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Supplementary Materials for

Vaccine breakthrough hypoxemic COVID-19 pneumonia in patients with auto-Abs neutralizing type I IFNs

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The PDF file includes:

Other Supplementary Material for this manuscript includes the following:

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Vaccine breakthrough hypoxemic COVID-19 pneumonia in patients with auto-Abs neutralizing type I IFNs

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Martinez-Picado[80-83], Tayfun Ozcelik[84], Sevgi Keles[51], Luisa Imberti[25], Luigi D. Notarangelo[14], Jesus Troya[85], Xavier Solanich[58], Shen-Ying Zhang[1-3], Anne Puel[1-3], Michael R Wilson[11], Sophie Trouillet-Assant[86], Laurent Abel[1-3], Emmanuelle Jouanguy[1-3], Chun Jimmie Ye[10,87-90,§], Aurélie Cobat[1-3,§], Leslie M. Thompson[91,§], Evangelos Andreakos[16,§], Qian Zhang[1-3,§], Mark S. Anderson[7,92,#,@], Jean-Laurent Casanova[1-4,93,#,@] and Joseph L. DeRisi[8,10,#,@]

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This PDF file includes:

Supplementary table S1 and legends to supplementary table (S1)
Legends to supplementary figure S1
Supplementary figure S1

Supplementary materials and methods

Subjects and samples

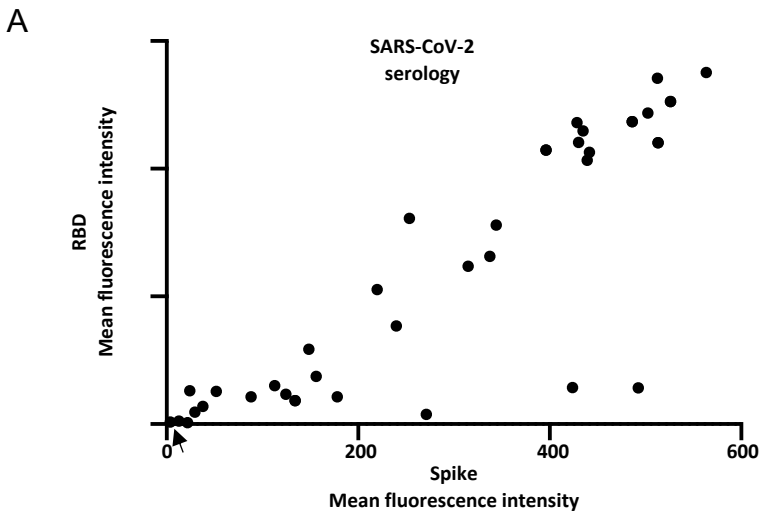
We enrolled, from 6 countries, 48 patients with proven hypoxemic COVID-19 pneumonia, 12 unvaccinated controls, and 11 vaccinated controls in this study. We collected plasma or serum samples for all these individuals to test by immuno-assay for the presence of IgG Abs against SARS-CoV-2 and auto-Abs to type I IFNs. All individuals were recruited according to protocols approved by local Institutional Review Boards (IRBs). For patients were enrolled in the French COVID cohort (clinicaltrials.gov NCT04262921), ethics approval was obtained from the CPP IDF VI (ID RCB: 2020-A00256-33). For patients enrolled at UCSF, IRB number was: 20-30497. All protocols conformed to local ethics recommendations and informed consent was obtained when required.

