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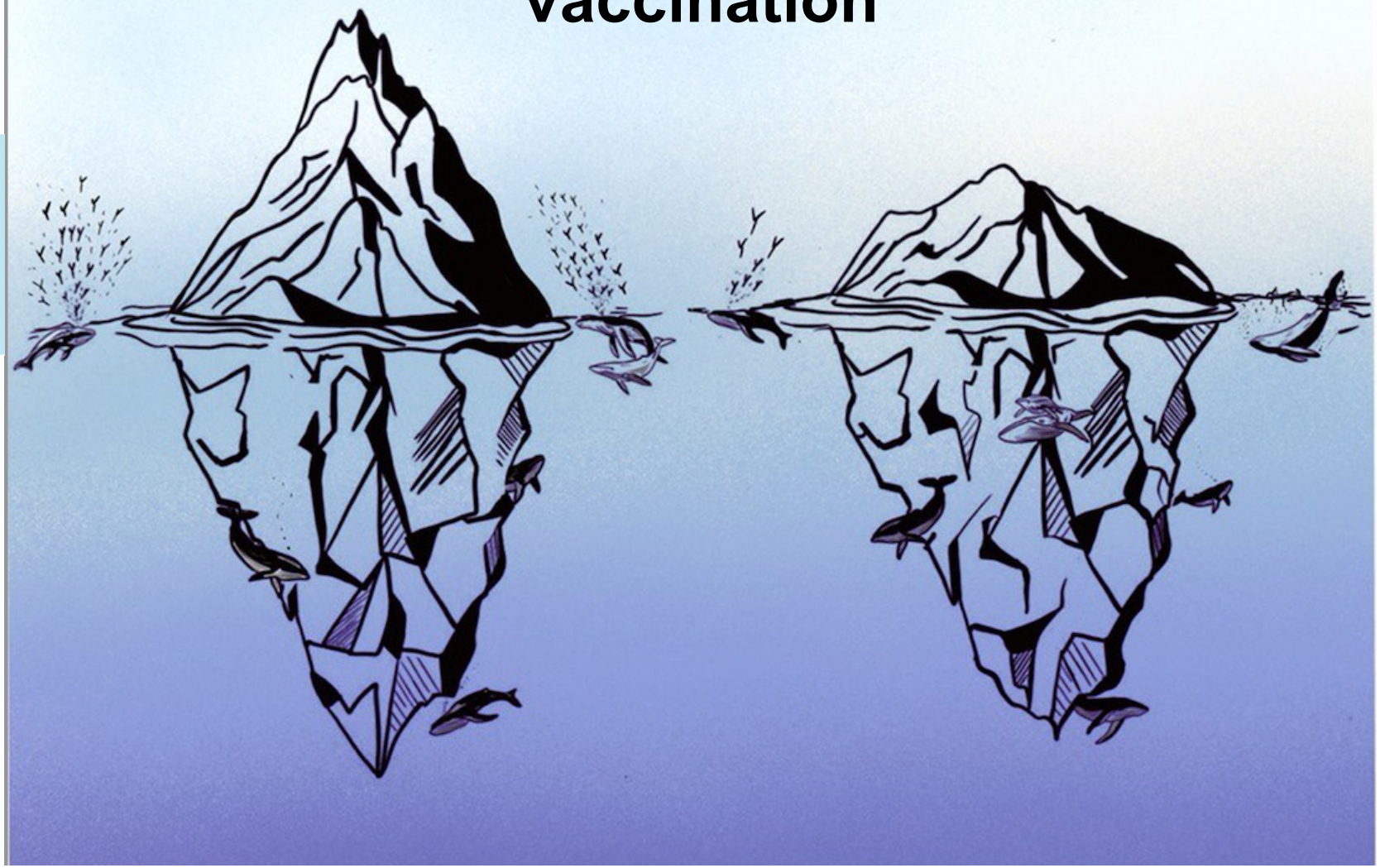
ESCCA 2022
21-24 SEPTEMBER 2022

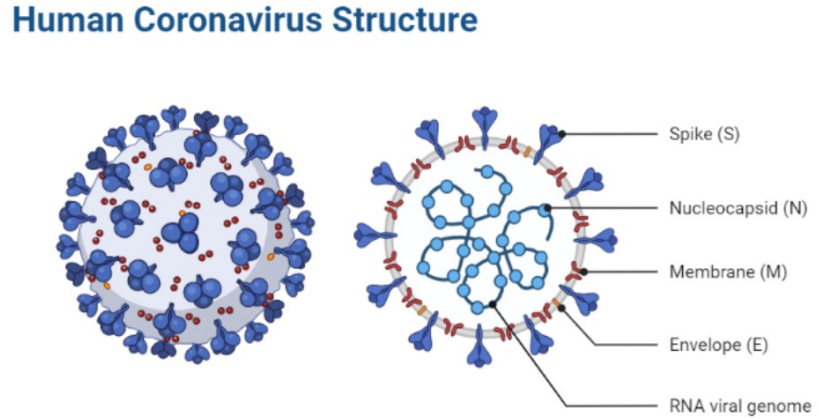
Development and performance of Spike-specific memory B cells after SARS-CoV-2 vaccination



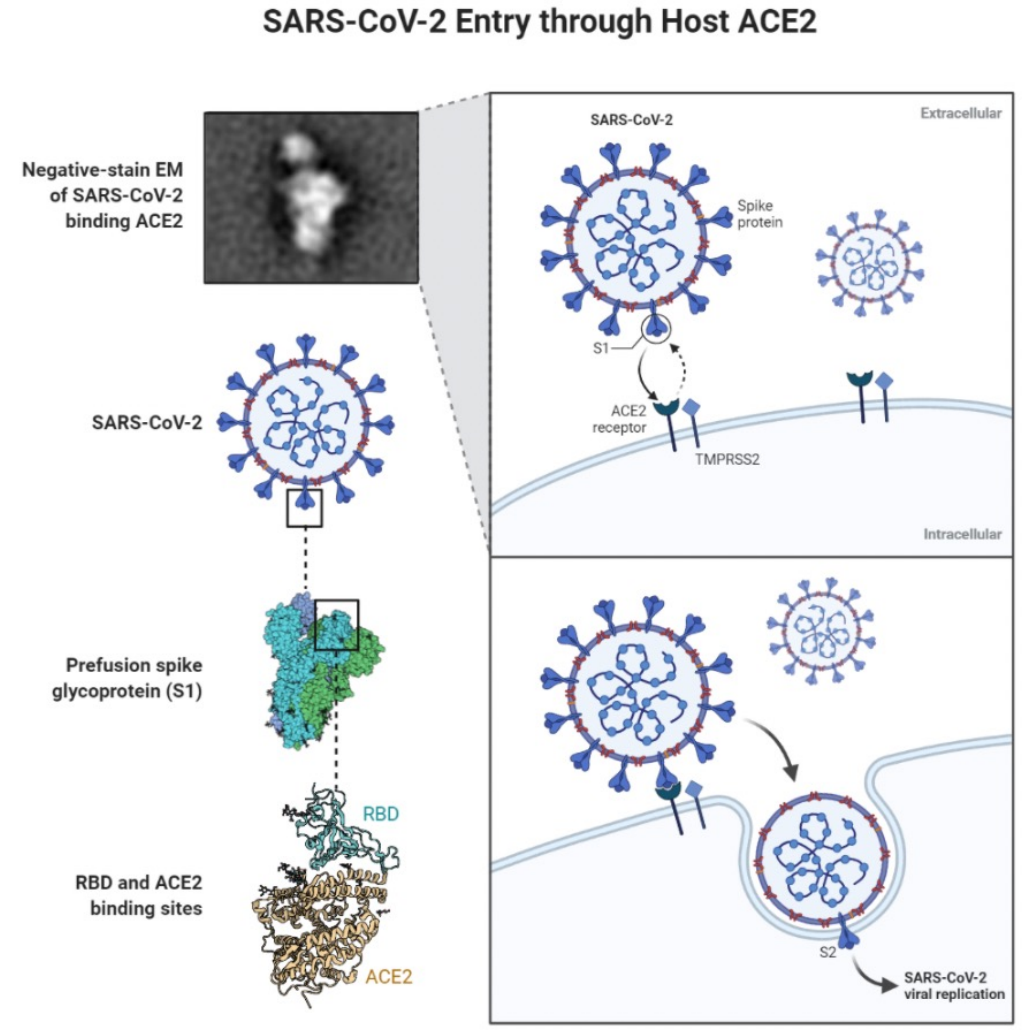
Eva Piano Mortari, PhD
B cell Research Unit
Immunology Area

