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.

better in patients on maintenance HD in comparison to patients on PD treatment, at 94% and 83%, respectively ($P = 0.25$). There was also a marginally significant trend of greater seroconversion rates among healthy controls than patients with ESKD (100% vs. 88%; $P = 0.051$). There were 12 (60%) patients in the control group and 21 (35%) patients in the ESKD group who reported mild adverse reactions in the early postvaccination period. Those adverse reactions included low-grade fever, headache, myalgia, and pain around the injection site.

Our preliminary report suggests that patients with ESKD requiring maintenance dialysis raised satisfactory humoral seroconversion response rates at 2 weeks after the second dose of an inactivated whole-virus SARS-CoV-2 vaccine. However, patients with ESKD developed lower levels of anti-RBD antibodies compared with healthy individuals. Adverse reactions were infrequent and relatively mild. Although obtained in a small number of patients, these data suggest that the immune response to CoronaVac is comparable to that achieved with mRNA and adenoviral-vectored vaccines. Further study including neutralizing antibody and cell-mediated immunity, is encouraged to better explore immunogenicity in these specific populations (Thai Clinical Trials Registry, TCTR20210226002).

ACKNOWLEDGMENTS

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Angiotensin-converting enzyme 2 decreased expression during kidney inflammatory diseases: implications to predisposing to COVID-19 kidney complications

To the editor: Although angiotensin-converting enzyme 2 (ACE2) is the receptor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) entry into target cells, it has a major anti-inflammatory role by hydrolyzing angiotensin II, a proinflammatory mediator, to angiotensin 1-7, an anti-inflammatory molecule.

Kidneys are a common target of SARS-CoV-2 infection. Both roles for direct viral infection and downstream effects of a cytokine storm syndrome have been suggested as mechanisms driving kidney injury in patients with coronavirus disease 2019 (COVID-19).[1]

It was recently reported that patients with glomerulonephritis have higher mortality and risk of acute kidney injury associated with SARS-CoV-2 infection.[2] We hypothesize that downregulation of the ACE2/angiotensin 1-7 pathway may account for higher kidney complications in these patients. We found both mRNA and protein expression of ACE2 is reduced in models of inflammation targeting glomeruli (anti–glomerular basement glomerulonephritis) and the tubulointerstitium (tubulointerstitial nephritis) compared with a normal kidney (Figure 1a–c). This is consistent with reduced ACE2 mRNA and protein expression in human kidney inflammatory diseases, including diabetic and IgA nephropathies.[3] We also identified that angiotensin 1-7, the product of ACE2, inhibits macrophage migration to C-X-C Motif Chemokine Ligand 16 (CXCL16), C-C Motif Chemokine Ligand 2 (CCL2)/Monocyte chemoattractant protein-1 (MCP-1), and C-C Motif Chemokine Ligand 5 (CCL5)/Regulated upon Activation, Normal T-Cell Expressed and Presumably Secreted (RANTES) chemokines (Figure 1d). Angiotensin 1-7 also suppresses glomerular endothelial cell CXCL10/interferon-γ–inducible protein 10 (IP10)–angiotensin II dependent induction (Figure 1e). Notably, angiotensin 1-7 infusion in rats with anti–glomerular basement glomerulonephritis

