Devarajan et al. [17] have even hypothesized as to the possibility of using serum NGAL as a new marker of renal function, on the basis of evidence that the protein correlated with effective GFR better than creatinine and cystatin C.

The exact mechanism at the basis of that correlation has not yet been well-defined. The most likely hypothesis still remains that of anti-apoptotic tubular compensatory mechanism to chronic renal damage, while the lower reduction of renal clearance would not, in the first place at least, be held responsible.

In conclusion, although we have highlighted a close link between uNGAL and severity of renal disease in our proteinuric patients, the findings reported cannot clarify the pathophysiological significance of this relationship. The hypothesis formulated should therefore be confirmed by further in-depth studies.

Conflict of interest statement. None declared.

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The Cys(311)Ser polymorphism of paraoxonase 2 (PON2) is associated with albumin-to-creatinine ratio (ACR) in Mexican Americans

Sir.

Alteration of paraoxonase 2 (PON2) enzyme activity due to genetic variations in the PON2 gene is thought to influence the development of oxidative stress and contribute to the pathophysiology of microvascular complications of diabetes. Of the genetic variants examined, two nonsynonymous coding variants (rs11545942; Arg148Gly and rs7493; Cys311Ser) and an intronic variant (rs12794795; A/C) of PON2 have been shown to be associated with microvascular complications of type 1 and type 2 diabetes including microalbuminuria [1,2]. The aim of this study is to investigate whether these three polymorphisms examined by others are associated with type 2 diabetes (T2DM) and its correlated subclinical cardiovascular and renal traits using data (N = 670, mean age = 45 years; females = 60%; T2DM = 29%) from the San Antonio Family Diabetes/Gallbladder Study (SAFDGS), a Mexican American population at high risk for T2DM and diabetes-related traits.

The SAFDGS family member recruitment and data collection procedures including estimation of urinary albuminto-creatinine ratio (ACR) were described previously [3,4]. The quantitative trait values of ACR (ln ACR) were log transformed and used in the association analysis since their raw data were non-normally distributed. The Institutional Review Board of the University of Texas Health Science Center at San Antonio approved all procedures, and all subjects gave informed consent.

Genotyping of rs11545942 (G/A), rs7493 (C/G) and rs12704795 (A/C) were performed by TaqMan assay (Applied Biosystems, CA, USA). Of the three polymorphisms examined, the rs11545942 failed to be polymorphic in our
SAFDFS data. Genotypic data of rs7493 and rs12704795 were polymorphic and verified for Mendelian inconsistencies and allele and genotype frequencies were measured using the programme PEDSYS subroutines. The allele frequencies of rs7493 were 77% (C) and 23% (G). In regard to the rs12704795, the A and C allele frequencies were 76% and 24%, respectively. Genotypic data of rs7493 [CC (60%), CG (35%), GG (5%)] and rs12704795 [AA (55%), AC (39%), CC (6%)] were consistent with the Hardy–Weinberg Equilibrium expectations, and there was no evidence for hidden population stratification. Association analysis in our family data was carried out using the measured genotype approach within the variance components analytical framework implemented in SOLAR [5].

Of the phenotypes examined for association [T2DM, body mass index (BMI), blood pressure measures, total cholesterol, high density lipoprotein-cholesterol, triglycerides and ln ACR], the C/G variant (rs7493) exhibited significant association only with ACR ($P = 0.013$) after adjusting for the effects of age, age$^2 \times$ sex, diabetes, duration of diabetes, systolic blood pressure, and antihypertensive treatment with ACE inhibitors or AT1R antagonists. The mean ACR values for genotypes were as follows: CC = 2.28 ± 0.05, CG = 2.16 ± 0.05 and GG = 2.03 ± 0.09. In addition, we reanalysed the association analysis by replacing the systolic blood pressure with the diastolic blood pressure values as a covariate in our model (together with antihypertensive covariates), and the association findings were found to be similar to ACR ($P = 0.019$). The analyses also indicate that the rs7493 variant explained ~8% of the total genetic variance in ACR. The biological relevance of our findings remains to be identified. Alterations in the activity of PON2 due to rs7493 are likely to influence the composition as well as the oxidation of lipoproteins [1]. For example, oxidized LDL may induce oxidative damage in kidney cells, therefore contributing to the pathogenesis of albuminuria. The precise biological relevance of this variant to albuminuria will therefore depend on its effect on the enzymatic activity of PON2. Our association analysis failed to show significant association between the phenotypes examined and genotypic data of rs12704795. The absence of relationships between the examined variants and the serum lipids and lipoproteins, BMI and blood pressure measures, is consistent with a previous report [1]. This study has limitation in that it focused on three variants in PON2 gene examined previously and has not attempted comprehensive tagging of all common variations within PON2 that could influence variation in ACR. In addition, it is possible that the associated variant is in linkage disequilibrium with (a) potential functional variant(s) in PON2 or with other variants in the flanking genes. These possibilities remain to be explored.

In conclusion, our data support the findings by others [1,2] that the Cys(311)Ser variant of PON2 may contribute to albumin excretion rate. Although the susceptibility to albuminuria due to this variant is found in different ethnic groups, the genetic influences attributable to this polymorphism appear to be rather minor in their magnitude.

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Posterior reversible encephalopathy induced by intravenous immunoglobulin

Sir,

Intravenous immunoglobulin (IVIg) is commonly used in nephrology units for the treatment of auto-immune diseases, antibody-mediated renal allograft rejection and immune deficiencies. Minor adverse effects, such as myalgia, headache, shiver, nausea, vomiting or fever occur in <20% of patients. Major reactions including renal failure, thromboembolism, aseptic meningitis and anaphylaxis are less common. Whereas osmotic nephropathy resulting from maltose and saccharose toxicity is well-known to nephrologists, posterior reversible encephalopathy syndrome (PRES) is a rare and potentially severe adverse event of IVIg therapy.

A 42-year-old man was admitted for end-stage renal failure secondary to myeloma cast nephropathy in the context of plasma cell leukaemia, diagnosed 2 months previously. His past medical history was otherwise unremarkable. Haematological tests showed increased white blood cells (12380/mm$^3$) with 27% of circulating plasma