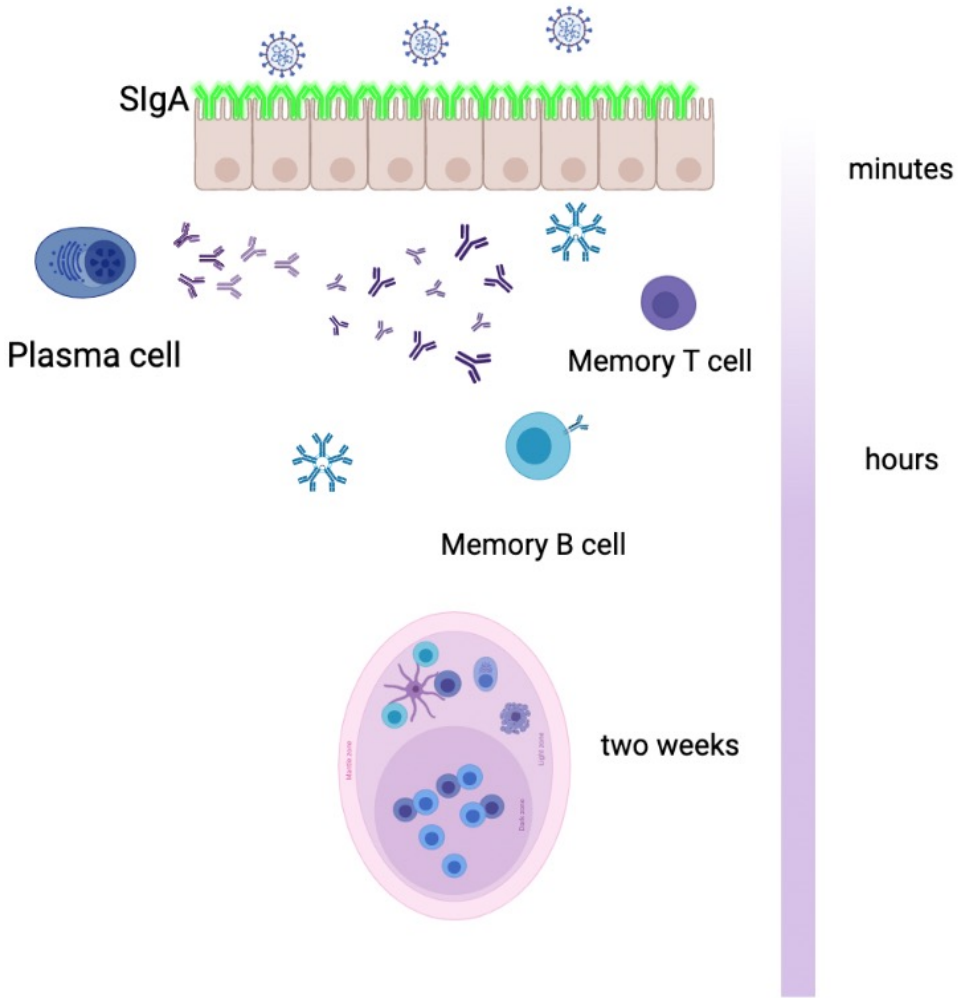
Bambino Gesù
OSPEDALE PEDIATRICO

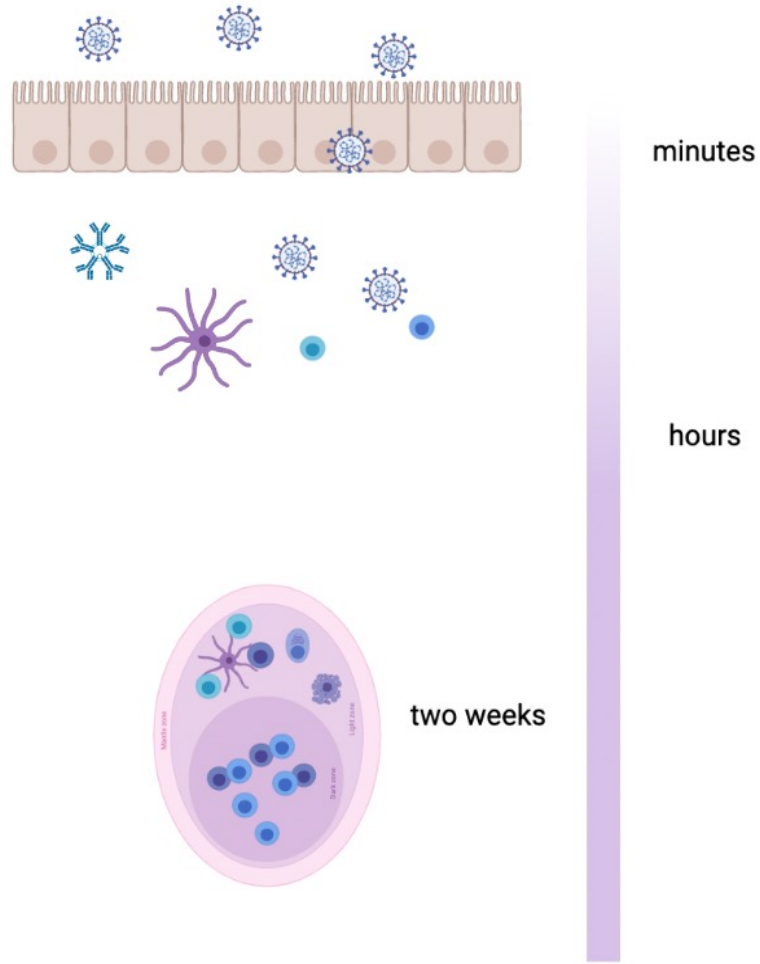
SAPIENZA
UNIVERSITÀ DI ROMA

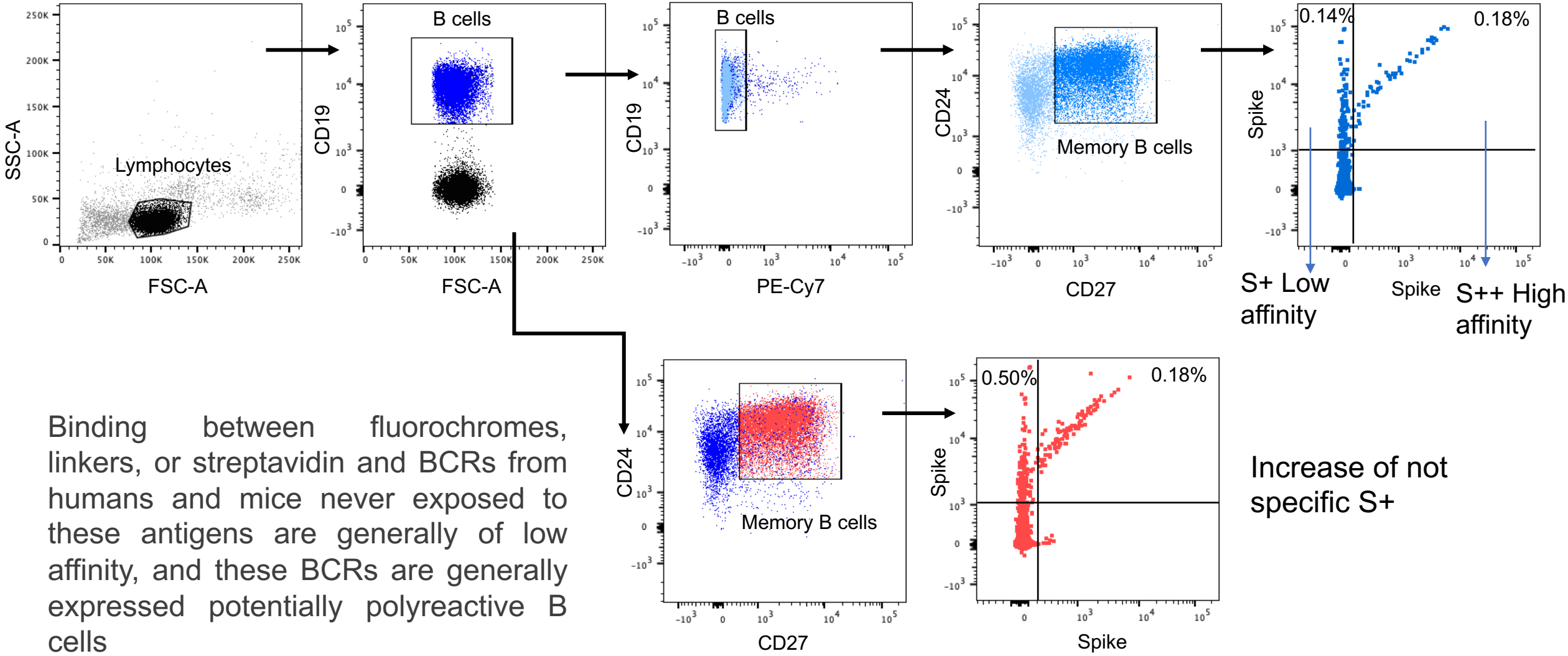


The high infectivity of SARS-CoV-2 and rapid rise of number of patients is explained by the lack of pre-existing immunity to a virus never encountered before




SIgA
Plasma cell
Memory T cell
Memory B cell
minutes
hours
two weeks


minutes
hours
two weeks



Binding between fluorochromes, linkers, or streptavidin and BCRs from humans and mice never exposed to these antigens are generally of low affinity, and these BCRs are generally expressed potentially polyreactive B cells

Increase of not specific S+

B cell performance after vaccination

1. Development of memory B cells

2. Performance of memory B cells

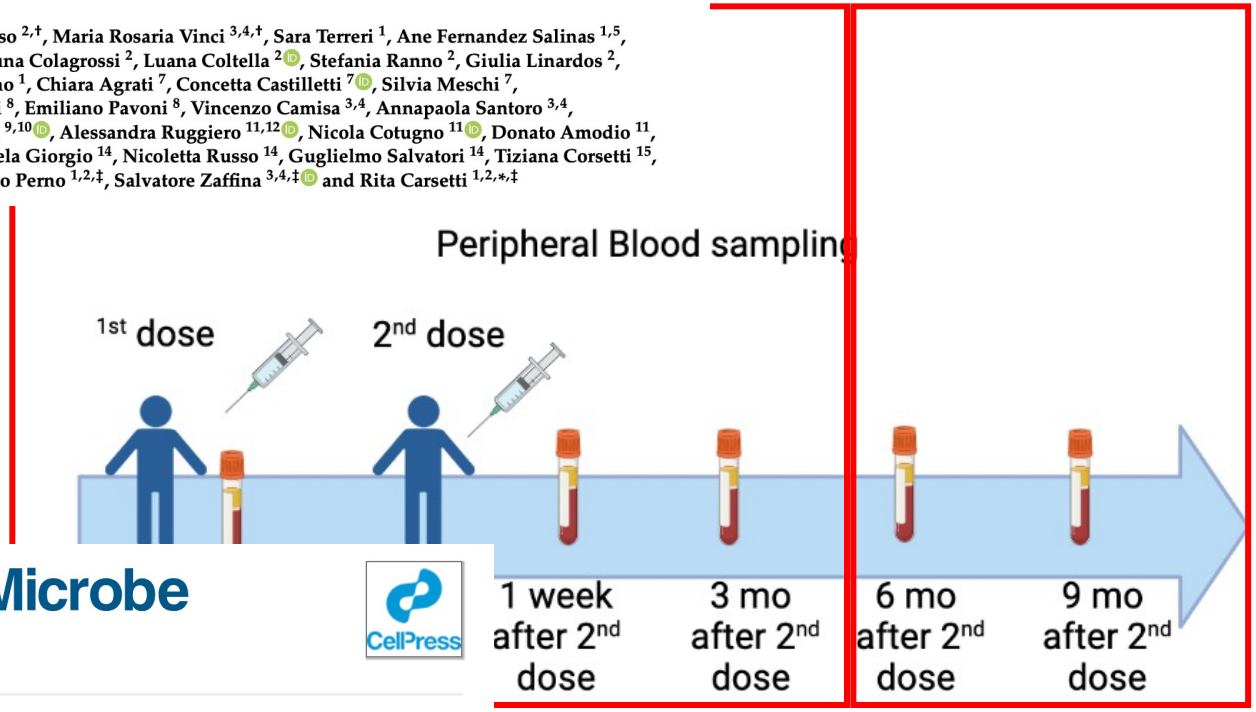
cells

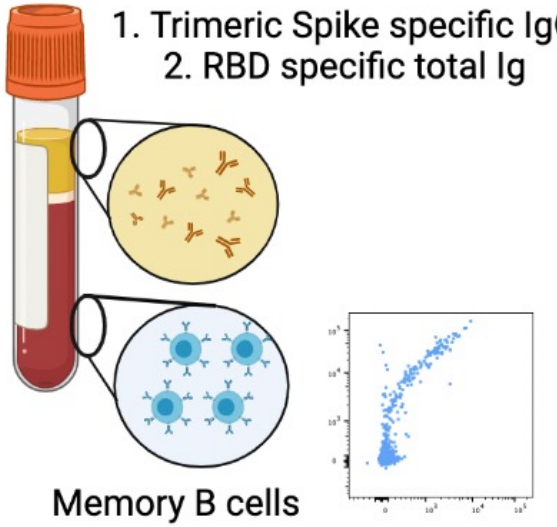
MDPI

Article

Highly Specific Memory B Cells Generation after the 2nd Dose of BNT162b2 Vaccine Compensate for the Decline of Serum Antibodies and Absence of Mucosal IgA

Eva Piano Mortari [1,†], Cristina Russo [2,†], Maria Rosaria Vinci [3,4,†], Sara Terreri [1], Ane Fernandez Salinas [1,5], Livia Piccioni [2], Claudia Alteri [1,6], Luna Colagrossi [2], Luana Coltella [2], Stefania Ranno [2], Giulia Linardos [2], Marilena Agosta [2], Christian Albano [1], Chiara Agrati [7], Concetta Castilletti [7], Silvia Meschi [7], Paolo Romania [1,5], Giuseppe Roscilli [8], Emiliano Pavoni [8], Vincenzo Camisa [3,4], Annapaola Santoro [3,4], Rita Brugaletta [3,4], Nicola Magnavita [9,10], Alessandra Ruggiero [11,12], Nicola Cotugno [11], Donato Amodio [11], Marta Luisa Ciofi Degli Atti [13], Daniela Giorgio [14], Nicoletta Russo [14], Guglielmo Salvatori [14], Tiziana Corsetti [15], Franco Locatelli [16,17], Carlo Federico Perno [1,2,‡], Salvatore Zaffina [3,4,‡] and Rita Carsetti [1,2,*,‡]





