kidney disease who were matched for age, sex and HIV status. The researchers found a single peak on the MALD scan that was centered on *MYH9*, indicating a strong association of African ancestry with FSGS at this locus. Several *MYH9* alleles that occurred at a higher frequency among African Americans than European Americans were associated with an increased risk of FSGS. Further analyses revealed certain *MYH9* alleles to be associated with hypertensive nephrosclerosis—but not with diabetic nephropathy—in African Americans.

An independent study by Kao and colleagues involved genome-wide MALD scanning of 1,372 individuals with end-stage renal disease and 806 controls without albuminuria or increased serum creatinine levels. Multiple common single nucleotide polymorphisms were found in the *MYH9* gene that were associated with a 2–4-fold increased risk of nondiabetic end-stage renal disease in African Americans. As in the study by Kopp *et al.*, African ancestry at this locus was not associated with diabetic nephropathy.

Original articles Kopp JB *et al.* (2008) *MYH9* is a major-effect risk gene for focal segmental glomerulosclerosis. *Nat Genet* **40:** 1175–1184
Kao WHL *et al.* (2008) *MYH9* is associated with nondiabetic end-stage renal disease in African Americans. *Nat Genet* **40:** 1185–1192

Losartan and vitamin D analog synergistically prevent diabetic nephropathy in mice

Renin–angiotensin system blockers are widely used to treat diabetic nephropathy, but compensatory renin release reduces their efficacy. Since vitamin D is known to repress renin gene transcription, Zhang *et al.* investigated whether combining a vitamin D analog (paricalcitol) and an angiotensin receptor blocker (losartan) leads to more effective inhibition of the renin–angiotensin system and prevention of renal injury in a mouse model of diabetic nephropathy.

Streptozotocin was used to induce diabetes in 8-week-old mice. At 2 weeks after streptozotocin injection, mice were randomly allocated to receive treatment with vehicle, losartan, paricalcitol or to a combination of losartan and paricalcitol. Vehicle-treated mice developed progressive albuminuria, with an almost fourfold increase in urinary albumin-to-creatinine ratio at 13 weeks. Although the development of albuminuria was ameliorated in mice receiving losartan or paricalcitol, the combination of losartan and paricalcitol prevented albuminuria completely; mice receiving combination therapy had a urinary albumin-to-creatinine ratio similar to that of untreated nondiabetic controls after 5 weeks and 10 weeks of treatment. In addition, combination therapy with losartan and paricalcitol prevented thickening of the glomerular basement membrane, prevented podocyte foot process effacement, reduced glomerulosclerosis, and suppressed induction of factors such as transforming growth factor β, which is implicated in the development of glomerulosclerosis.

These promising findings in a mouse model of diabetes might have important implications for the treatment of diabetic nephropathy in humans. The heightened therapeutic effects of the combination treatment are attributed to the suppression of renin and angiotensin II accumulation in the kidney.

Original article Zhang Z *et al.* (2008) Combination therapy with AT1 blocker and vitamin D analog markedly ameliorates diabetic nephropathy: blockade of compensatory renin increase. *Proc Natl Acad Sci USA* **105:** 15896–15901

Combination therapy is the most effective option for severe lupus nephritis

Treatment of severe lupus nephritis generally involves monotherapy with cyclophosphamide, tacrolimus or mycophenolate mofetil, but remission rates remain low. Bao *et al*. have now shown that, compared with monotherapy, a combination of mycophenolate, tacrolimus and a corticosteroid leads to improved remission rates in patients with class V + IV (combined diffuse-proliferative and membranous) lupus nephritis.

In this open-label study, 40 Chinese patients with proteinuria and class V + IV lupus nephritis, as defined by the International Society of Nephrology and the Renal Pathology Society, were randomly allocated to receive either combination therapy or intravenous cyclophosphamide. In the intention-to-treat analysis, 13 (65%) patients in the combination-therapy group had achieved complete remission by