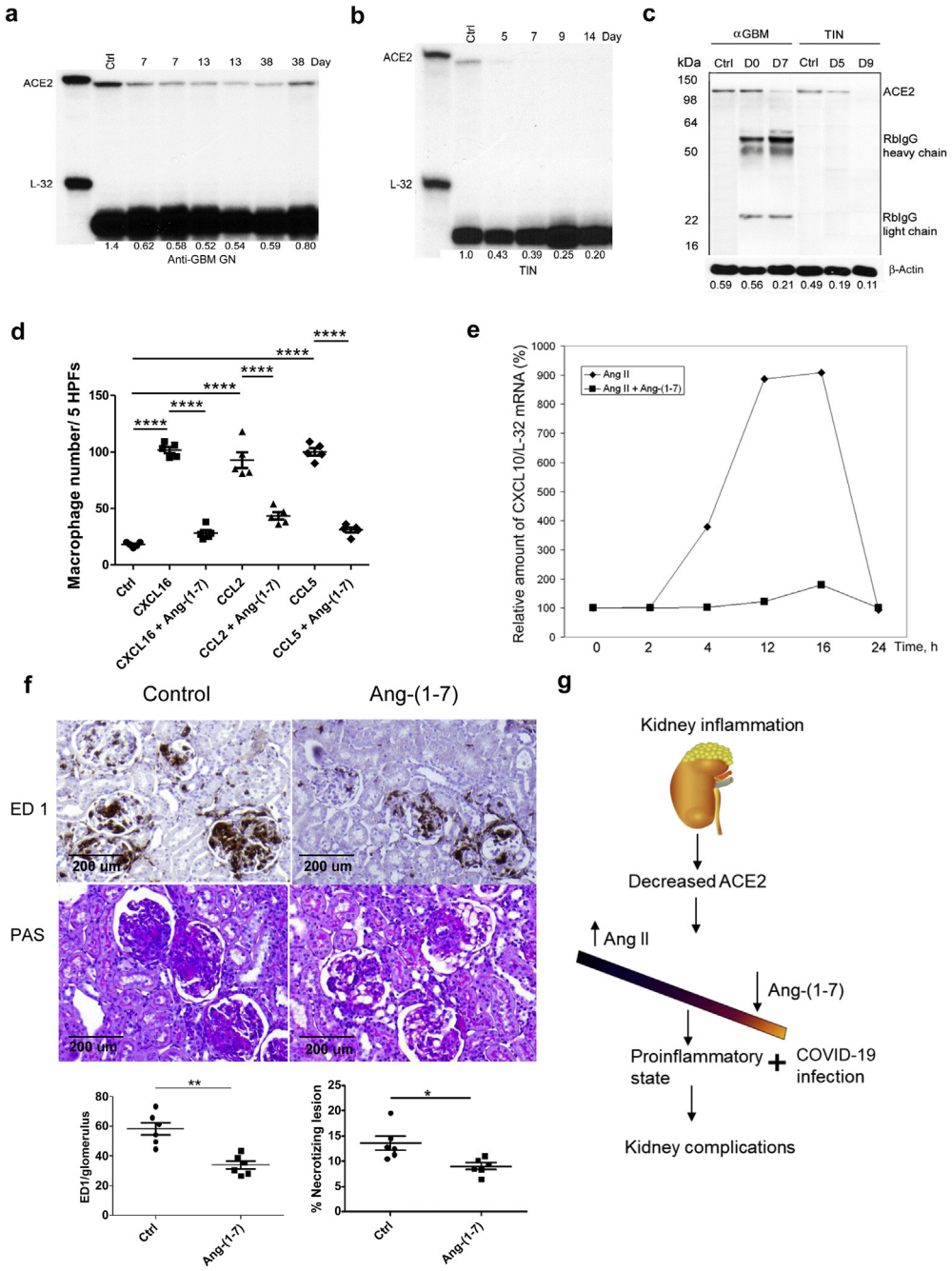

Figure 1 | Potential effect of reduction of angiotensin-converting enzyme 2 (ACE2) in kidney inflammation. (**a,b**) RNase protection analysis of ACE2 mRNA expression. (**a**) In the nephritic kidney of WKY rats, ACE2 mRNA expression is downregulated through day 38. (**b**) In the tubulointerstitial nephritis (TIN) model, the downregulation of ACE2 is observed at day 3 through day 7 (D7), with almost complete suppression from day 9 (D9) through day 14. Each line represents a single rat sample. Probes contain polylinker regions and are longer than the protected bands. Rat ribosomal *L-32* gene was used as a housekeeping gene. (**c**) Western blot analysis shows the reduction of ACE2 protein expression in anti–glomerular basement glomerulonephritis (GBM GN) and TIN. Anti-ACE2 antibody detects rabbit IgG (RbIgG) from anti-GBM antibody. As expected, these bands are not observed in TIN or a normal kidney (Ctrl). (**d**) Chemotaxis analysis of macrophages in the presence or absence of angiotensin 1-7 (Ang-[1-7]). Ang-(1-7) inhibits chemotactic activities of C-X-C Motif Chemokine Ligand 16 (CXCL16), C-C Motif Chemokine Ligand 2 (CCL2)/ Monocyte chemoattractant protein-1 (MCP-1), and C-C Motif Chemokine Ligand 5 (CCL5)/Regulated upon Activation, Normal T-Cell Expressed and Presumably Secreted (RANTES) on macrophages. The chemotactic responses are expressed as the number of migratory cells per 5 high-power fields (HPFs). (**e**) Densitometric analysis of blot from RNase protection assay of CXCL10/interferon-γ–inducible protein 10 (IP10) expression in glomerular endothelial cells with or without incubation with Ang-(1-7). Angiotensin II induction of CXCL10/IP10 in glomerular endothelial cells is prevented by Ang-(1-7). Data are presented as a ratio of the counts per minute for the specific mRNA/*L-32* mRNA to ensure a constant quantity of RNA in each sample. (**f**) Periodic acid–Schiff (PAS) staining and immunohistochemistry stained for ED1^{+} monocytes/macrophages of WKY rats with anti-GBM GN treated with Ang-(1-7) or vehicle. (**g**) Proposed mechanism for the development of kidney complications associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. *$P < 0.05$; **$P < 0.01$; ****$P < 0.0001$; COVID-19, coronavirus disease 2019; D0, day 0; D5, day 5. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.