Cell Host & Microbe

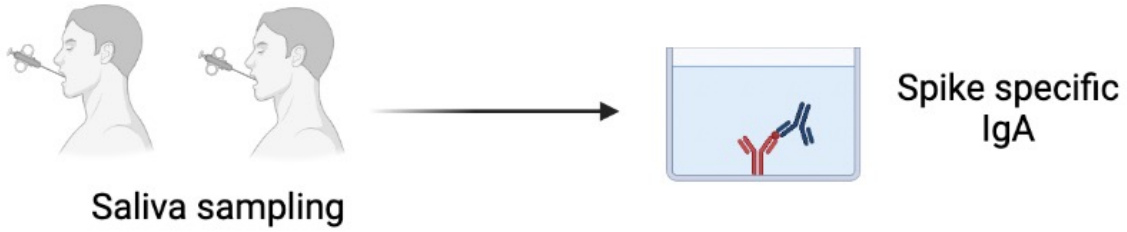
Available online 25 January 2022

In Press, Corrected Proof

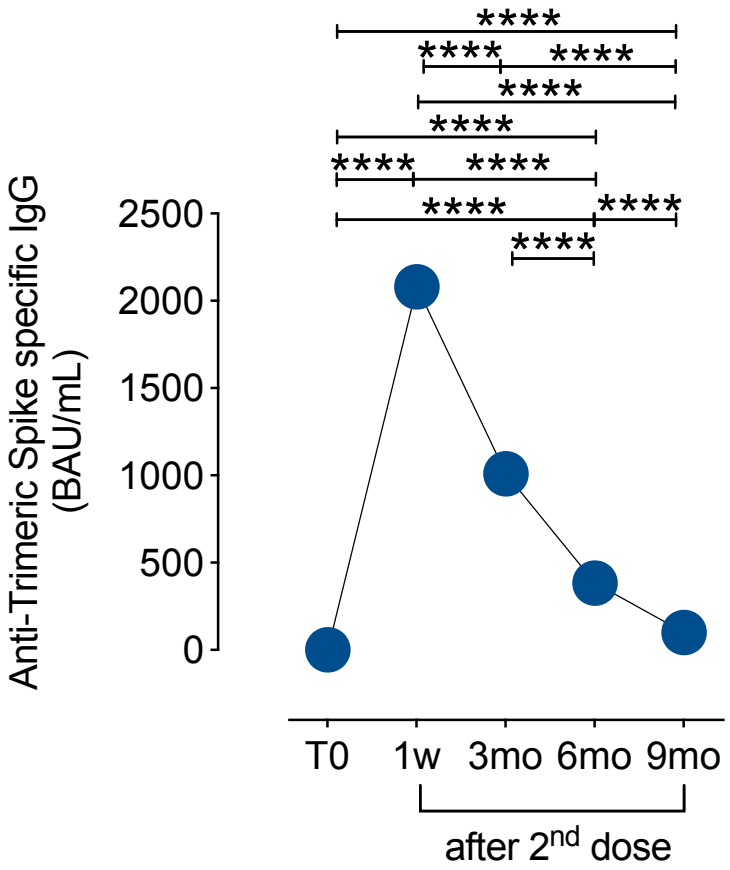
Article

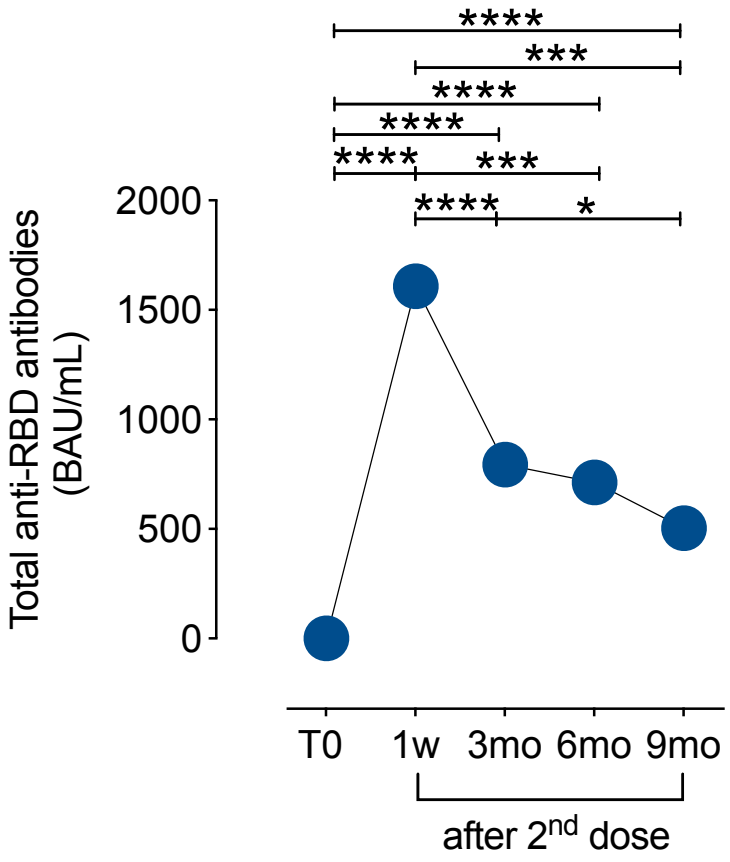
Persistent B cell memory after SARS-CoV-2 vaccination is functional during breakthrough infections

Sara Terreri [1, 16], Eva Piano Mortari [1, 16], Maria Rosaria Vinci [2], Cristina Russo [3], Claudia Alteri [3, 4], Christian Albano [1], Francesca Colavita [5], Giulia Gramigna [5], Chiara Agrati [6], Giulia Linardos [3], Luana Coltella [3], Luna Colagrossi [3], Gloria Deriu [2], Marta Ciofi Degli Atti [7], Caterina Rizzo [7], Marco Scarsella [8], Rita Brugaletta [2], Vincenzo Camisa [2] ... Rita Carsetti [1, 3, 15, 17]



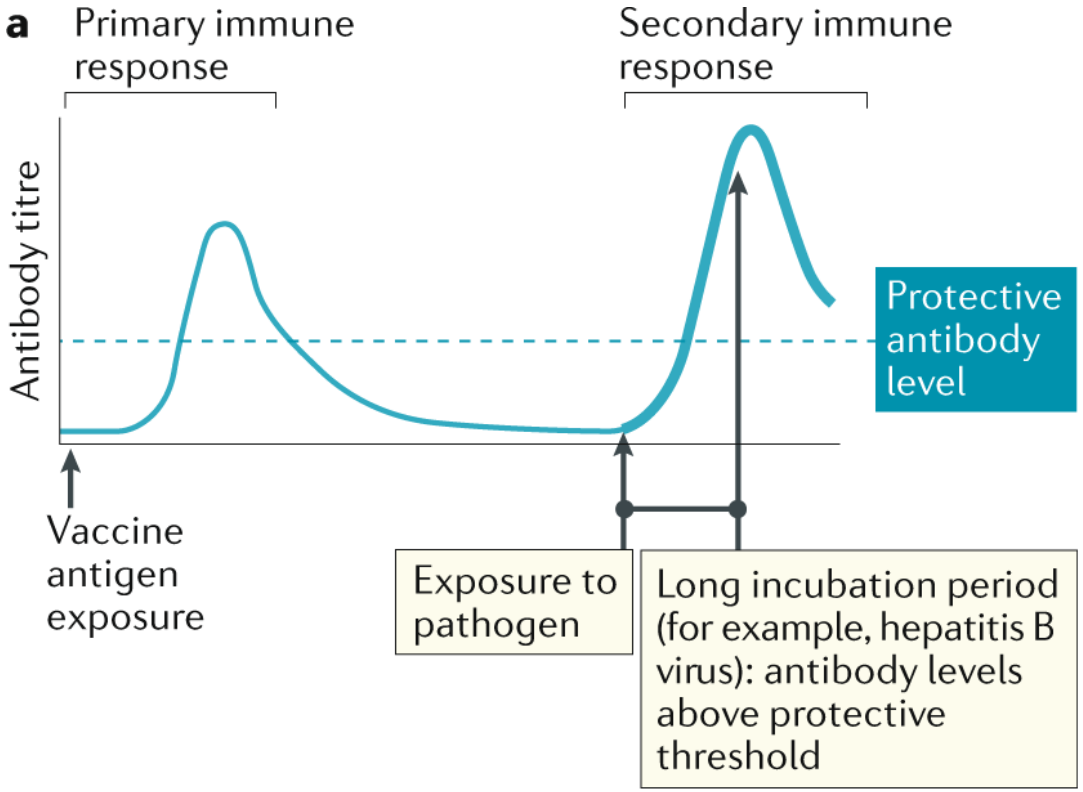
Serum specific antibodies to RBD and Trimeric Spike reach the maximum level after the 2nd dose and decline three months later

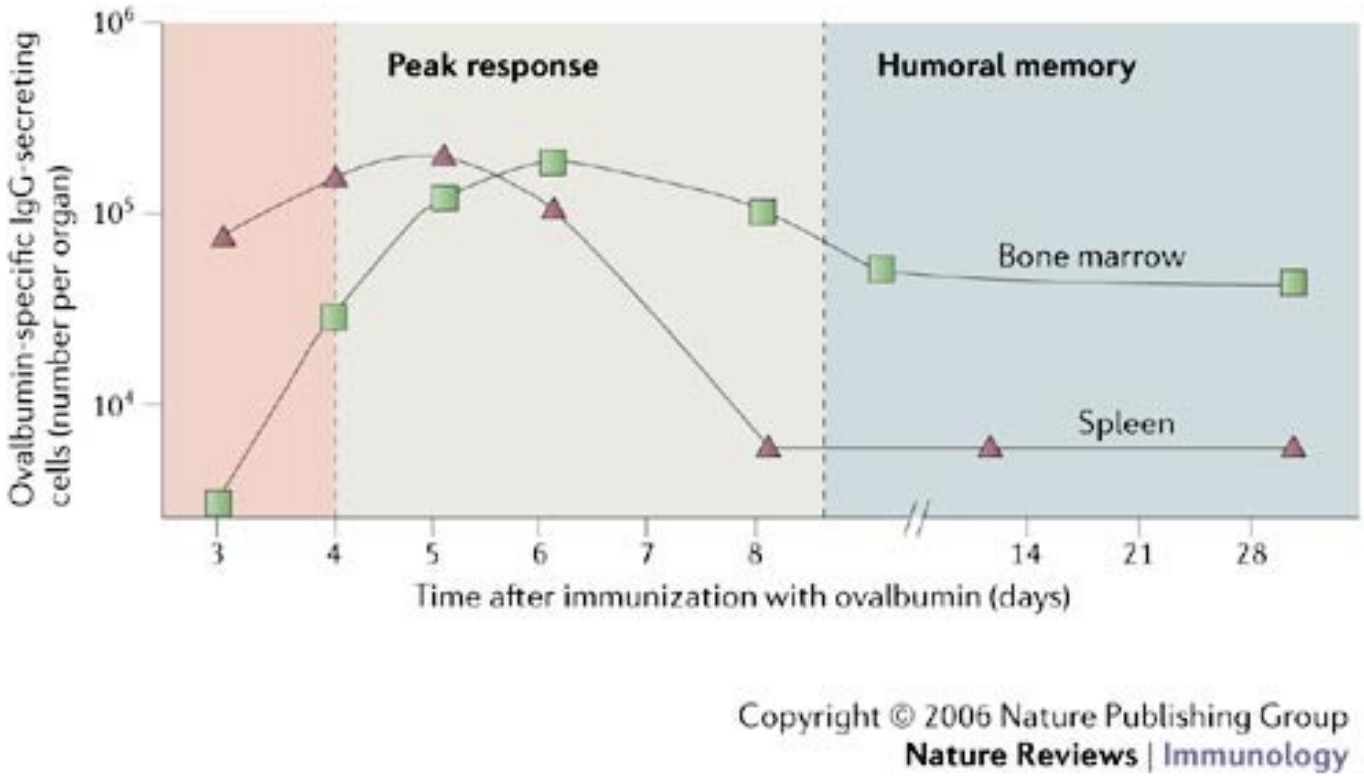




Stabilization of antibody titers between 6 and 9 months after 2nd dose

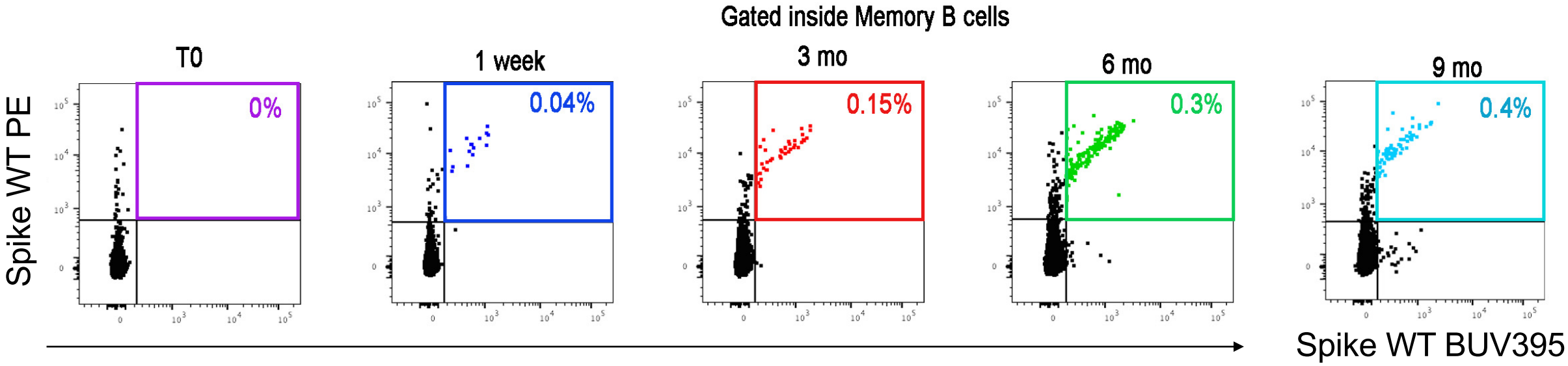
Terreri, Piano Mortari et al. *Cell Host&Microbes* 2022