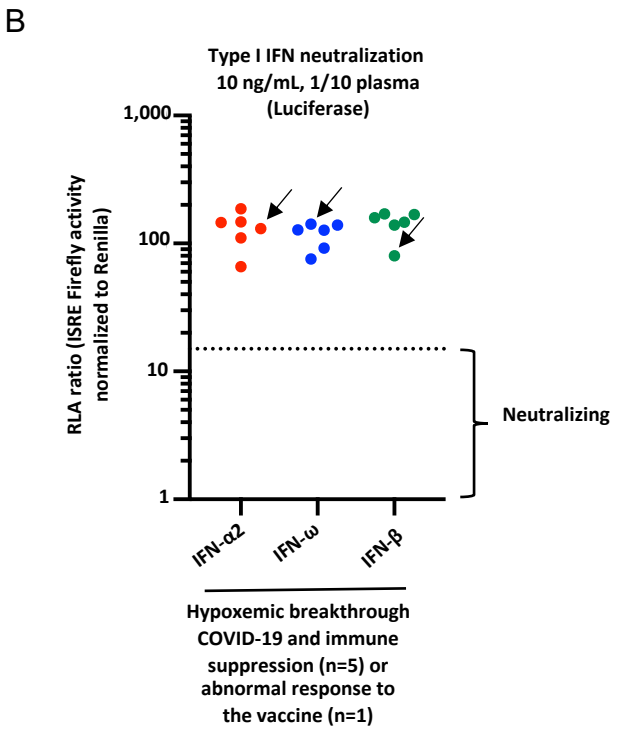
Table S1: Antibody response to the vaccine

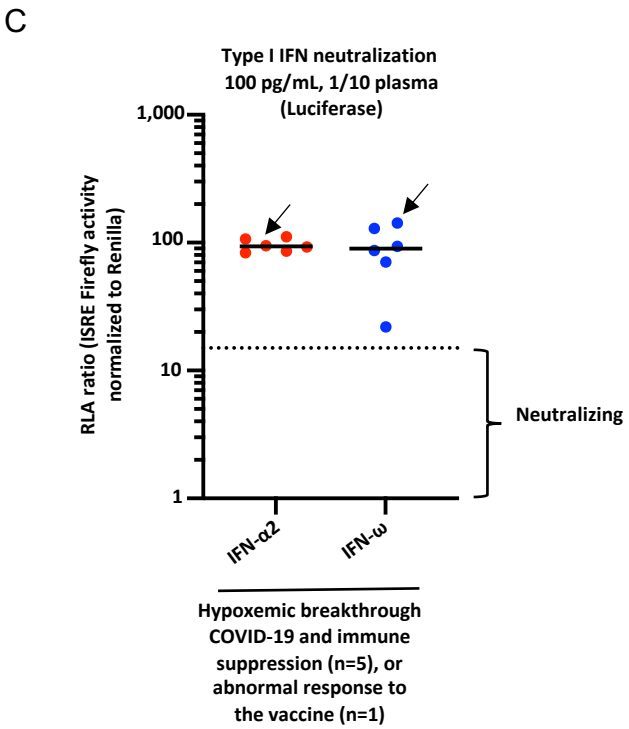
	Spike p-val	**RBD p-val**
NOVAX vs POSTVAX	8,46E-18	8,98E-15
NOVAX vs all breakthrough (n=40)	1,95E-06	0,000147706
aab+ (n=10) vs aab- breakthrough (n=30)	0,4320157	0,259816689

Figure S1: No neutralizing auto-Abs against IFN-α2 and IFN-ω in patients with hypoxemic breakthrough COVID-19 and an insufficient serological response or immunodeficiencies. Serological response in auto-Ab positive patients. (A) Spike(S)-protein and receptor binding domain (RBD) serological titers, plotted against each other for breakthrough COVID-19 patients **(B)** Neutralization of 10 ng/mL IFN-α2, IFN-ω or IFN-β in the presence of plasma 1/10 from patients with hypoxemic breakthrough COVID-19 and previously known immunodeficiency (N=5) or with low Ab response to the virus (n=1). The patients with low Ab response to the virus is shown with an arrow. Relative luciferase activity is shown (ISRE dual luciferase activity, with normalization against *Renilla* luciferase activity) after stimulation with 10ng/mL IFN-α2 or IFN-ω in the presence of plasma 1/10. RLA: relative luciferase activity. **(C)** Neutralization of 100 pg/mL IFN-α2 or IFN-ω in the presence of plasma 1/10 from patients with hypoxemic breakthrough COVID-19 and previously known immunodeficiency (N=5) or with low Ab response to the virus (n=1). **(D)** Spike(S)-protein and receptor binding domain (RBD) serological titers of the 10 auto-Ab positive patients. **(E)** Spike(S)-protein and receptor binding domain (RBD) serological titers of the 10 auto-Ab positive patients, represented individually.

