



Perspective

The Immunologic Downsides Associated with the Powerful Translation of Current COVID-19 Vaccine mRNA Can Be Overcome by Mucosal Vaccines

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Perspective

Rethinking next-generation vaccines for coronaviruses, influenzaviruses, and other respiratory viruses

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Table 1. Epidemiologic and immunologic parameters of selected human respiratory viruses and vaccines used to control them

Virus	Incubation period ^a	Marked viremia	Infection elicits long-term protective immunity	Re-infections are rare	Vaccines elicit long-term protective immunity	Vaccine type
Measles (to prodrome)	≈ 10 days	yes	yes	yes	yes	replicating
Mumps	≈ 16 days	yes	yes	yes	yes	replicating
Rubella	≈ 16 days	yes	yes	yes	yes	replicating
Smallpox ^b	≈ 12 days	yes	yes	yes	yes	replicating
VZV ^c	≈ 14 days	yes	yes	yes	yes	replicating
Endemic coronaviruses	≈ 5 days	no	no	no	no	none
Influenza virus	≈ 2 days	no	no	no	no	replicating, other
Parainfluenzaviruses	≈ 4 days	no	no	no	no	none
RSV	≈ 5 days	no	no	no	no	none
SARS-CoV-2	≈ 4 days	no ^d	no	no	no	non-replicating

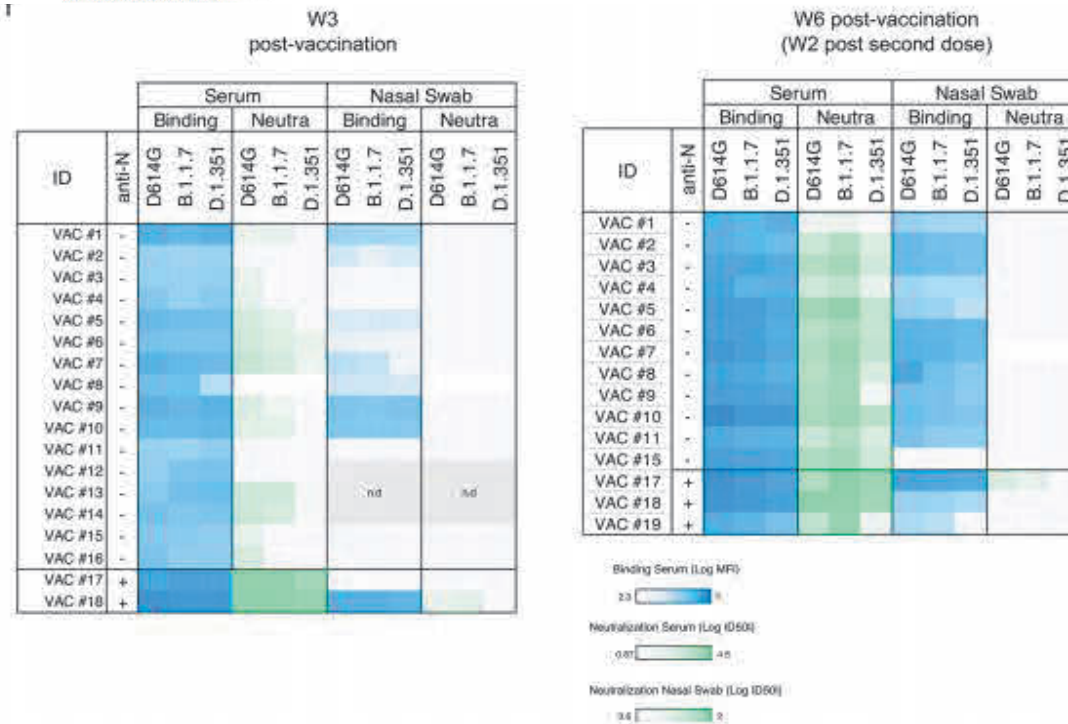
respiratory, lower respiratory tract, and systemic vaccination^{144,145,146,147}; or optimized combinations of these. Attempting to control mucosal respiratory viruses with systemically administered non-replicating vaccines has thus far been largely unsuccessful, indicating that new approaches are needed. For example,

respiratory disease often reflects host genetic susceptibility factors.^{148,149,150,151}

PUBLIC HEALTH CONSIDERATIONS RELATING TO NEXT-GENERATION RESPIRATORY VACCINES MUST

Sensitivity of infectious SARS-CoV-2 B.1.1.7 and B.1.351 variants to neutralizing antibodies

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Either low or absent anti-Spike immunity in lungs of vaccinees