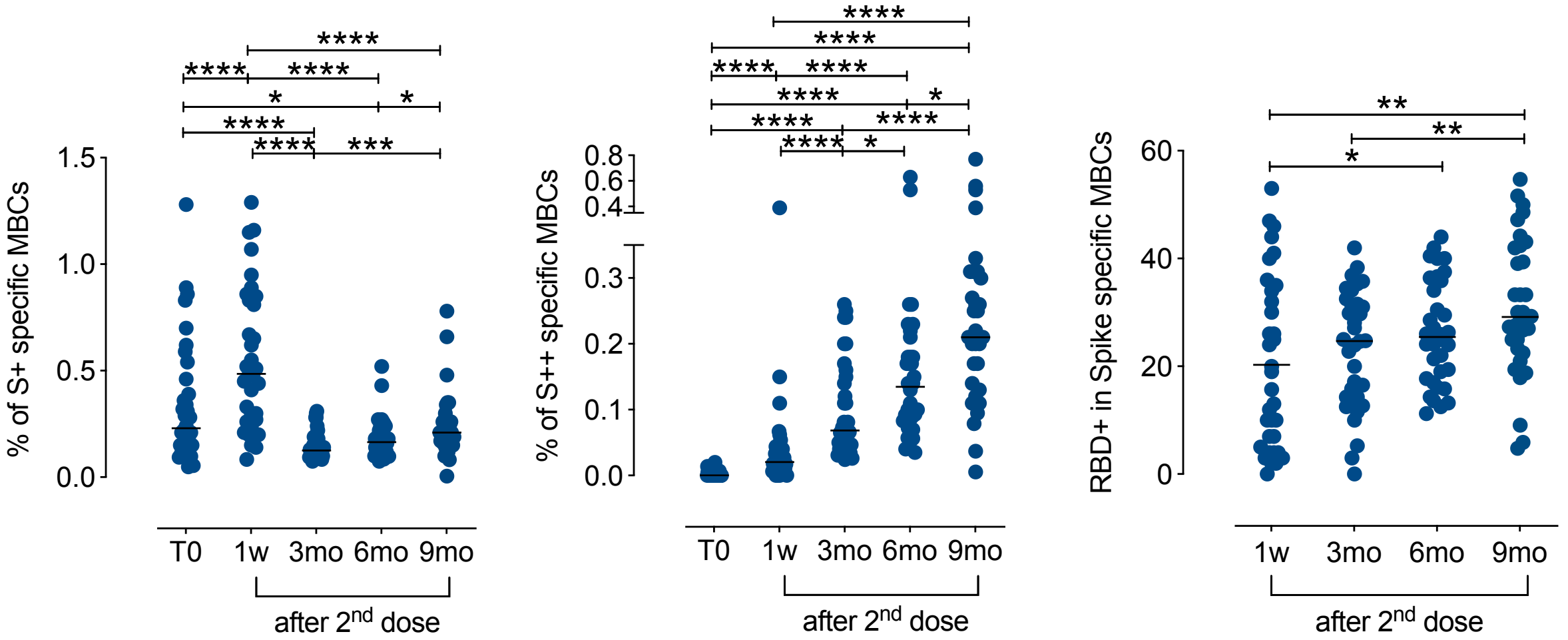




Nature Reviews Immunology **volume 21**, pages83–100(2021)

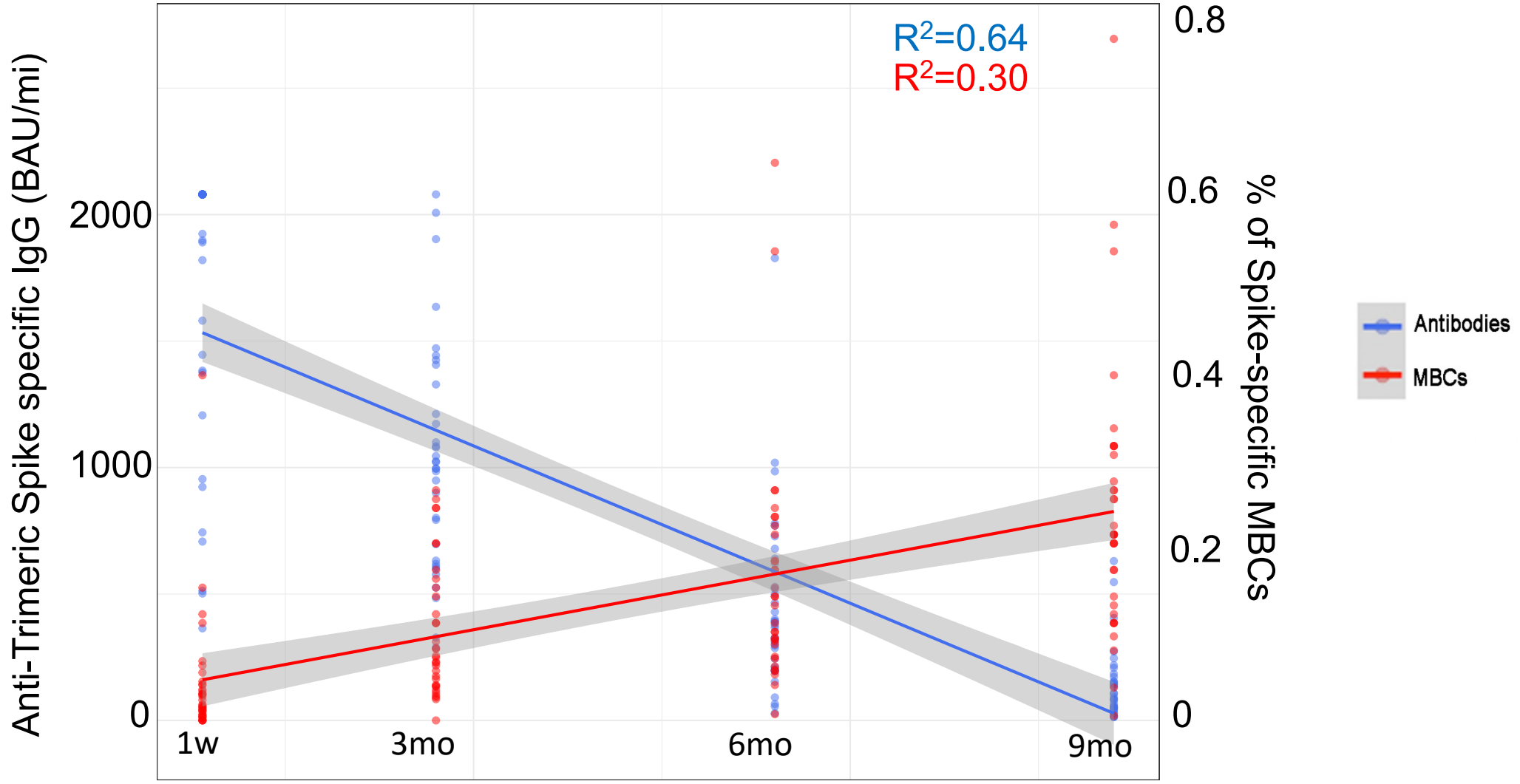
Memory B cells development following vaccination

