



*vaccines*

Perspective

---

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

---

Maurizio Federico

Special Issue

[Efficacy, Immunogenicity and Safety of COVID-19 Vaccines and COVID-19 Vaccination Strategies](#)

Edited by  
Dr. Pedro Plans-Rubió



<https://doi.org/10.3390/vaccines12111281>

Perspective

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

David M. Morens,<sup>1</sup> Jeffery K. Taubenberger,<sup>2,\*</sup> and Anthony S. Fauci<sup>1</sup>

<sup>1</sup>Office of the Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892, USA

<sup>2</sup>Viral Pathogenesis and Evolution Section, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892, USA

\*Correspondence: [taubenbergerj@niaid.nih.gov](mailto:taubenbergerj@niaid.nih.gov)

<https://doi.org/10.1016/j.chom.2022.11.016>

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

Virus	Incubation period <sup>a</sup>	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 <sup>b</sup>	≈ 12 days	yes	yes	yes	yes	replicating
VZV <sup>c</sup>	≈ 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 <sup>d</sup>	no	no	no	non-replicating

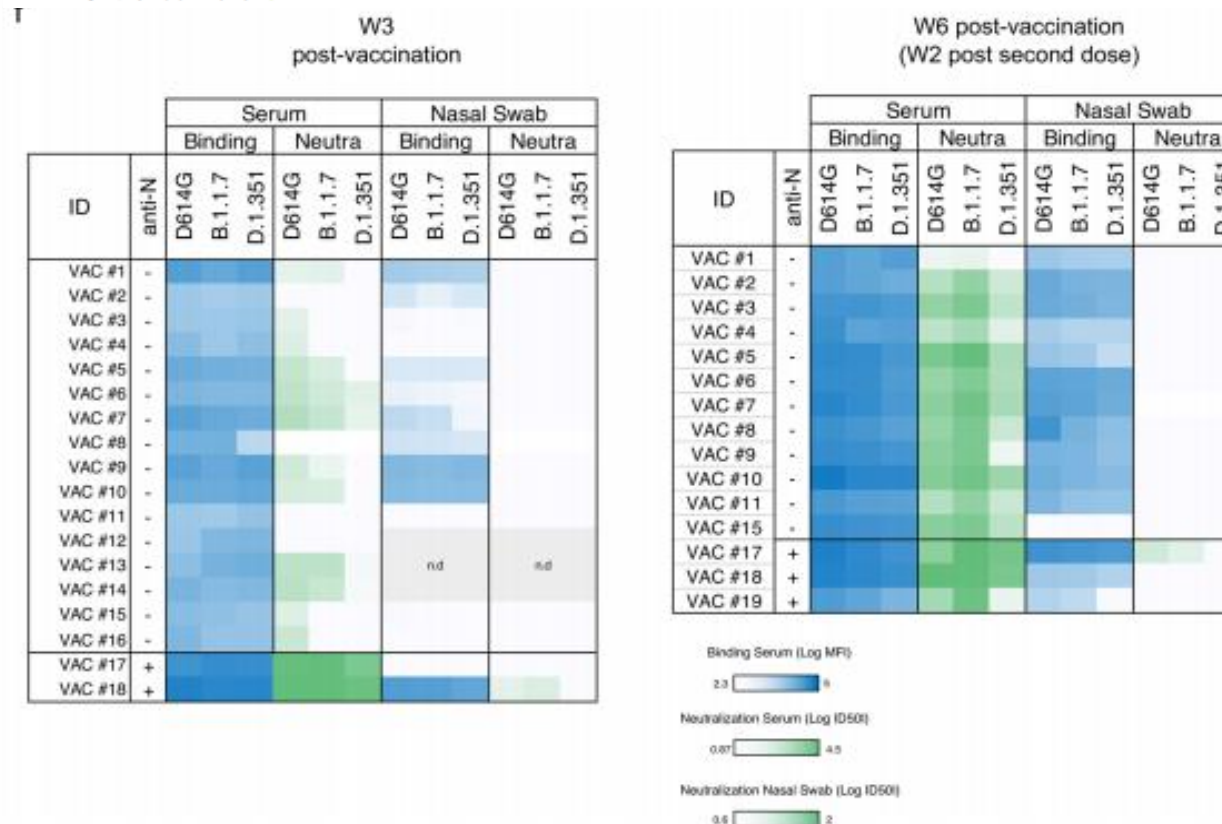
respiratory, lower respiratory tract, and systemic vaccination<sup>16,76,134-147</sup>; or optimized combinations of these. Attempting to control mucosal respiratory viruses with systemically administered non-replicating vaccines has thus far been largely unsuccessful, indicating that new approaches are needed. For example,

