FSGS is a podocyte disease.

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Focal and segmental glomerulosclerosis is progressive kidney disease frequently undergo chronic renal failure. The morphology of FSGS varies, even it includes “non-sclerotic” lesions, which is particularly seen in the collapsing and cellular variants of FSGS by Columbia Classification. These “pre-sclerotic” glomerular lesions that progress to typical sclerosis show an initiation of FSGS morphology, podocyte loss. Podocyte loss plays central roles not only FSGS but also other glomerular diseases, including diabetic glomerulosclerosis, Lupus nephritis and IgA nephropathy. Although genetic and experimental studies uniformly showed podocyte injury causes cell loss that promotes glomerulosclerosis, sequence of event from podocyte loss leading to glomerulosclerosis is not fully known. Under podocyte loss, what happens in the glomeruli next and how glomeruli deteriorate their function? Podocyte specific toxin models have shown variety of glomerular changes by cellular/molecular responses in endothelial cells and parietal cells. The failure of homeostatic cross-talk system among glomerular resident cells together with the response of bone marrow cells are the critical step toward sclerosis. Podocyte loss initiates endothelial plasminogen activator inhibitor amplification that leads to podocyte domino effects. In addition, podocyte loss-driven intracapillary lipid peroxidization and up-regulation of chemokine and adhesion molecules causes segmental foam cells infiltration, as commonly seen in FSGS in humans. Podocyte loss stimulates Notch-mediated changes of parietal cell polarity that also promote segmental scar. These features seem to mimic wound healing process particularly occurred in glomerular microenvironment with high levels of vascular permeability that needs to halt protein leakage.

FSGS may be an end product of glomerular responses for abnormal filtration barrier particularly caused by podocyte loss.

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