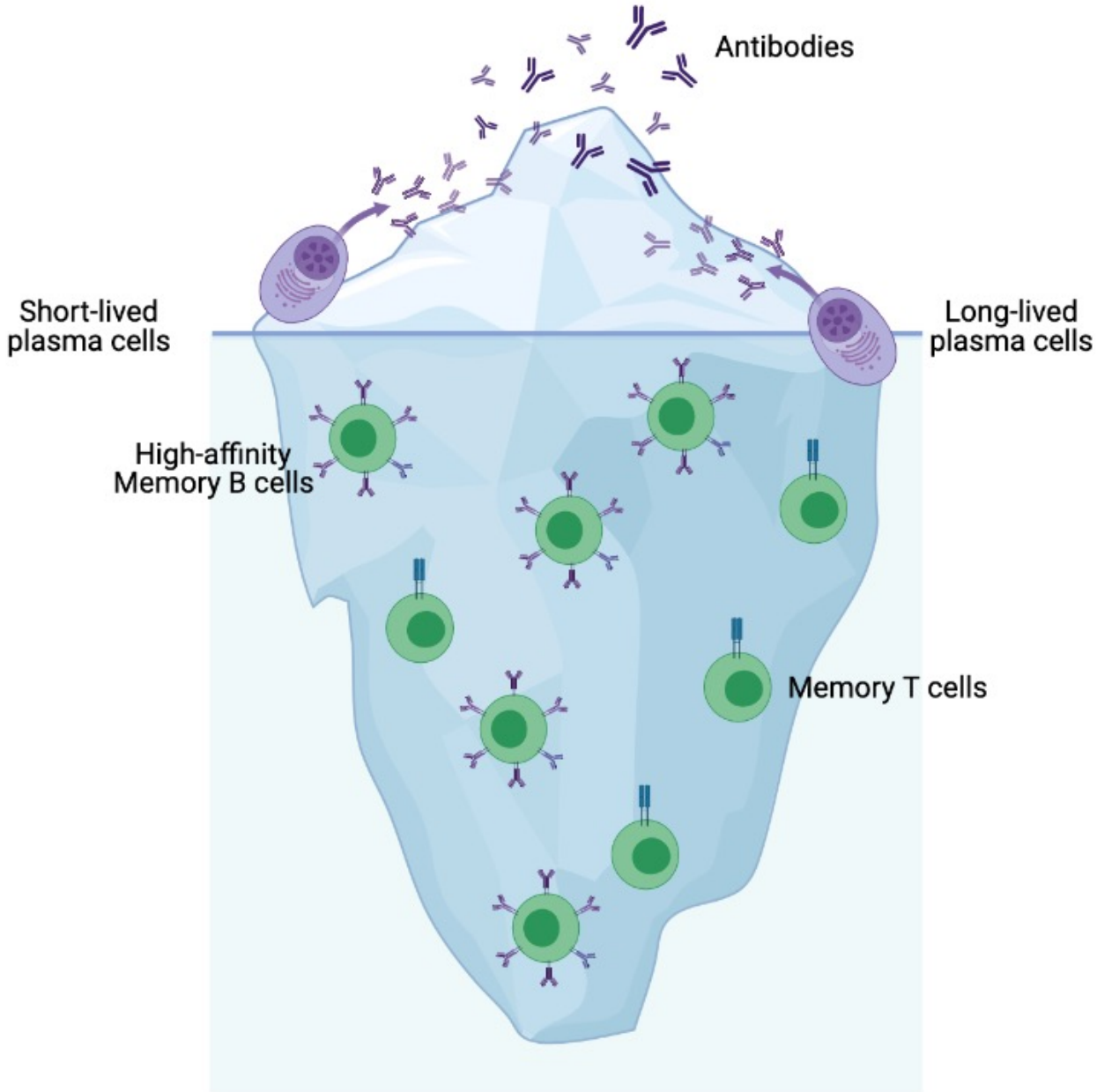


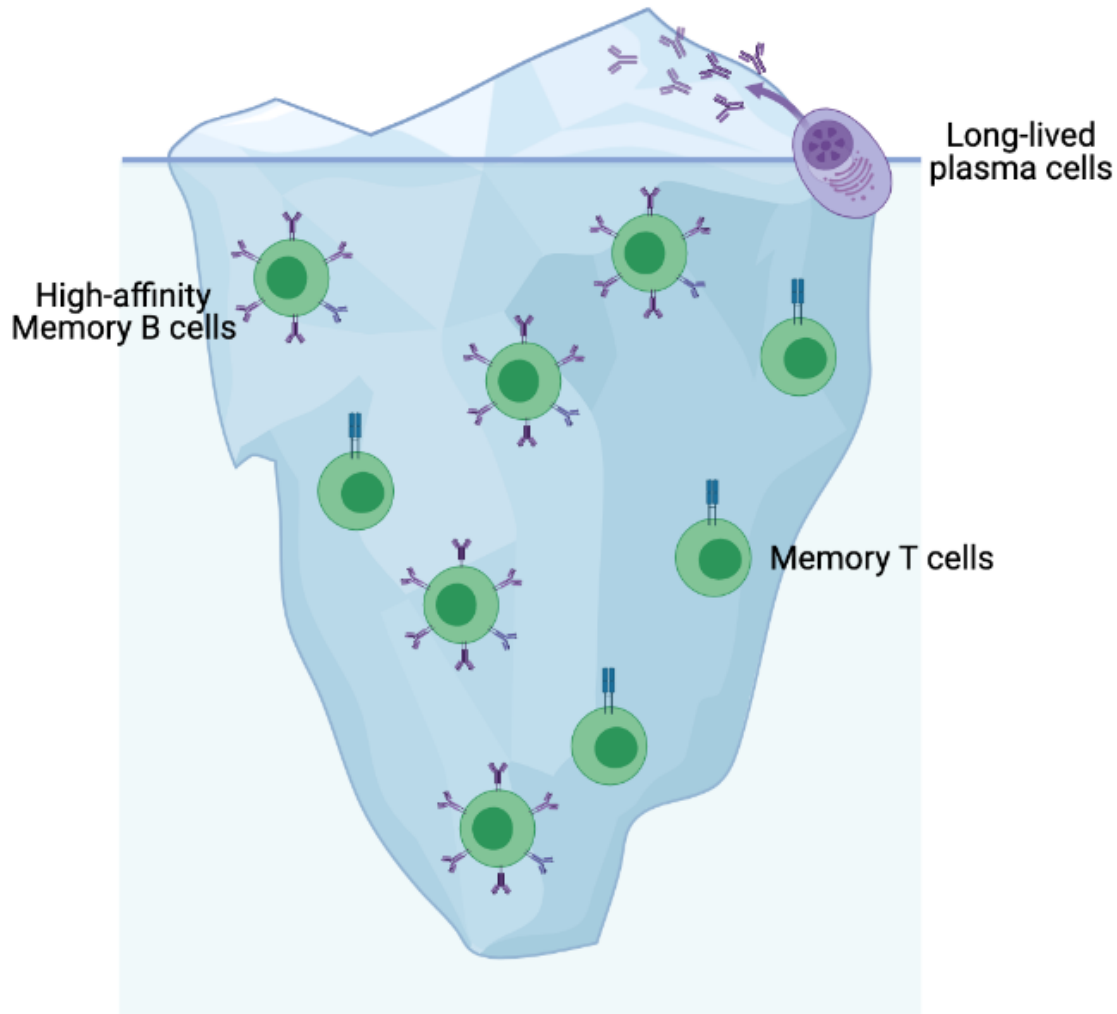


Spike-specific MBCs continue to increase for 9 months after vaccination

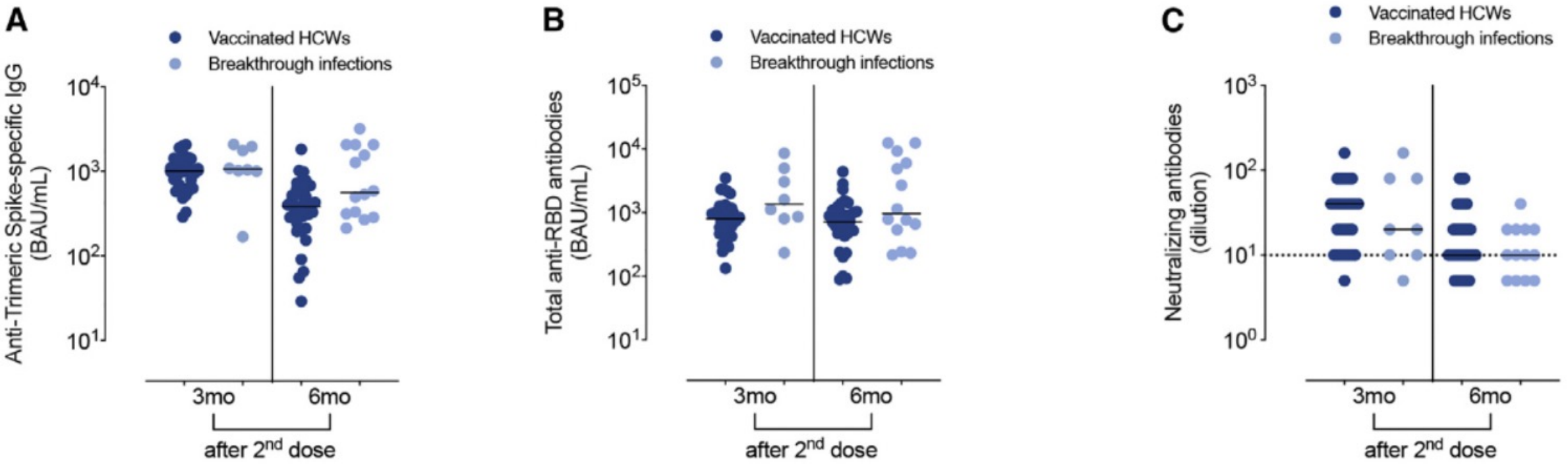
Terreri, Piano Mortari et al. *Cell Host&Microbes* 2022

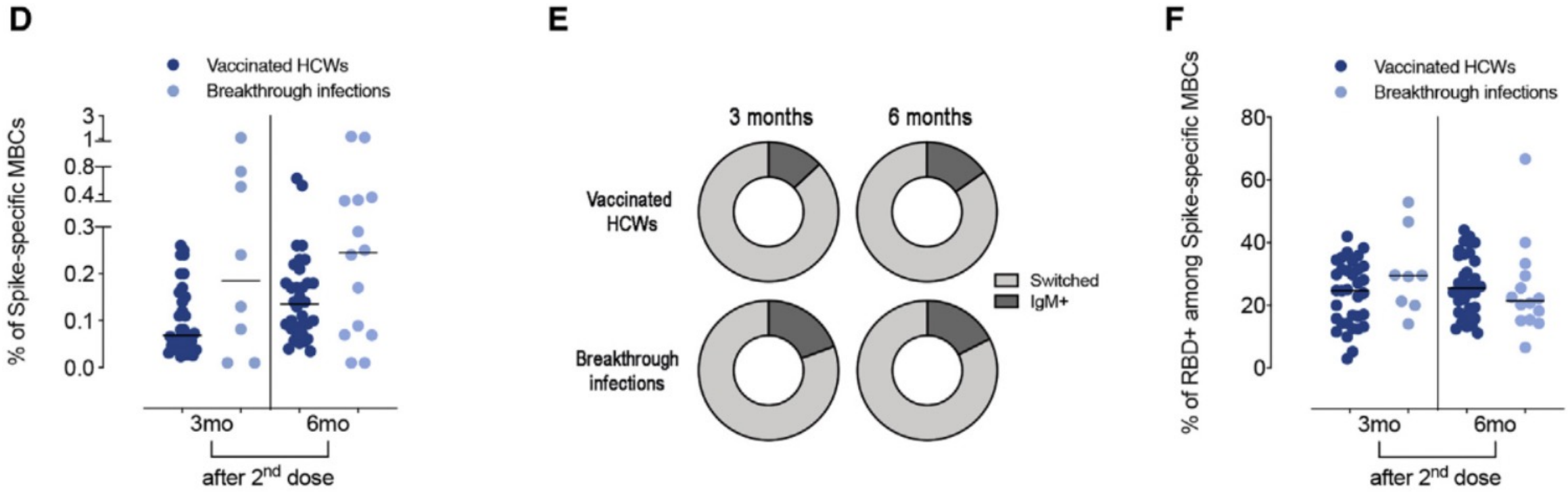

R2=0.64
R2=0.30
Anti-Trimeric Spike specific IgG (BAU/mi)
2000
1000
0
0.8
0.6
0.4
0.2
0
% of Spike-specific MBCs
1w
3mo
6mo
9mo
Antibodies
MBCs


Antibodies
Short-lived
plasma cells
Long-lived
plasma cells
High-affinity
Memory B cells
Memory T cells


Long-lived
plasma cells
High-affinity
Memory B cells
Memory T cells

Why people have breakthrough infections?

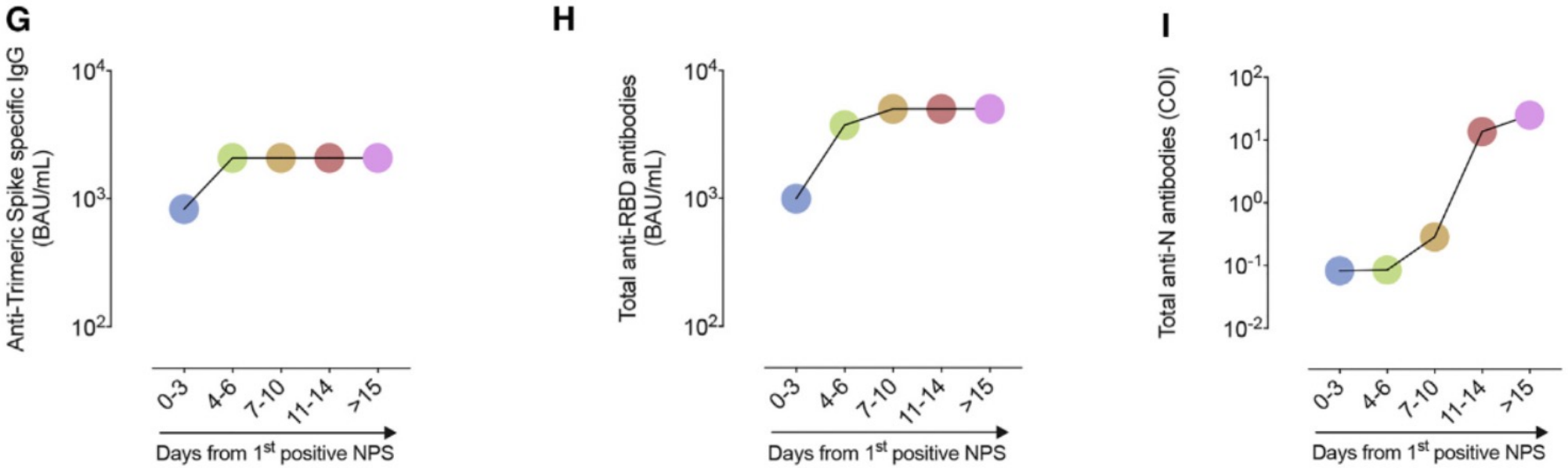



D
Vaccinated HCWs
Breakthrough infections
% of Spike-specific MBCs
3
1
0.8
0.4
0.3
0.2
0.1
0.0
3mo
6mo
after 2nd dose
E
3 months
6 months
Vaccinated HCWs
Breakthrough infections
Switched
IgM+
F
Vaccinated HCWs
Breakthrough infections
% of RBD+ among Spike-specific MBCs
80
60
40
20
0
3mo
6mo
after 2nd dose

