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REPLY

SuPAR and FSGS: is the jury still out?

Lorenzo Gallon and Susan E. Quaggin

We thank L. Mesnard, Y. Luque and E. Rondeau for their comments (Experimental concerns regarding suPAR-related proteinuria. *Nat. Rev. Nephrol.* http://dx.doi.org/10.1038/nrneph.2017.108; 2017)[1] regarding our News & Views commentary (Gallon, L. and Quaggin, S. E. A suPAR kidney connection found in the bone marrow. *Nat. Rev. Nephrol.* **13**, 263–264; 2017)[2] on the recent study by Hahm *et al.* that reported a role of circulating soluble urokinase plasminogen activator receptor (suPAR) produced by bone marrow cells in the development of focal segmental glomerulosclerosis (FSGS) (Bone marrow-derived immature myeloid cells are a main source of circulating suPAR contributing to proteinuric kidney disease. *Nat. Med.* **23**, 100–106; 2017)[3]. In their correspondence, Mesnard and colleagues correctly highlight the difficulty in confirming a causal role for suPAR in the development of FSGS. Indeed, in the closing paragraph of our commentary, we state that additional studies are required to confirm whether or not suPAR is causing disease in the models presented by Hahm *et al.* As Mesnard and colleagues correctly point out, the effects of suPAR might be enhanced in *Plaur*-deficient mice, although the underlying mechanism(s) are unclear.

Despite the remaining uncertainties and additional observations that raise questions about the role of suPAR in the pathogenesis of FSGS (for example, the finding that patients with paroxysmal nocturnal haemoglobinuria have high circulating levels of suPAR but do not develop the disease[4,5]), the study by Hahm and colleagues provides experimental support for the important possibility of involvement of bone-marrow-derived cells in recurrent FSGS. As such this study provides the foundation for additional future studies to confirm or refute the role of suPAR and/or other bone-marrow derived factors/cells in the pathogenesis of FSGS. If such bone marrow-derived factors are conclusively identified, this finding may lead to much needed new therapeutic strategies for FSGS.

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1. Mesnard, L., Luque, Y. & Rondeau, E. Experimental concerns regarding suPAR-related proteinuria. *Nat. Rev. Nephrol.* http://dx.doi.org/10.1038/nrneph.2017.108 (2017).
2. Gallon, L. & Quaggin, S. E. A. suPAR kidney connection found in the bone marrow. *Nat. Rev. Nephrol.* **13**, 263–264 (2017).
3. Hahm, E. *et al.* Bone marrow-derived immature myeloid cells are a main source of circulating suPAR contributing to proteinuric kidney disease. *Nat. Med.* **23**, 100–106 (2017).
4. Sloand, E. M. *et al.* Increased soluble urokinase plasminogen activator receptor (suPAR) is associated with thrombosis and inhibition of plasmin generation in paroxysmal nocturnal hemoglobinuria (PNH) patients. *Exp. Hematol.* **36**, 1616–1624 (2008).
5. Brodsky, R. A. Paroxysmal nocturnal hemoglobinuria. *Blood* **124**, 2804–2811 (2014).

Competing interests statement
L.G. is a consultant for Alexion. S.E.Q. owns stock in and is a director of Mannin Research.