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On the Cover

What's the diagnosis? Over the past decade, intravitral multiphoton excitation fluorescence microscopy has provided stunning images and movies of the structure and function of the intact kidney with unparalleled spatial and temporal resolution. Because of its ability to directly visualize dynamic intrarenal processes in vivo without causing tissue damage, this noninvasive optical sectioning technique and imaging approach has revolutionized kidney research. This multiphoton image shows a glomerulus (lower right) in the living rat kidney that has been treated with puromycin aminonucleoside (PAN), a model of focal segmental glomerulosclerosis (FSGS). The red is albumin conjugated to Alexa594 to label the blood (plasma); green-yellow is Lucifer yellow, a freely filtered fluid marker labeling the glomerular filtrate. The nuclear dye Hoechst33342 was added to label cell nuclei (green). In this early phase of FSGS, small cysts in podocytes (unlabeled dark cells outside the glomerular capillary loops), and increased permeability of the glomerular filtration barrier (red-labeled albumin uptake in the early proximal tubule), are visible. Also, Lucifer yellow intensity in the tubular fluid nicely demonstrates the renal concentrating mechanism (intense fluorescence in the adjacent collecting duct versus the Bowman’s space and proximal tubule at the right). A corresponding video shows the filtration of Lucifer yellow injected into the carotid artery and the appearance of unlabeled podocytes (negative image). (Image and video, available online at www.cjasn.org, provided by Janos Peti-Peterdi and James Burford)