PERFORMANCE OF SPECIFIC MEMORY B CELLS

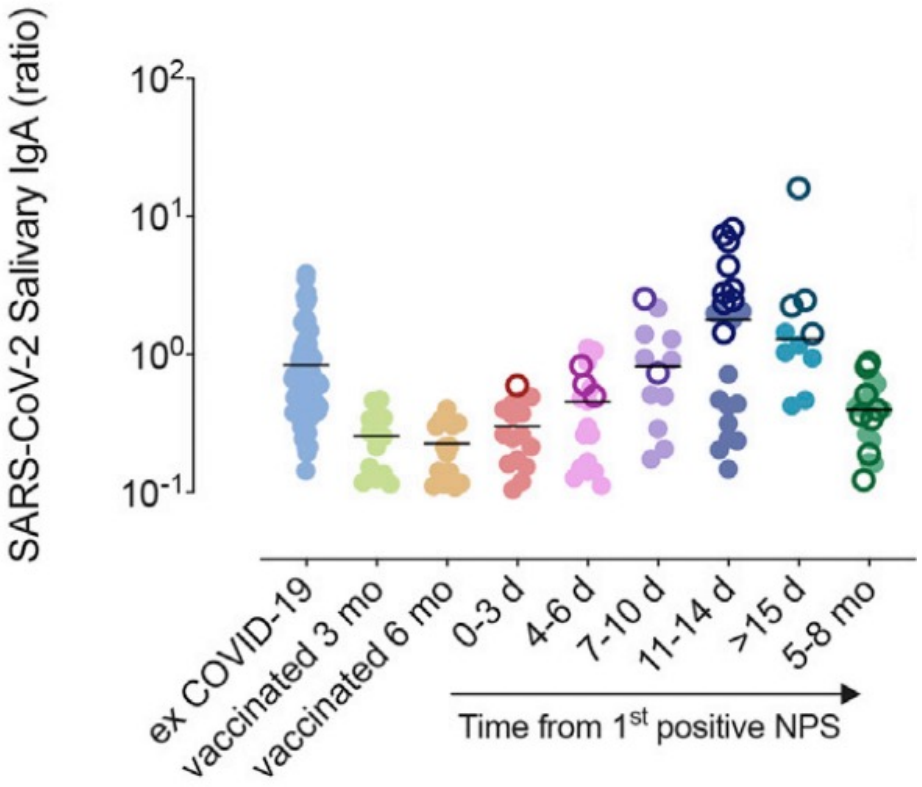
In 21 HCWs with breakthrough infections, specific antibodies against Spike and RBD rapidly increase in the serum and reach the highest levels 4 to 6 days after the positive NPS.

In contrast, Anti N antibodies start to increase after 10 days



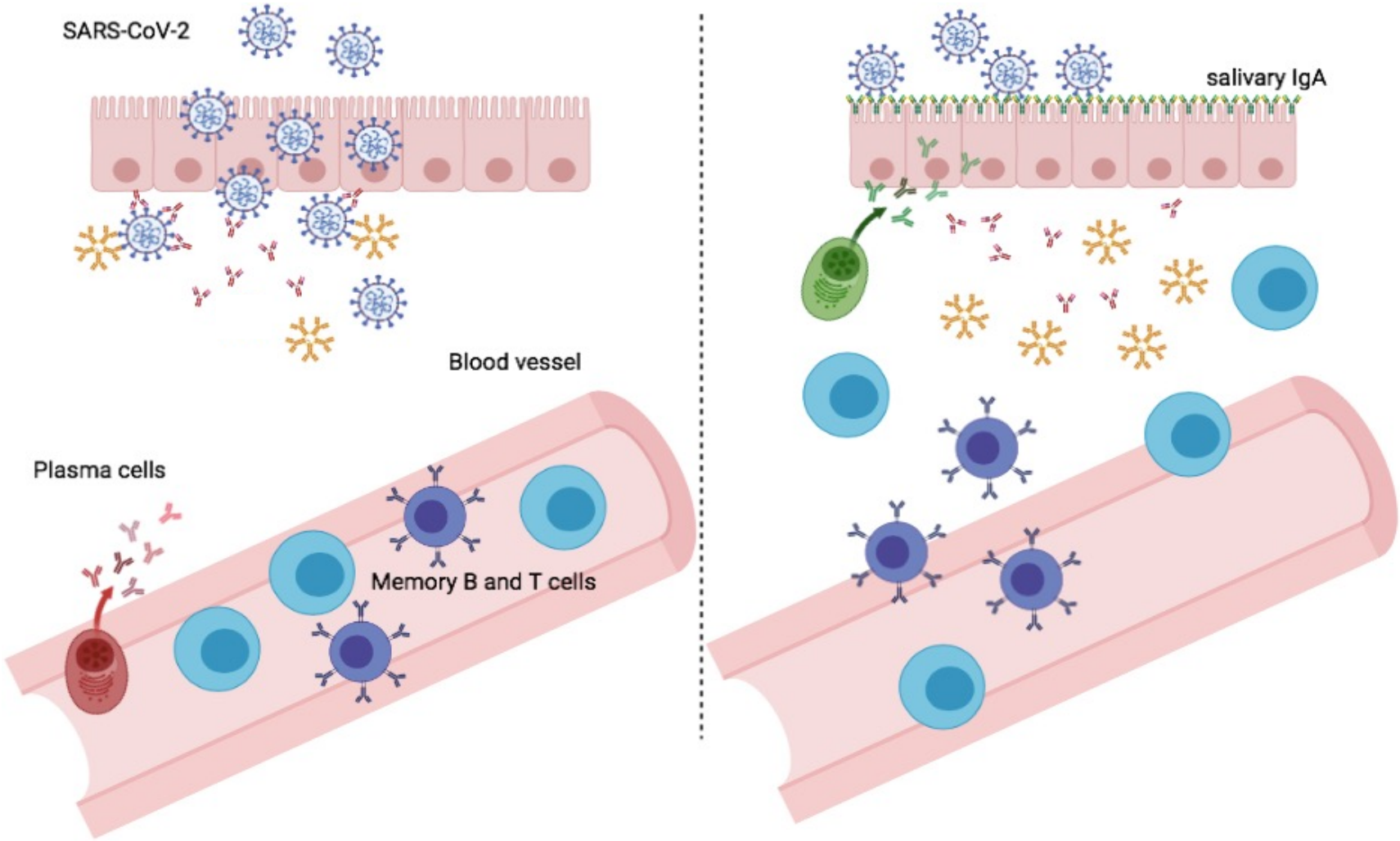
Salivary IgA rapidly increase

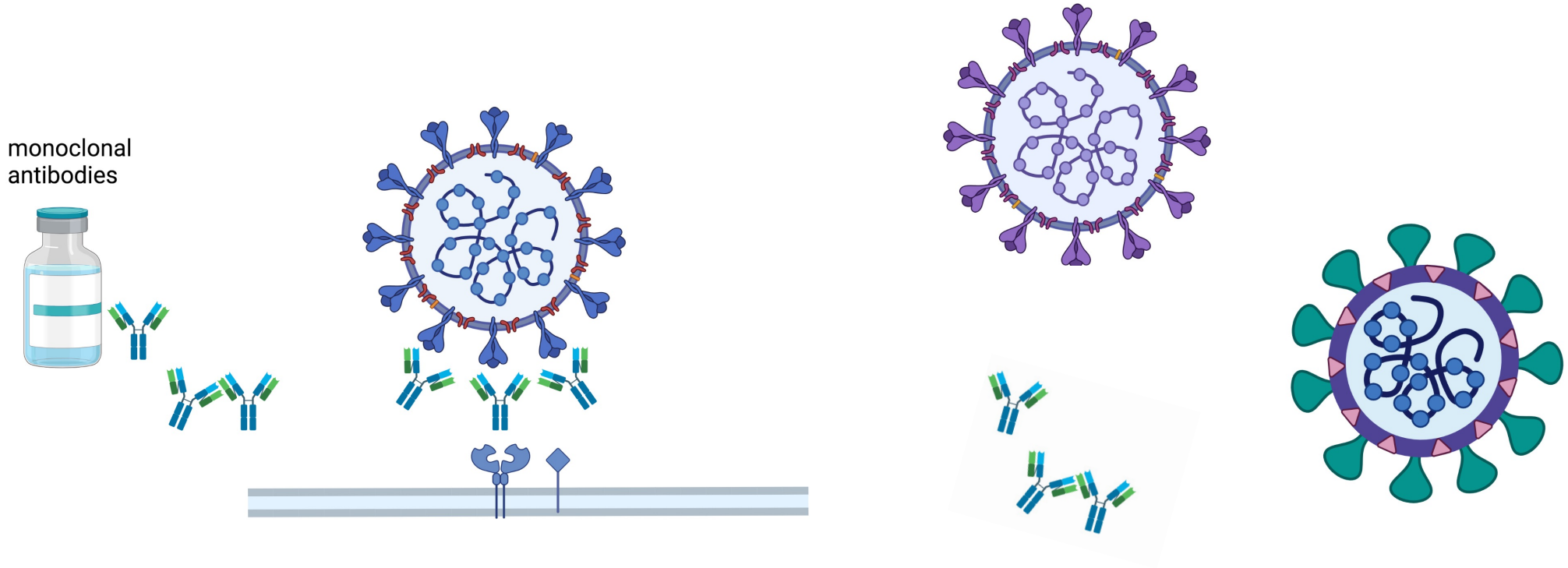
Upon encounter with the pathogen for which they are specific MBCs have the function of rapidly producing antibodies in the serum and at the site of invasion, the oropharinx for SARS-CoV-2



After vaccination

In response to a breakthrough infection





Monoclonal antibodies effective against the ancestral wuhan virus may not work against new variants