respiratory disease often reflects host genetic susceptibility factors.<sup>16,51,146,147</sup>

**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

Delphine Planas<sup>1,2,3,22</sup>, Timothée Bruel<sup>1,2,3,22</sup>, Ludivine Grzelak<sup>1,2,3,4</sup>, Florence Guivel-Benhassine<sup>1,2,3</sup>, Isabelle Staropoli<sup>1,2,3</sup>, Françoise Porrot<sup>1,2,3</sup>, Cyril Planchais<sup>5</sup>, Julian Buchrieser<sup>1,2,3</sup>, Maaran Michael Rajah<sup>1,2,3,4</sup>, Elodie Bishop<sup>1,2,3,4</sup>, Mélanie Albert<sup>6,7</sup>, Flora Donati<sup>6,7</sup>, Matthieu Prot<sup>8</sup>, Sylvie Behillil<sup>6,7</sup>, Vincent Enouf<sup>6,7</sup>, Marianne Maquart<sup>9</sup>, Mounira Smati-Lafarge<sup>10</sup>, Emmanuelle Varon<sup>10</sup>, Frédérique Schortgen<sup>11</sup>, Layla Yahyaoui<sup>12</sup>, Maria Gonzalez<sup>13</sup>, Jérôme De Sèze<sup>14,15</sup>, Hélène Péré<sup>16</sup>, David Veyer<sup>16,17</sup>, Aymeric Sève<sup>18</sup>, Etienne Simon-Lorière<sup>8</sup>, Samira Fafi-Kremer<sup>19,20</sup>, Karl Stefic<sup>9,21</sup>, Hugo Mouquet<sup>5</sup>, Laurent Hocqueloux<sup>18</sup>, Sylvie van der Werf<sup>6,7,23</sup>, Thierry Prazuck<sup>18,23</sup> and Olivier Schwartz<sup>1,2,3,23</sup> ✉



