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# Response to *COL4A3/COL4A4* heterozygous mutations with TBMN presenting as focal segmental glomerulosclerosis

**Rasheed A Gbadegesin**

Department of Pediatrics and Duke Molecular Physiology Institute, Duke University Medical Center, Durham, NC

We thank Drs. Deltas and Pierides for their comments on our paper[1-2]. They were concerned that we had failed to refer to their earlier work, which has similarities but also differences with our report. We certainly want to acknowledge the contributions of Dr Deltas and other investigators and apologize for our oversight. We also want to reassure them that we did not intentionally omit or wanted to negate their prior contributions to the subject. In our study, we reported the frequency of *COL4A3/COL4A4* rare variants in a cohort of patients with a diagnosis of familial FSGS. After excluding mutations in known FSGS genes in a family, we performed whole exome sequencing to identify new gene for FSGS and found a segregating mutation in *COL4A3*. We then screened the rest of our cohort (cohort referred to us with a diagnosis of familial FSGS) and found that 10% of families have potential pathogenic mutations in *COL4A3/A4.* Thus, we reported the frequency of *COL4A3/A4* mutations in patients with presumed familial FSGS. This differs somewhat from the findings in the references cited by Deltas and Pierides, which alluded to FSGS as an **associated finding** in patients with familial hematuria/thin glomerular basement membrane disease[3-7]. In our paper, we emphasized the fact that there are numerous reports of secondary FSGS in patients with COL4 nephropathy and nowhere did we claim that we were reporting secondary FSGS in COL4 nephropathy for the first time. Rather, we simply stated that our report is on *COL4A3/A4* variants in a cohort of patients with a **primary diagnosis** of familial FSGS[2]. We believe that this observation is important because: 1) it has implications for the approach to clinical management of patients with FSGS and finding new genes for familial FSGS, and, 2) as rightly stated in your letter and the accompanying commentary to our paper[8], our observation as well as yours and other investigators extend the spectrum of phenotype associated with collagenopathies and emphasize the need for new classification of glomerular diseases that will integrate clinical, morphologic and genomic findings.

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To whom correspondence should be addressed: rasheed.gbadegesin@duke.edu.

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