The human B cell response is not monoclonal

nature

https://doi.org/10.1038/s41586-021-03207-w

Accelerated Article Preview

Evolution of antibody immunity to SARS-CoV-2

Received: 3 November 2020

Accepted: 6 January 2021

Accelerated Article Preview

Published online 18 January 2021

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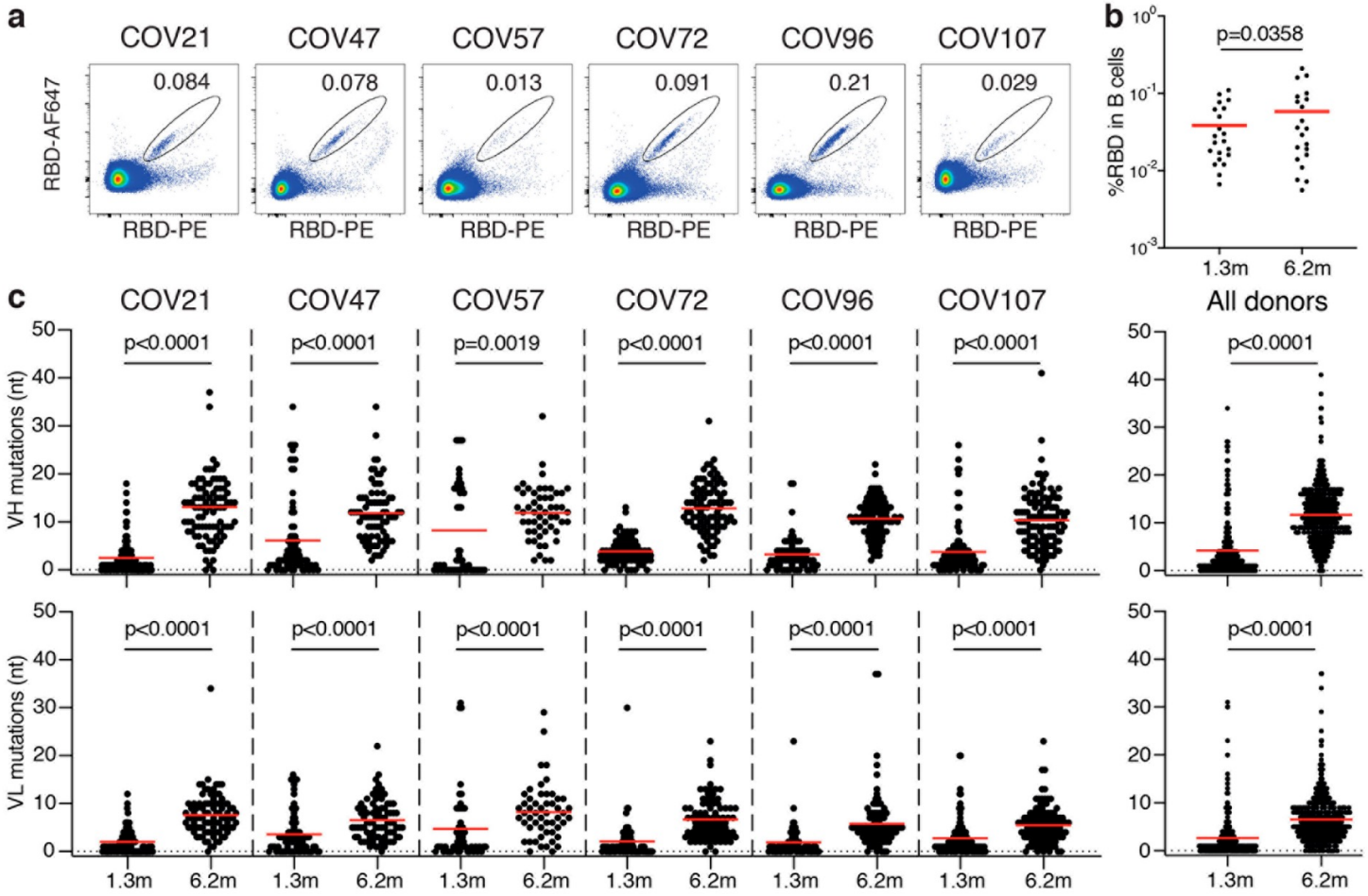
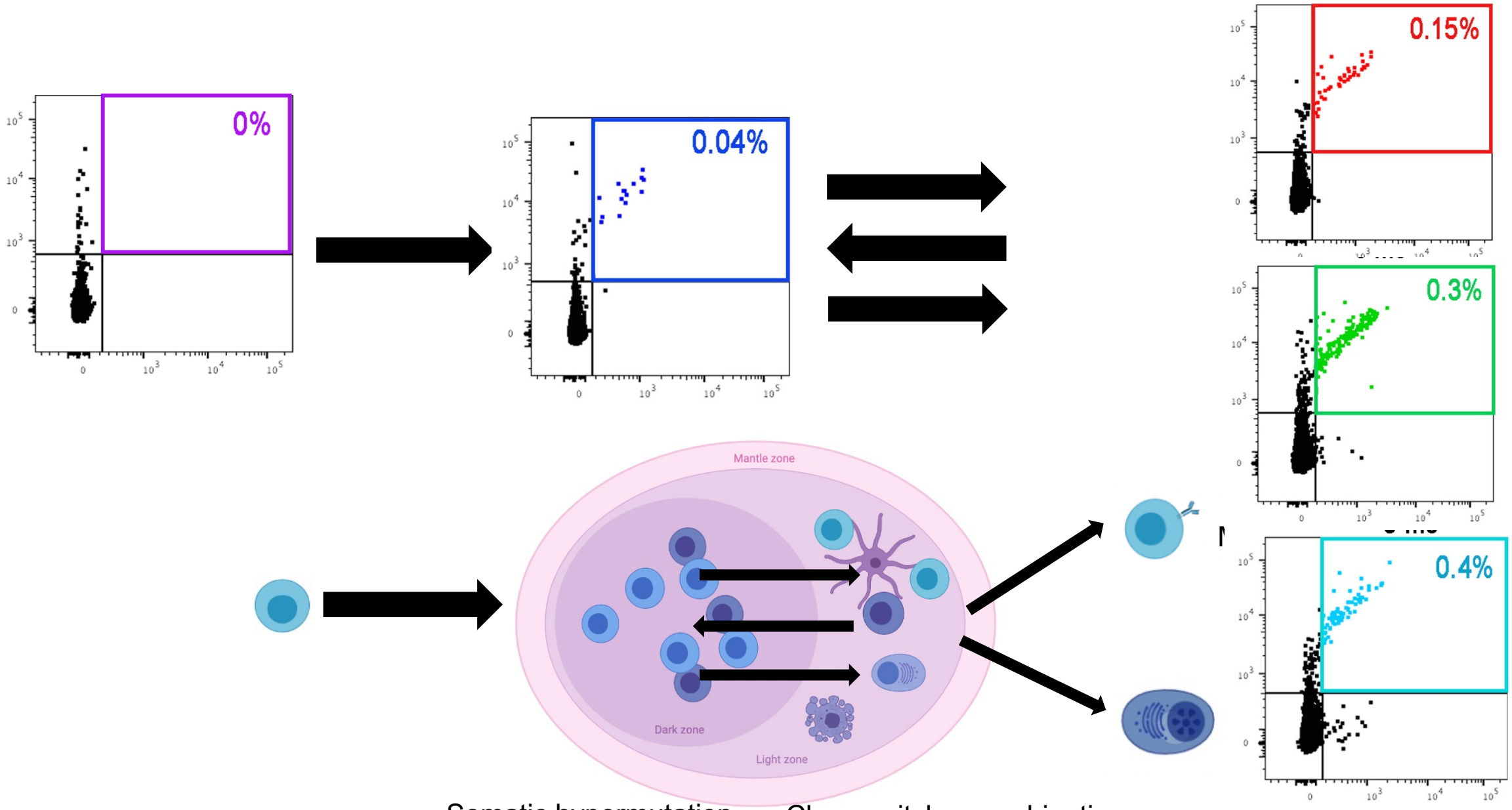
Christian Gaebler, Zijun Wang, Julio C. C. Lorenzi, Frauke Muecksch, Shlomo Finkin, Minami Tokuyama, Alice Cho, Mila Jankovic, Dennis Schaefer-Babajew, Thiago Y. Oliveira, Melissa Cipolla, Charlotte Viant, Christopher O. Barnes, Yaron Bram, Gaëlle Breton, Thomas Hägglöf, Pilar Mendoza, Arlene Hurley, Martina Turroja, Kristie Gordon, Katrina G. Millard, Victor Ramos, Fabian Schmidt, Yiska Weisblum, Divya Jha, Michael Tankelevich, Gustavo Martinez-Delgado, Jim Yee, Roshni Patel, Juan Dizon, Cecille Unson-O'Brien, Irina Shimeliovich, Davide F. Robbiani, Zhen Zhao, Anna Gazumyan, Robert E. Schwartz, Theodora Hatziioannou, Pamela J. Bjorkman, Saurabh Mehandru, Paul D. Bieniasz, Marina Caskey & Michel C. Nussenzweig

MBCs persist, evolve and mature overal several months by progressive acquisition of somatic mutation in their variable region genes to improve affinity through an ongoing germinal center response (Gabbler et al 2021, Rodda et al. 2021, Sokal et al. 2021b)

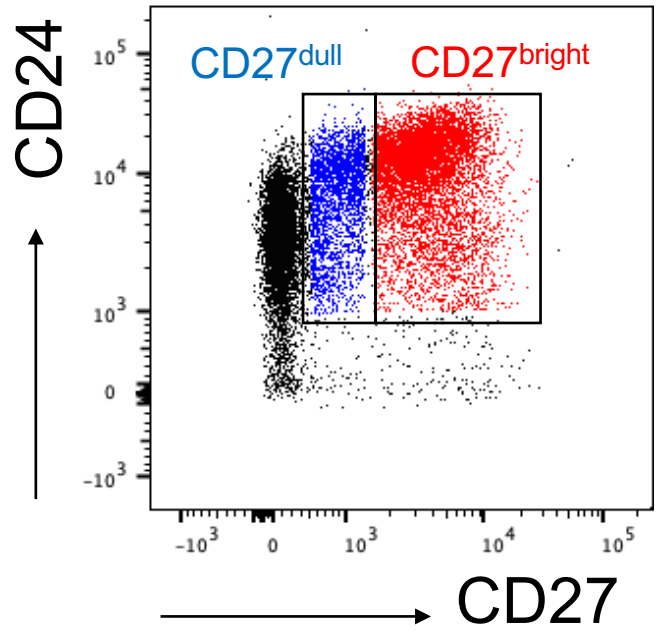



0%
0.04%
0.15%
0.3%
0.4%
Mantle zone
Dark zone
Light zone
Somatic hypermutation
Class switch recombination
Plasma cells

A major concern about Omicron is the large number of mutations in the spike protein, including mutations associated with immune escape and mutations rarely detected in previous variants.

~10-fold to ~40-fold reduction in neutralization capacity compared with the wild-type virus at 6 months after the primary 2-dose vaccine series.

Serological data indicate that antibody response to Omicron can be at least partially boosted in the short term (up to 1 months) after a 3rd vaccine dose suggesting that immunological memory generated by 2nd dose vaccination had some reactivity against the Omicron spike protein.