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

July 19, 2022

Science Immunology

Current Issue First release papers Archive About

HOME > SCIENCE IMMUNOLOGY > FIRST RELEASE > RESPIRATORY MUCOSAL IMMUNITY AGAINST SARS-COV-2 FOLLOWING MRNA VACCINATION

REPORTS | CORONAVIRUS

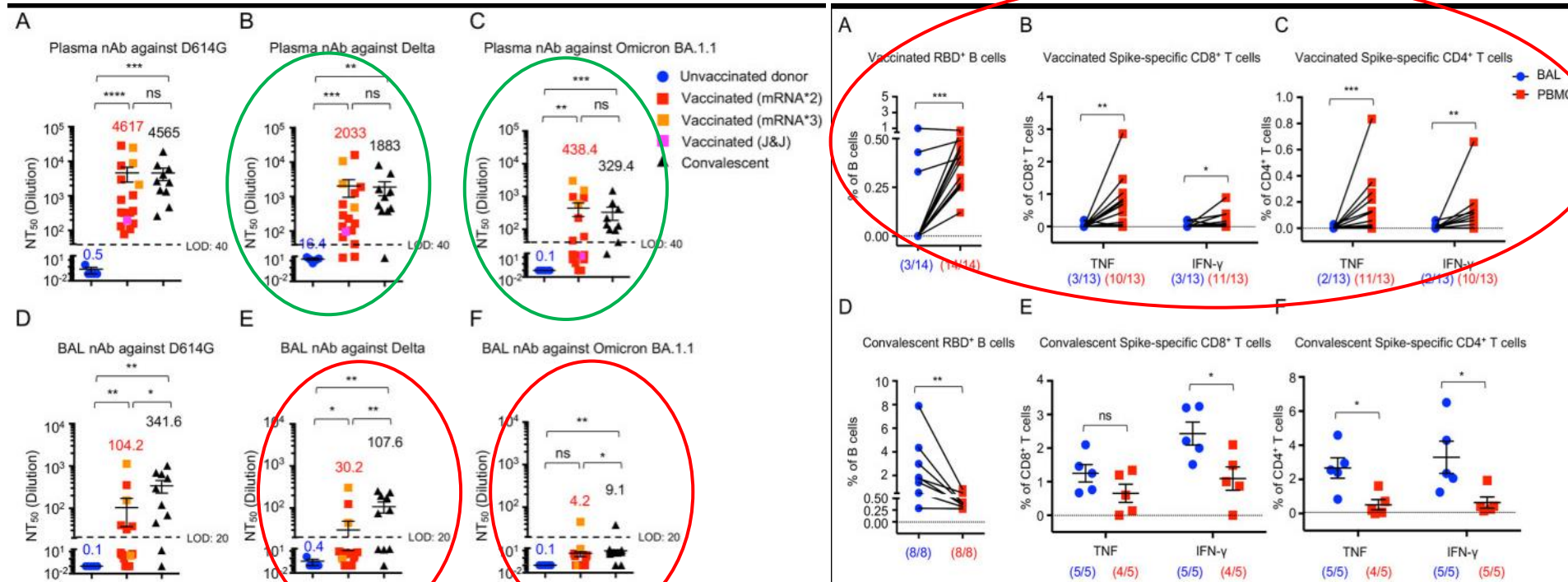


## Respiratory mucosal immunity against SARS-CoV-2 following mRNA vaccination

JINYI TANG, CONG ZENG, THOMAS M. COX, CHAOFAN LI, YOUNG MIN SON, IN SU CHEON, YUE WU, SUPRIYA BEHL, JUSTIN J. TAYLOR, [...]

JIE SUN, +18 authors, Authors Info & Affiliations

SCIENCE IMMUNOLOGY • 19 Jul 2022 • First Release • DOI: 10.1126/sciimmunol.add4853




