cause of end stage renal disease. Understanding the contribution of individual cell types to glomerular degeneration and regeneration may open new avenues for treatment. It is now firmly established that podocyte damage and the associated loss of glomerular barrier function is a central event in glomerulosclerosis. Identifying ways to replace podocytes after damage is a key challenge for the future. A novel concept is that there is extensive cellular cross-talk between podocytes and glomerular parietal cells. Experimental evidence suggests that once parietal cells are activated (but yet ill-defined stimuli) they can form bridges with the glomerular tuft and replace/displace podocytes thus initiating the processes that ultimately lead to glomerulosclerosis. Extensive mesangial disease, such as in IgA nephropathy, may also result in secondary podocyte damage. Limiting mesangioproliferative changes, e.g. by interfering with platelet-derived growth factor (PDGF), represents an attractive new therapeutic action (in particular, since PDGFs also contribute to secondary tubulointerstitial damage). Finally, maintaining glomerular endothelial integrity is of therapeutic relevance. While the key factor vascular-endothelial growth factor (VEGF) needs to be very tightly regulated in this process and thus may be difficult to manipulate, PDGF-C is of interest in instances where endothelial damage is prominent in the glomeruli. In this lecture I will attempt to synthesize these various processes into one integrative concept.