

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:

Materials and Methods
Table S1
Fig. S1

Other Supplementary Material for this manuscript includes the following:

Data file 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- α 2 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- α 2, 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- α 2 or IFN- ω in the presence of plasma 1/10. RLA: relative luciferase activity. **(C)** Neutralization of 100 pg/mL IFN- α 2 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.