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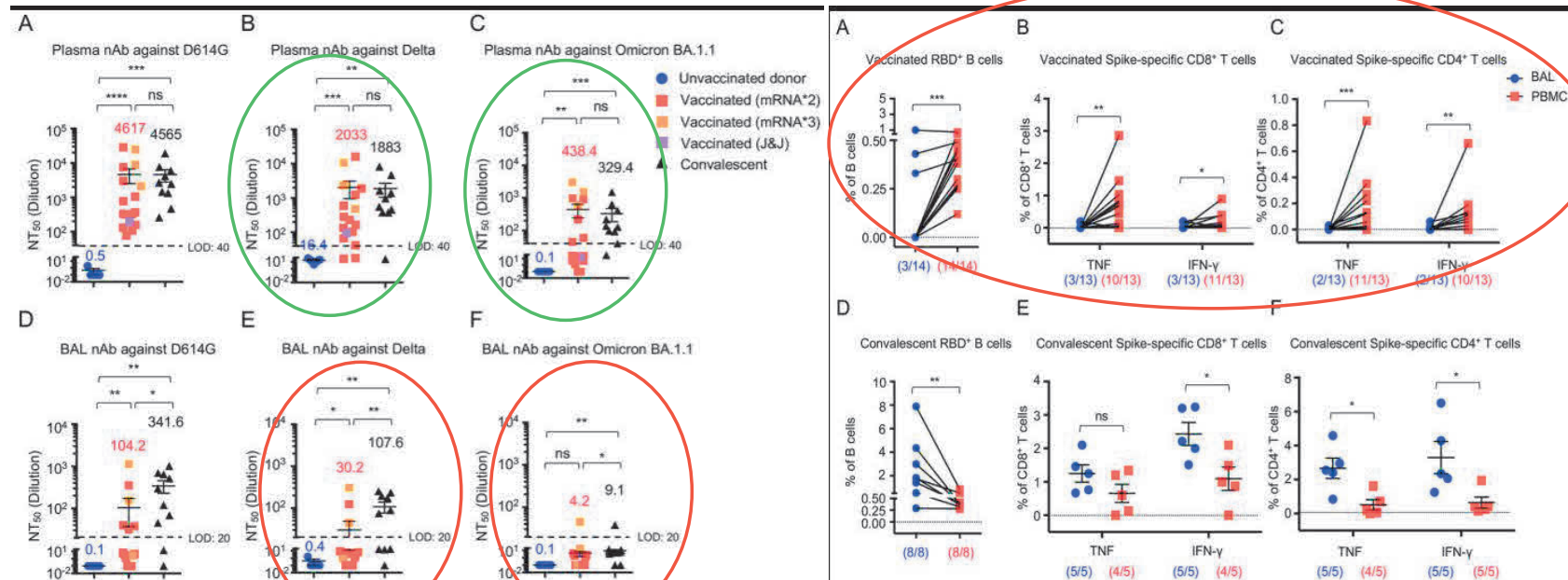
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Respiratory mucosal immunity against SARS-CoV-2 following mRNA vaccination