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

nature  
immunology

ARTICLES

<https://doi.org/10.1038/s41590-018-0260-6>

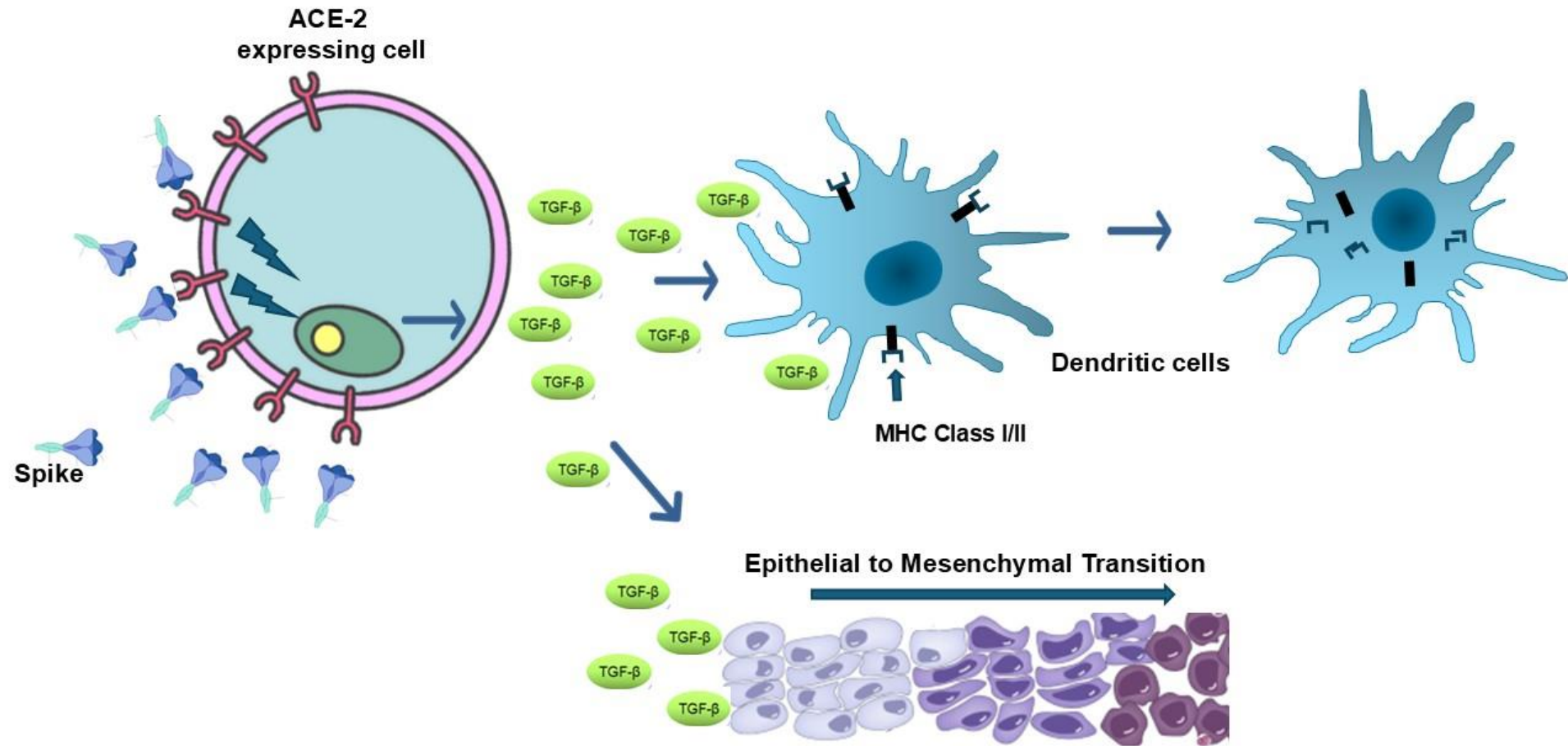
## The establishment of resident memory B cells in the lung requires local antigen encounter

S. Rameeza Allie<sup>1</sup>, John E. Bradley<sup>1</sup>, Uma Mudunuru<sup>1</sup>, Michael D. Schultz<sup>2</sup>, Beth A. Graf<sup>2</sup>, Frances E. Lund<sup>2</sup> and Troy D. Randall <sup>1\*</sup>

Memory B cells are found in lymphoid and non-lymphoid tissues, suggesting that some may be tissue-resident cells. Here we show that pulmonary influenza infection elicited lung-resident memory B cells (BRM cells) that were phenotypically and functionally distinct from their systemic counterparts. BRM cells were established in the lung early after infection, in part because their placement required local antigen encounter. Lung BRM cells, but not systemic memory B cells, contributed to early plasmablast responses following challenge infection. Following secondary infection, antigen-specific BRM cells differentiated in situ, whereas antigen-non-specific BRM cells were maintained as memory cells. These data demonstrate that BRM cells are an important component of immunity to respiratory viruses such as influenza virus and suggest that vaccines designed to elicit BRM cells 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



## OPEN ACCESS

EDITED BY  
Anastas Dimitrov Pashov,  
Bulgarian Academy of Sciences (BAS),  
Bulgaria

REVIEWED BY  
Nesir Abu Rached,  
Ruhr University Bochum, Germany  
Heinz Kohler,  
Retired, Carlsbad, CA, United States

