Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Multivesicular bodies mimicking SARS-CoV-2 in patients without COVID-19

To the editor: It is now well known that patients with novel coronavirus disease 2019 (COVID-19) due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) commonly have kidney complications, including acute kidney injury, proteinuria, and hematuria. Recent publications in *Kidney International* used electron microscopy (EM) to detect the virus in autopsy or biopsy specimens of the kidney.[1,2] Most of the published images depicting the suspected virus are very similar, if not identical, to multivesicular bodies (MVBs). MVBs have been well-known since the 1960s and their appearance and occurrence is detailed in the classic monograph of Feroze Ghadially;[3] however, their exact significance and function is unclear. We suspect that the EM images of SARS-CoV-2 published to date are in fact MVBs.

To address this question, we examined the EMs of 11 current consecutive kidney biopsies and 10 kidney biopsies from the pre–COVID-19 era (Table 1). Every EM contained renal cortex with 1 to 2 glomeruli. MVBs were found in all 20 kidney biopsies, irrespective of the underlying kidney disease (Figure 1). To our surprise, MVBs were always identified in podocytes (1 to 4 podocytes per glomerulus), but we have not seen them in tubular epithelial cells. MVBs were occasionally seen in endothelial cells (mainly arterial or arteriolar) and in a parietal glomerular epithelial cell of 1 biopsy. MVBs theoretically may represent podocyte endocytosis with subsequent formation of intracytoplasmic microvesicles resembling viruses. Seeing an MVB by EM is just a snapshot and we do not know how and when they evolved or how long they remain. MVBs contain microvesicles. However, microvesicles are commonly "free floating" in the cytoplasm of many cell types, including tubular epithelial cells (frequently representing endocytotic vesicles). Su *et al.*[1] show such cytoplasmic microvesicles in tubular epithelial cells in their Figure 2, but the particles in Figure 2a may have come from an MVB after its membrane dissolved. While these "free floating" cytoplasmic microvesicles could represent viral particles, they are

Table 1 | Renal cells with MVB

Case no.	Year of biopsy	Age (yr)	Sex	Podocyte	Endothelial cell	Parietal epithelial cell	Diagnosis
1	2015	56	F	+	+		Membranous glomerulonephritis
2	2015	58	M	+	+		Minimal change disease
3	2015	56	M	+			Focal segmental glomerular sclerosis
4	2015	59	M	+			Immune complex glomerulonephritis with membranoproliferative pattern
5	2016	60	M	+			Immune complex glomerulonephritis focal crescents
6	2016	72	M	+			AL amyloidosis
7	2016	25	M	+			IgA nephropathy
8	2016	48	M	+			Cryoglobulinemic glomerulonephritis
9	2016	82	M	+		+	Oxalate nephropathy
10	2016	69	F	+			Thin basement membrane nephropathy
11	Current	32	F	+			Class V+III lupus nephritis (COVID-19–negative)
12	Current	80	F	+			Membranous glomerulonephritis
13	Current	52	M	+			Diabetic nephropathy
14	Current	80	M	+	+		Diabetic nephropathy
15	Current	66	F	+			Fibrillary glomerulonephritis
16	Current	79	M	+			IgA nephropathy
17	Current	26	M	+	+		Chronic active antibody-mediated rejection
18	Current	40	M	+	+		Chronic active antibody-mediated rejection
19	Current	54	F	+			Thrombotic microangiopathy
20	Current	86	F	+	+		Pauci-immune crescentic glomerulonephritis
21	Current	68	F	+			Acute tubular necrosis

AL, amyloid λ light chain amyloidosis; COVID-19, coronavirus disease 2019; MVB, multivesicular body.

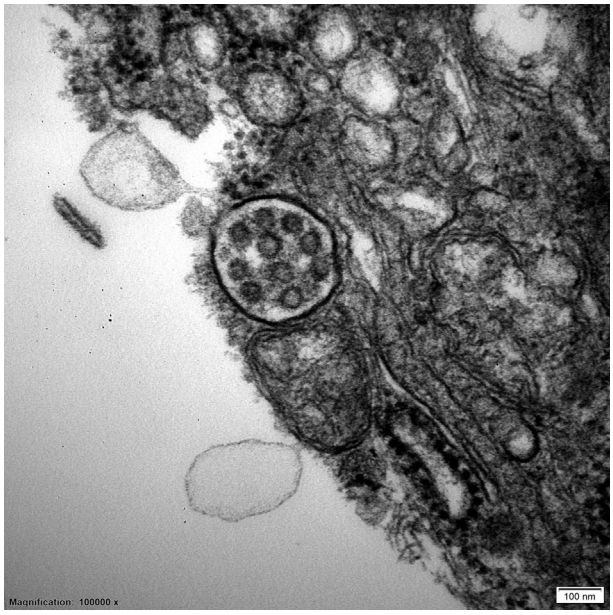

Figure 1 | Multivesicular body in a podocyte of a patient with lupus nephritis who tested negative for coronavirus disease 2019. Uranyl acetate-lead citrate, original magnification ×10,000. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.

nonspecific. Endocytic vesicles may be coated by proteins, such as clathrin. The presence of coating proteins may cause an electron-dense area around these vesicles giving the appearance of a viral "corona."[4] Su *et al.*[1] found SARS-CoV nucleoprotein in renal tubules by immunohistochemistry, but the presence of a viral protein does not necessarily mean the presence of complete viral particles. Why MVBs occur so commonly in podocytes and uncommonly in tubular epithelial cells is unclear.

Transmission EM of tissue sections is not a specific or sensitive method for the detection of viral particles; there are numerous structures found by EM that resemble viruses (so-called viral-like particles), such as the well-known endothelial tubuloreticular inclusions (also called myxovirus-like particles). Therefore, caution is suggested when identifying a virus by EM in tissue sections. Immunohistochemistry may also result in nonspecific staining, particularly in renal tubules. Two recent case reports of collapsing glomerulopathy in COVID-19–positive patients failed to identify the virus in the kidney biopsy by *in situ* RNA analysis.[5,6] Another case report describing a patient with collapsing glomerulopathy also failed to find viral RNA in tissue extracted from the biopsy but demonstrated "viral particles" (with the appearance of MVBs) in podocytes.[2] Further molecular studies for the presence of the viral genome in renal parenchymal cells would be important in deciding whether SARS-CoV-2 truly infects the kidney.

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Autophagy inhibition by chloroquine and hydroxychloroquine could adversely affect acute kidney injury and other organ injury in critically ill patients with COVID-19

To the editor: We read the letter by Izzedine *et al.*[1] with great interest, especially the discussion of renal adverse effects of drug treatment options for coronavirus disease 2019 (COVID-19). We would like to draw particular attention to the potential adverse effect of chloroquine and hydroxychloroquine, the lysosomotropic antimalarial drugs that may inhibit the infection of severe acute respiratory syndrome coronavirus 2 by reducing the entry and replication of the virus. Severe acute respiratory syndrome coronavirus 2 enters cells via endocytosis by binding of its trimeric spike protein to cell surface receptors including angiotensin-converting enzyme 2. Expression of angiotensin-converting enzyme 2 is high in proximal tubular cells in the human kidney (see Supplementary Figure S1 and Supplementary References). Based on the *in vitro* observation of inhibitory effects of chloroquine and hydroxychloroquine, clinical studies of their treatment in COVID-19 patients are under way. However, we believe that these lysosomotropic agents have the potential to make acute kidney injury (AKI) and other organ failures worse due to their known effect to increase lysosomal pH and inhibit autophagy,[2] a fundamental mechanism for the survival of injured cells. Chloroquine mainly inhibits autophagy by