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Hôpital Pasteur 2, Centre Hospitalier Universitaire de Nice, Nice, France; [11]*Department of Nephrology and Transplantation, Centre Hospitalier Universitaire Rennes, Rennes, France;* [12]*Department of Nephrology and Transplantation, University of Limoges, Limoges, France;* [13]*Department of Nephrology and Transplantation, University of Reims, Reims, France;* [14]*Nephrology and Renal Transplantation Department Assistance Publique-Hopitaux de Paris, Hôpital Tenon, Paris, France;* [15]*Department of Nephrology, University of Besançon, Besançon, France;* [16]*Department of Nephrology and Transplantation, University of Caen, Caen, France; and* [17]*Department of Nephrology and Transplantation, University of Angers, Angers, France*

Correspondence: *Sophie Caillard, Nephrology and Transplantation Department, Hôpitaux Universitaires de Strasbourg, 1 place de l'Hôpital, Strasbourg 67091, France. E-mail: Sophie.caillard@chru-strasbourg.fr*

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Evidence of cell-mediated immune response in kidney transplants with a negative mRNA vaccine antibody response

To the editor: Benotmane *et al.* have demonstrated that only 48% of renal transplant patients (RTxP) develop a serologic response after vaccination with an mRNA-based severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine.[1] Likewise, we reported that only 22% of RTxP develop anti–SARS-CoV-2 IgG after vaccination with the mRNA-based SARS-CoV-2 vaccine BNT162b2 (Pfizer-BioNTech).[2] To further characterize the immunologic response, we measured the cellular response to BNT162b2 vaccination in 7 RTxP