Figure S1


A
SARS-CoV-2
serology
RBD
Mean fluorescence intensity
0
200
400
600
Spike
Mean fluorescence intensity


B
Type I IFN neutralization
10 ng/mL, 1/10 plasma
(Luciferase)
1,000
100
10
1
RLA ratio (ISRE Firefly activity
normalized to Renilla)
Neutralizing
IFN-α2
IFN-ω
IFN-β
Hypoxemic breakthrough
COVID-19 and immune
suppression (n=5) or
abnormal response to
the vaccine (n=1)


C
Type I IFN neutralization
100 pg/mL, 1/10 plasma
(Luciferase)
1,000
100
10
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RLA ratio (ISRE Firefly activity
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Neutralizing
IFN-α2
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Hypoxemic breakthrough
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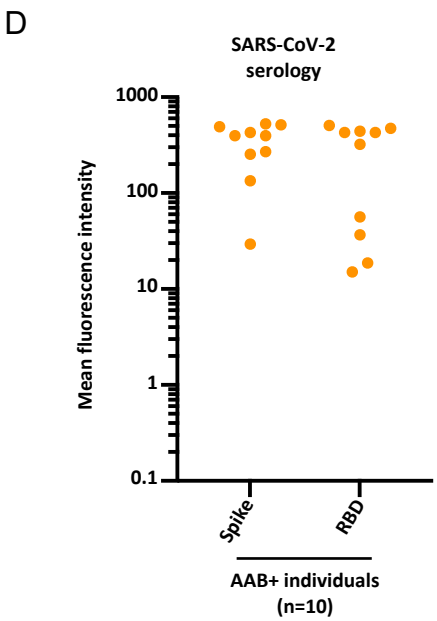
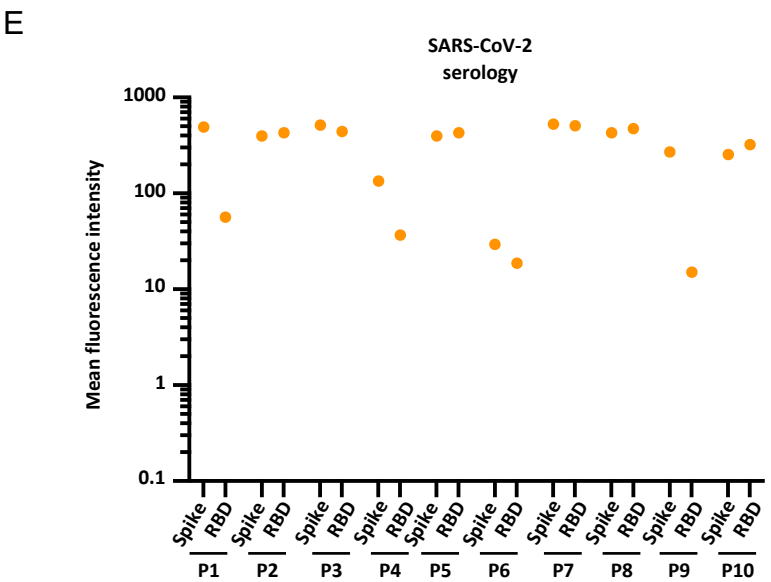

D
SARS-CoV-2
serology
1000
100
10
1
0.1
Mean fluorescence intensity
Spike
RBD
AAB+ individuals
(n=10)


E
SARS-CoV-2
serology
1000
100
10
1
0.1
Mean fluorescence intensity
Spike
RBD
P1
P2
P3
P4
P5
P6
P7
P8
P9
P10