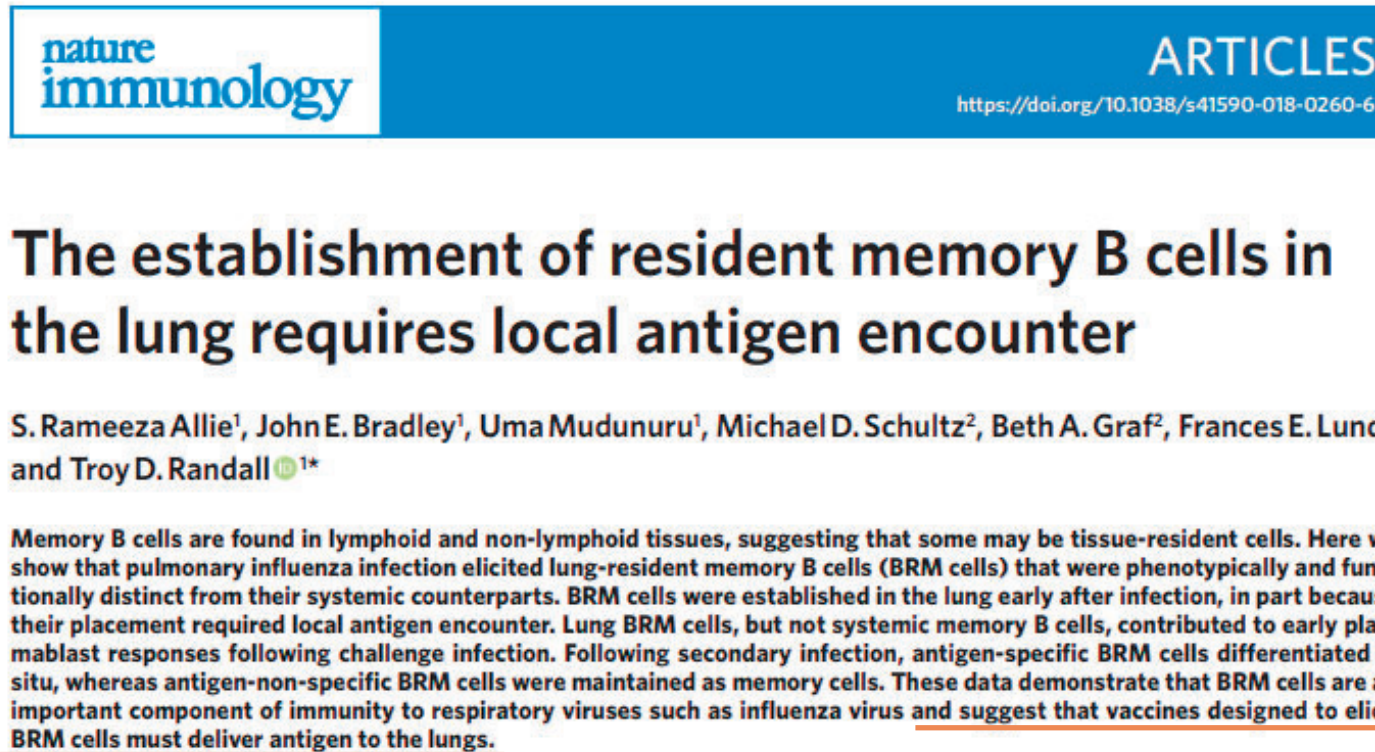
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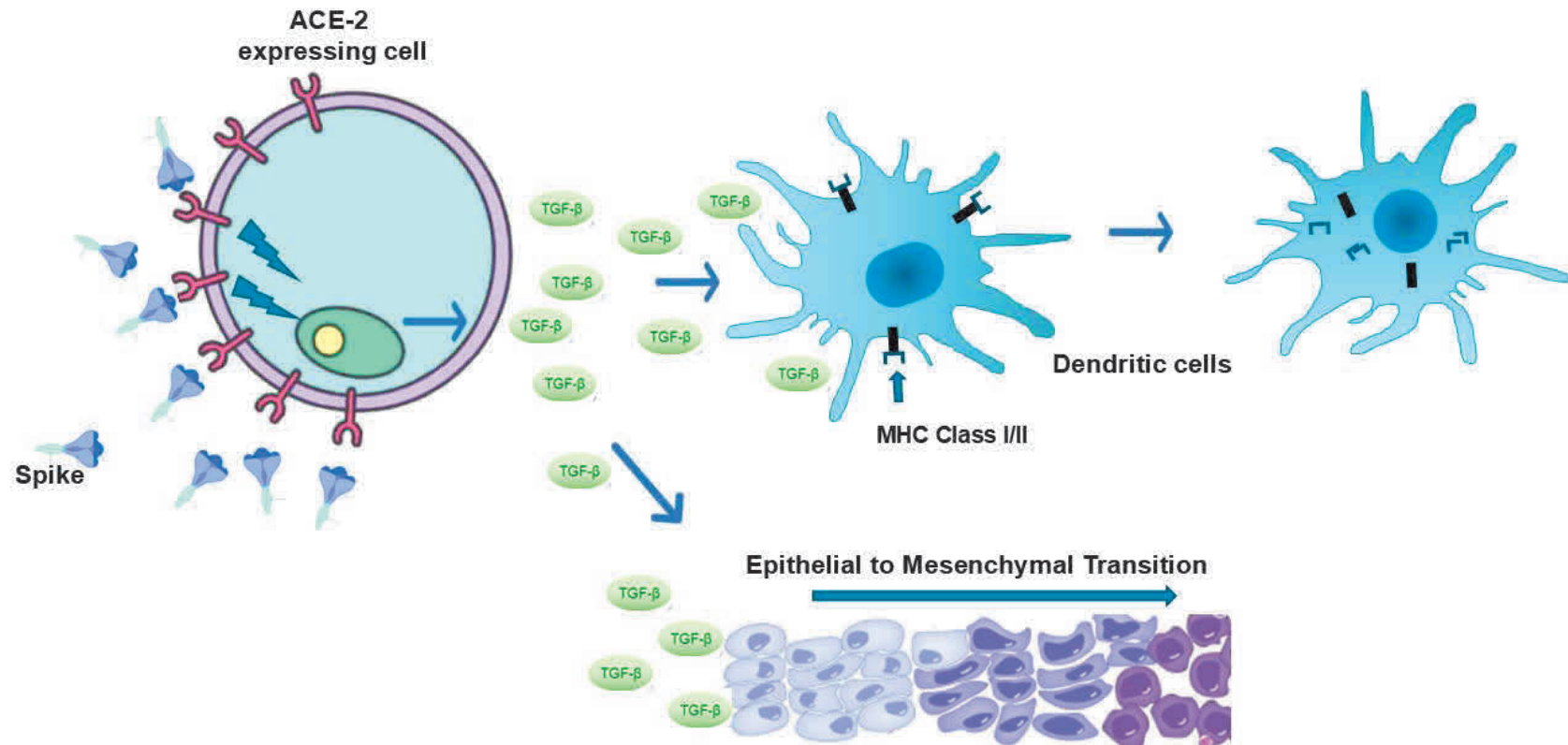