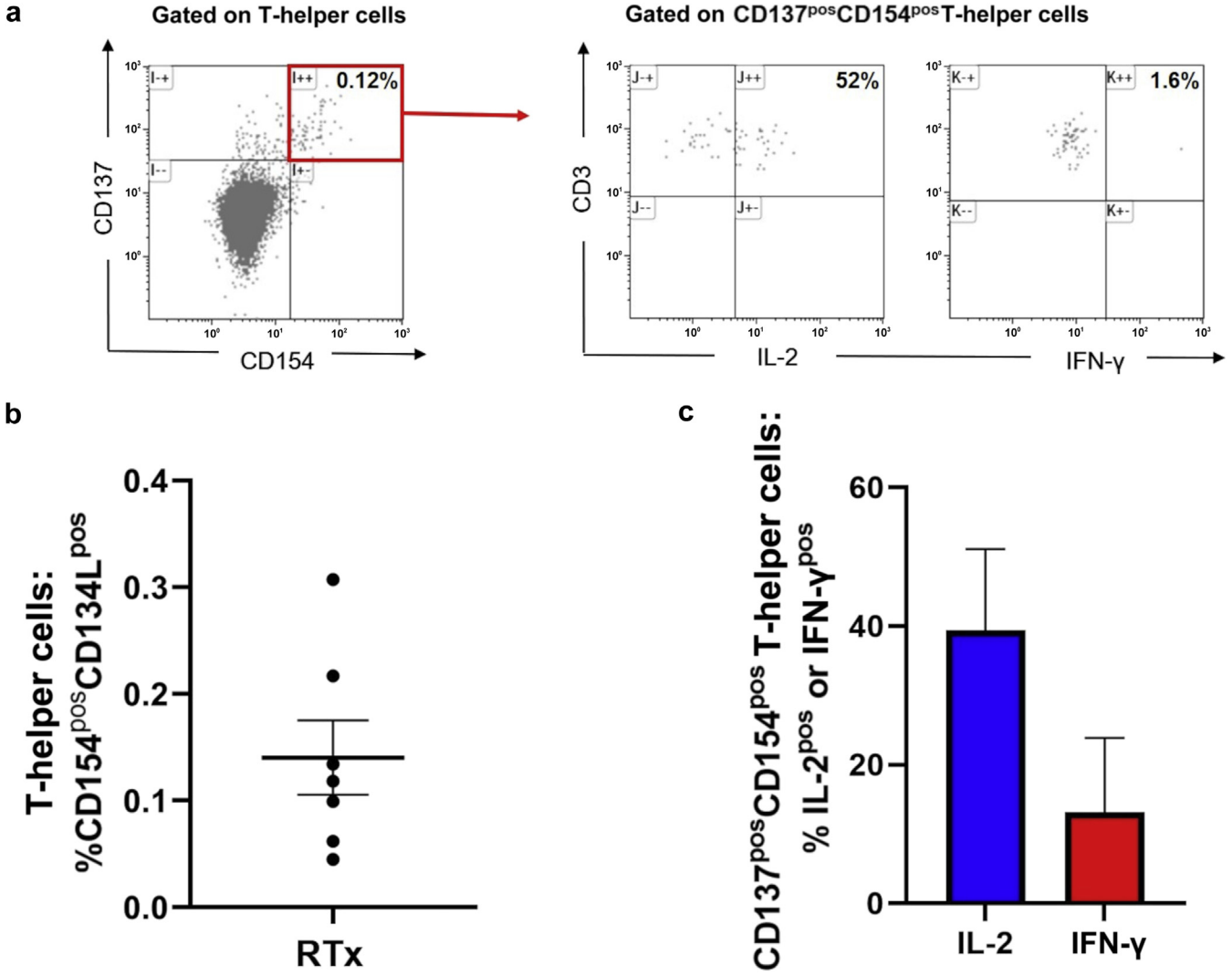

Figure 1 | S-protein–reactive T-helper cells in renal transplant patients after vaccination. (**a**) Peripheral blood mononuclear cells were freshly isolated from whole blood and cultured for 16 hours in the presence of overlapping peptide pools for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein and brefeldin A. T cells coexpressing CD154 and CD137 were defined as S-protein–specific. The cytokine profile of S-protein–specific T cells was characterized, and interleukin-2 (IL-2)/interferon-γ (IFN-γ) expression was determined. (**b**) In all 7 patients, S-protein–specific T-helper cells were detectable. (**c**) S-protein–specific T-helper cells produced IL-2 and IFN-γ. Pos, positive.

with triple immunosuppression lacking anti–SARS-CoV-2 IgG after vaccination with 2 dosages of BNT162b2 (measured 18–60 days after the second dose). For that purpose, peripheral blood mononuclear cells were isolated from patients and stimulated with overlapping peptide pools for the SARS-CoV-2 spike protein, according to previously published protocols.[3] In all 7 patients, S-protein–reactive T-helper cells were detected (Figure 1). All patients harbored interleukin-2–producing S-protein–reactive T-helper cells (Figure 1; 39% ± 11% of S-protein–reactive T-helper cells), and in 6 of the 7 patients, interferon-γ–positive S-protein–reactive T-helper cells were present (13% ± 11% of S-protein–reactive T-helper cells).

Thus, in all of the 7 RTxP, a cellular S-protein–specific immune response was induced by vaccination, despite the lack of S-protein–specific antibodies. The presence of a vaccine-induced T-cell response indicates that mRNA vaccines may well confer T cell–mediated vaccine-specific immunity in immunocompromised patients. Taken together, these findings underscore the importance for a comprehensive immune monitoring and the need for individualized schemes for booster vaccinations in this susceptible patient cohort.

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Sebastian Dolff[1], Baotong Zhou[2], Johannes Korth[2], De Luo[2], Yang Dai[2], Michael Jahn[2], Oliver Dorsch[3], Olympia Evdoxia Anastasiou[4], Oliver Witzke[1], Andreas Kribben[2] and Benjamin Wilde[2]

[1]Department of Infectious Diseases, West German Centre of Infectious Diseases, University Hospital Essen, University of Duisburg-Essen, Essen, Germany; [2]Department of Nephrology, University Hospital Essen, University of Duisburg-Essen, Essen, Germany; [3]KfH Kuratorium für Dialyse und Nierentransplantation e.V., Kronach, Germany; and [4]Institute for Virology, University Hospital Essen, University of Duisburg-Essen, Essen, Germany

Correspondence: *Benjamin Wilde, Department of Nephrology, University Hospital Essen, University of Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany. E-mail: benjamin.wilde@uk-essen.de*

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Paclitaxel-coated balloon angioplasty for recurrent arteriovenous fistula stenosis

To the editor: We read with interest the investigator-led Paclitaxel-assisted balloon Angioplasty of Venous stenosis in hEmodialysis access (PAVE) trial by Karunanithy *et al.*, evaluating the efficacy of paclitaxel-coated balloons (PCBs) in arteriovenous fistula (AVF).[1] In contrast to a recently published large-scale randomized controlled trial by Lookstein *et al.*,[2] the PAVE trial failed to demonstrate a difference in the treatment effect of PCBs versus standard balloons for AVF stenosis. The authors attributed this observation to the different PCB used in the study, which has a different excipient and paclitaxel dose, and a possible confounder of a shorter balloon inflation time.

Of interest to note, the PAVE trial included more than one-fifth of nonmaturing AVFs, which have not been used for dialysis. AVF nonmaturation may not be solely contributed by neointimal hyperplasia, and the response to paclitaxel, an antiproliferative agent that inhibits neointimal hyperplasia, may differ from AVF with recurrent stenosis. Specifically, investigator-initiated randomized controlled trials that recruited only matured AVFs have shown positive patency outcomes with PCBs.[3,4] Irani *et al.* suggested that PCBs offered more significant benefits for older dialysis accesses with recurrent stenosis,[3] whereas Swinnen *et al.* demonstrated that PCBs delay restenosis in matured AVF.[4] Also, our retrospective study showed that the types of balloons with different excipient and paclitaxel doses (Lutonix PCBs vs. IN.PACT PCBs) were not predictors of postintervention patency rates.[5] The nonmaturing AVFs likely confound the lack of benefit of PCBs in the PAVE trial. An individualized approach of PCB use in matured and repeatedly stenosed AVF may ensure the maximum possible benefit.

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Ru Yu Tan[1], Suh Chien Pang[1], Alvin Ren Kwang Tng[1] and Chieh Suai Tan[1]

[1]Department of Renal Medicine, Singapore General Hospital, Singapore