reduced macrophage infiltration and glomerular damage (Figure 1f). These data demonstrate that during kidney inflammation, ACE2 downregulation could dampen the ACE2/angiotensin 1-7 anti-inflammatory pathway, resulting in worse inflammation. Consequently, patients with kidney inflammatory diseases could be more susceptible to kidney complications from COVID-19 (Figure 1g), because inflammation and previous kidney disease predict acute kidney injury and mortality after acute kidney injury.[4]

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods.

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Membranous nephropathy following anti–COVID-19 mRNA vaccination

To the editor: A 76-year-old man with a history of hypertension and UV-treated cutaneous mycosis fungoid was vaccinated in January 2021 for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with Bnt162b2 and developed an antibody response. He had not had prior coronavirus disease 2019 (COVID-19) infection. He developed edema 4 days after vaccination with a random spot urine protein-to-creatinine ratio of 6.5 g/g, hypoalbuminemia (1.6 g/dl), hematuria, and normal serum creatinine (0.86 mg/dl). His anti–phospholipase A2 receptor autoantibody titer was found to be 1:800 (maximal dilution for this assay), supporting a diagnosis of membranous nephropathy (MN).[1] As there were no other clinical data to suggest an alternative diagnosis, a kidney biopsy was not performed. He was initially treated symptomatically, with dietary modification and renin-angiotensin system blockade, resulting in partial control of the nephrotic syndrome (body weight stabilized, serum albumin increased to 2.6 g/dl, urine protein-to-creatinine ratio decreased to 3 g/g, creatinine increased to 1.14 mg/dl, and the titer of anti–phospholipase A2 receptor did not change).

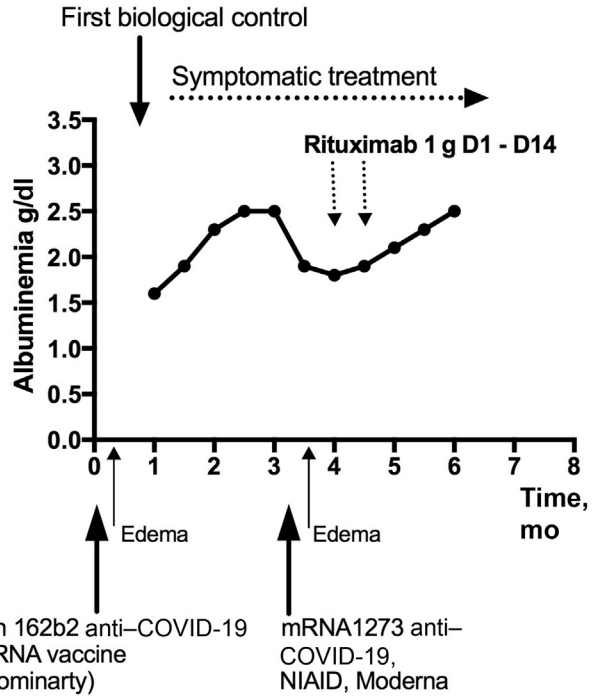

Figure 1 | Timeline. Treatment and clinical and biological evolution of the nephrotic syndrome from the first anti–coronavirus disease 2019 (COVID-19) vaccine injection. D1, day 1 Rituximab perfusion 1 g; D14, day 14 Rituximab perfusion 1 g; NIAID, National Institute of Allergy and Infectious Diseases.

He was given the SARS-CoV-2 mRNA-1273 vaccine for his second dose to maintain mRNA vaccination but avoid a second dose of Bnt162b2. Two days later, his edema worsened, serum albumin decreased to 2.2 g/dl, urine protein-to-creatinine ratio increased to 3.8 g/g, and serum creatinine was stable at 1.15 mg/dl. At this time, rituximab treatment was initiated and resulted in a partial remission at 2 months (Figure 1).

To our knowledge, this is the first case of MN occurring after anti–COVID-19 mRNA vaccination. A recurrence of previously diagnosed MN has been reported after administration of inactivated SARS-CoV-2 vaccination,[2] and a case of minimal change disease has been reported after mRNA-1273 vaccination.[3] Exacerbation of nephrotic syndrome following a second injection of an mRNA vaccine seems to suggest a role of these vaccines in triggering MN. Further studies are needed to elucidate the early postvaccination immune response mechanism.

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