Vaccines designed to elicit respiratory immunity must deliver antigen to the lungs



- The development of lung immune memory is largely not influenced by events occurring in both peripheral circulation and lymphoid organs;
- Lymphocytes in lungs are maintained independently of the pool of circulating lymphocytes, and their continuous loss through intraepithelial migration towards airways is constantly replenished by homeostatic proliferation

Bystander effects of the Spike/ACE-2 binding



COVID-19 vaccine-induced autoimmunity: auto-antibodies



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High serum prevalence of autoreactive IgG antibodies against peripheral nerve structures in patients with neurological post-COVID-19 vaccination syndrome

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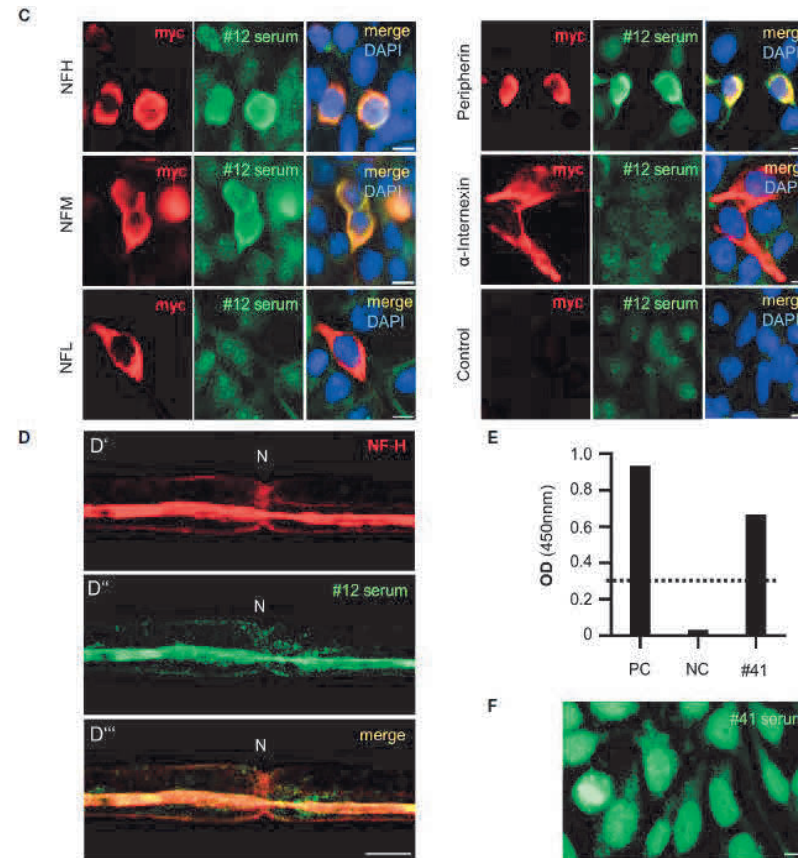


FIGURE 2

Antibody target identification and confirmation in PCVS sera. Volcano plot representing significantly enriched proteins (labeled in red) in patient #12 IgG IP (A) and patient #41 IgG IP (B) compared to a negative control; in A-B: the x-axis displays the log₂-transformed fold change, and the y-axis represents the -log₁₀-transformed p value. (C) Cell-based assays with patient #12 serum testing IgG reactivity against neurofilament subunits and control HEK293 cells. (D) Costaining of sciatic nerve teased fibers with a commercial NF-H antibody (D') and patient #12 serum (D'') showing clear signal overlap (D'''). (E) ELISA analysis of DFS-70 and patient #41 serum. PC: positive control serum. NC: negative control serum. The standard reference serum OD was 0.278 (dotted line). OD: optical density. (F) Hep2 staining of patient #41 serum resembling fine speckled nuclear staining typical of DFS-70 IgGs.



National Center for the Global Health

Un grazie e un saluto a tutti