\*CORRESPONDENCE  
Christiana Franke  
✉ christiana.franke@charite.de

†These authors have contributed equally to  
this work

RECEIVED 21 March 2024  
ACCEPTED 11 July 2024  
PUBLISHED 02 August 2024

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

Friederike A. Arlt<sup>1,2†</sup>, Ameli Breuer<sup>1†</sup>, Elli Trampenau<sup>1,2</sup>,  
Fabian Boesl<sup>1</sup>, Marieluise Kirchner<sup>3</sup>, Philipp Mertins<sup>3</sup>,  
Elisa Sánchez-Sendín<sup>1,2</sup>, Mahoor Nasouti<sup>1,2</sup>, Marie Mayrhofer<sup>4</sup>,  
Martin Blüthner<sup>4</sup>, Matthias Endres<sup>1,2,5,6,7</sup>, Harald Prüss<sup>1,2†</sup>  
and Christiana Franke<sup>1,4†</sup>

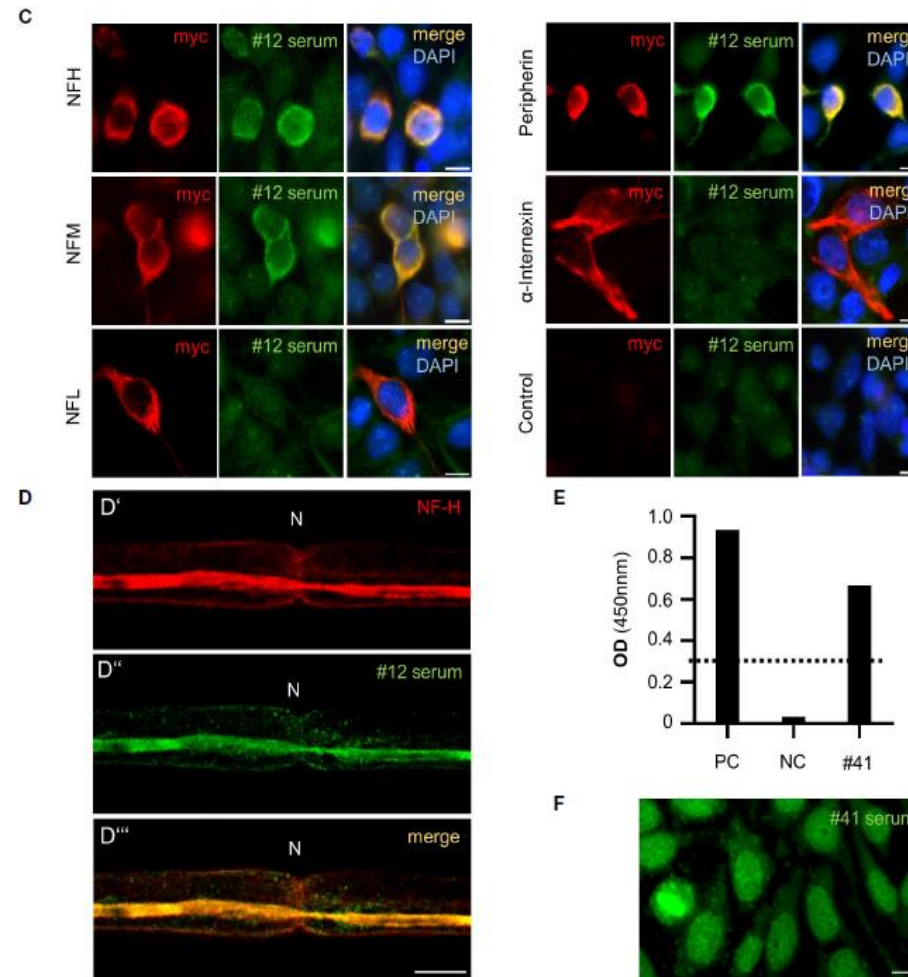


FIGURE 2

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 log<sub>2</sub>-transformed fold change, and the y-axis represents the -log<sub>10</sub>-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*