Article

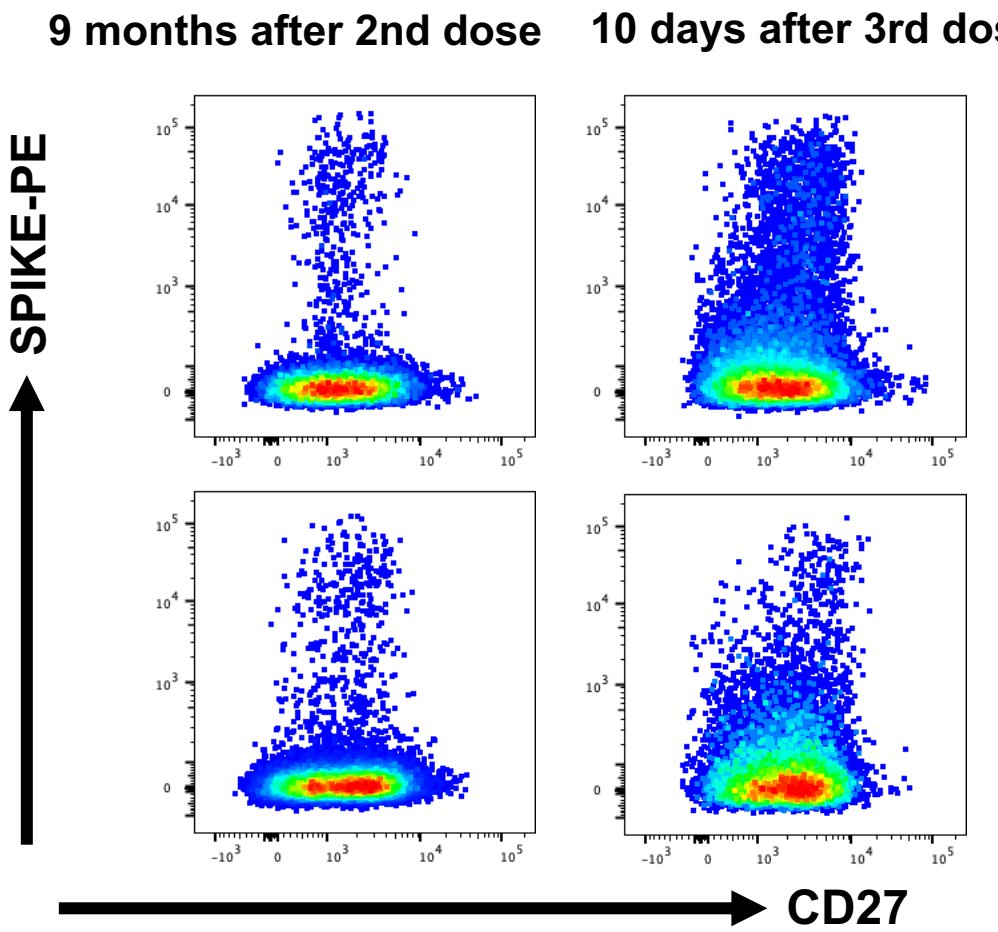
Cell Reports

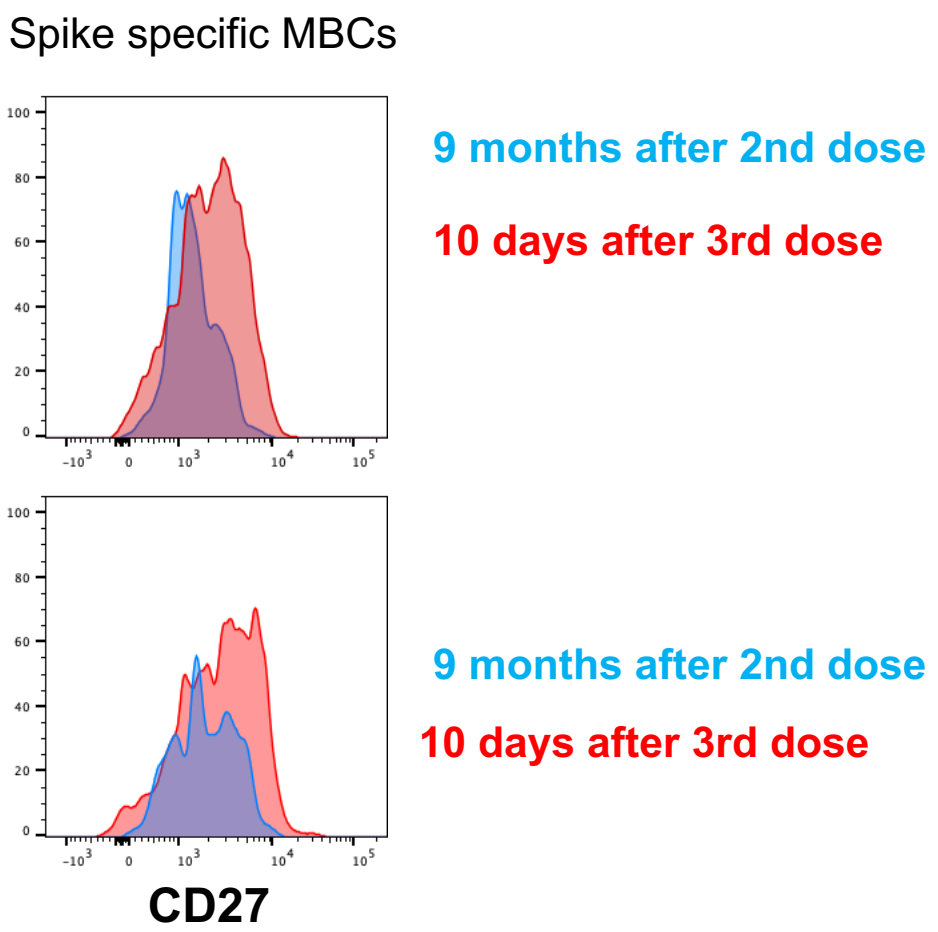
The Interplay between CD27^{dull} and CD27^{bright} B Cells Ensures the Flexibility, Stability, and Resilience of Human B Cell Memory

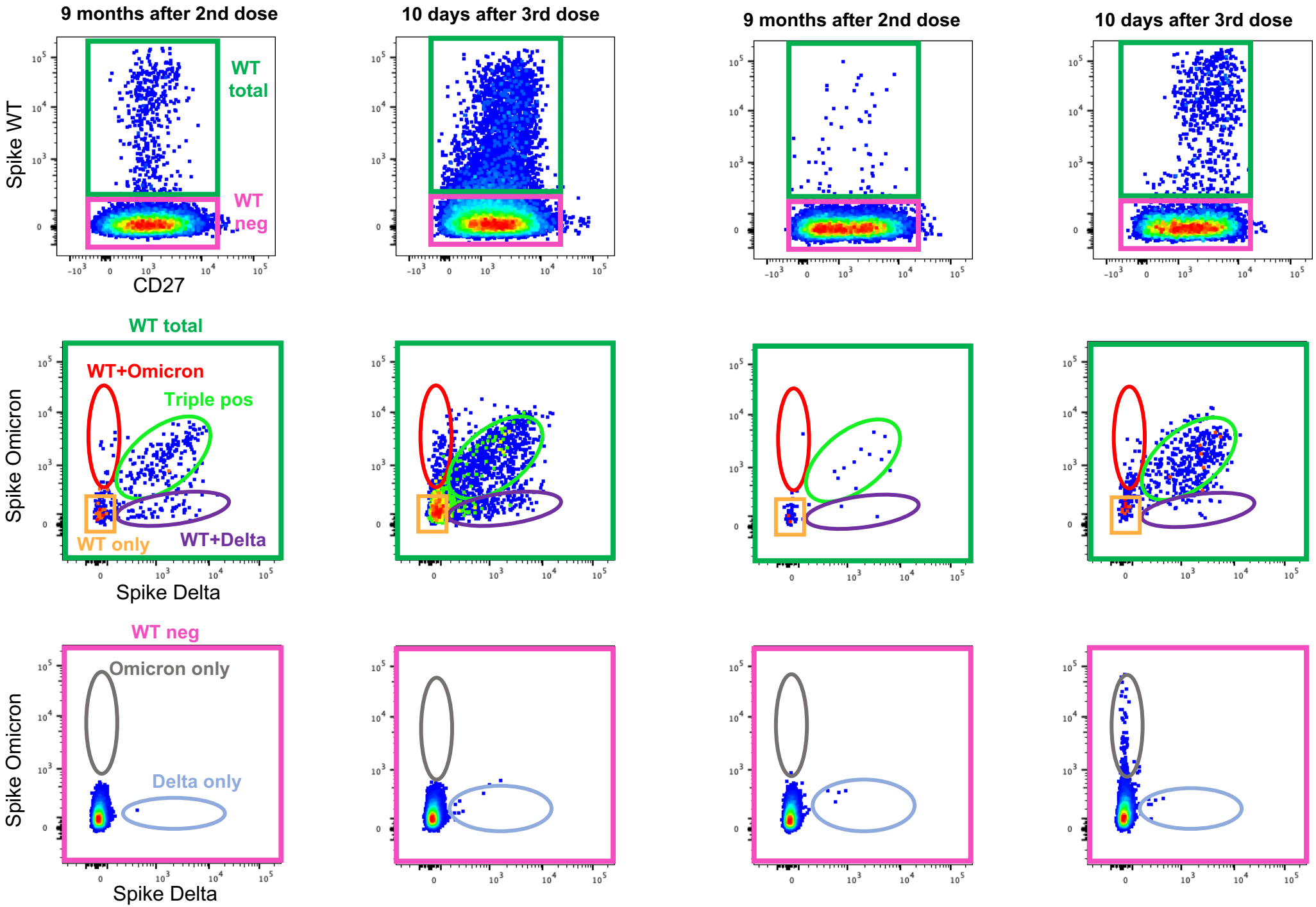
The less stringent selection of some MBCs is suggested to expand a breadth of MBCs.

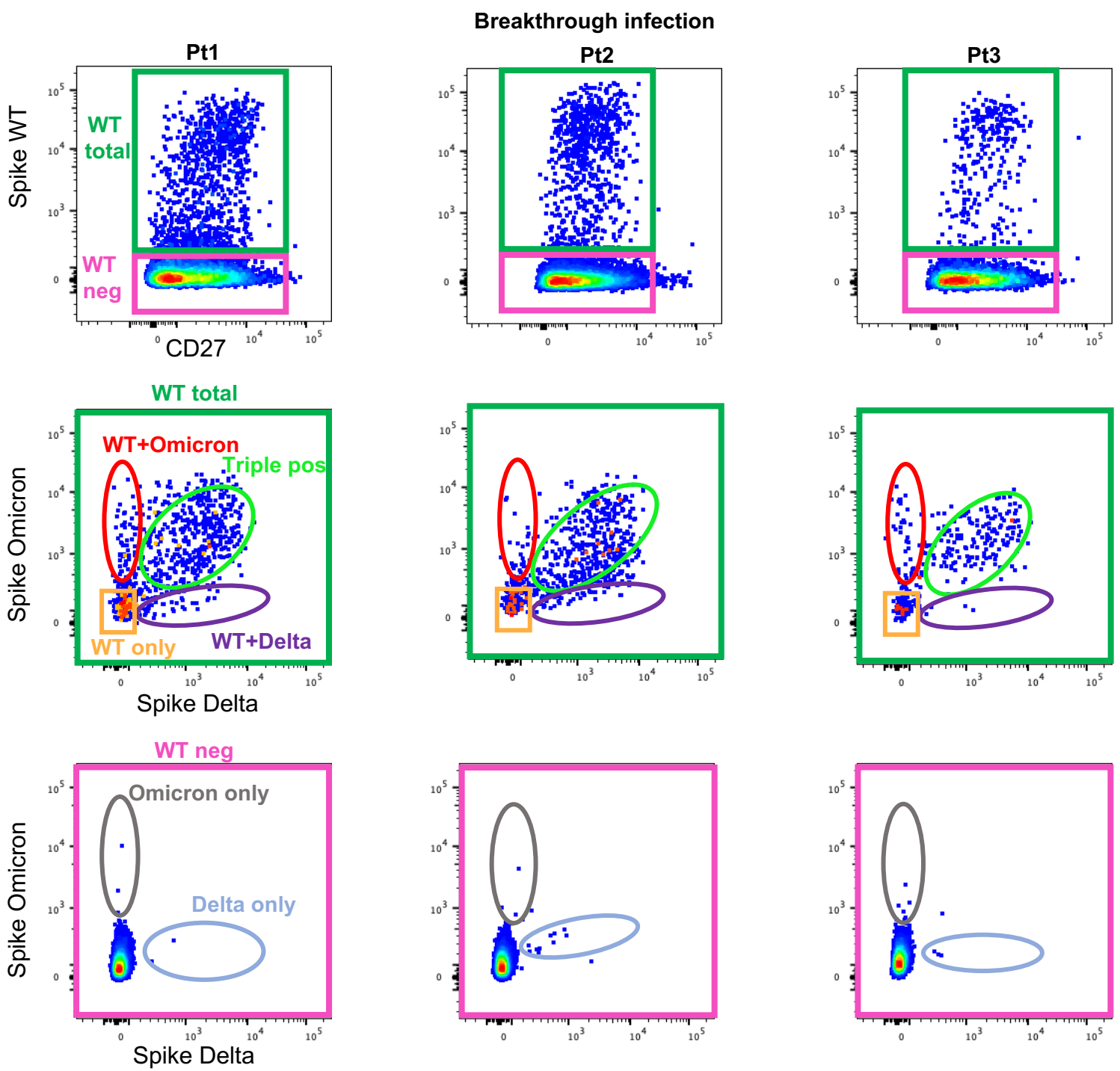
Results support the possible contribution of MBCs breadth to the broadly neutralizing antibody response after and additional boosting by mRNA vaccine or breakthrough infection.

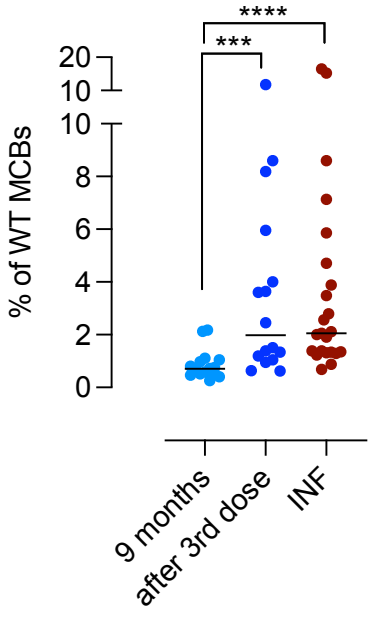
MEMORY B CELLS BECOME CD27^{bright} UPON CHALLENGE

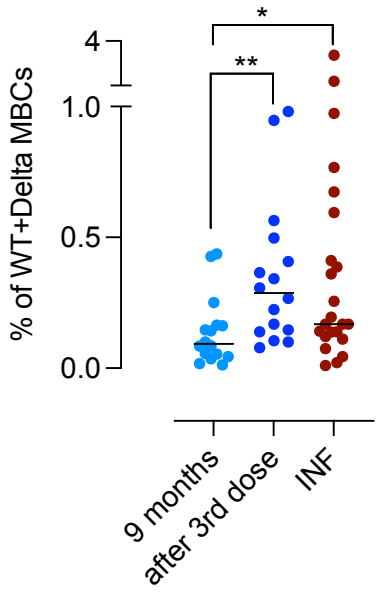


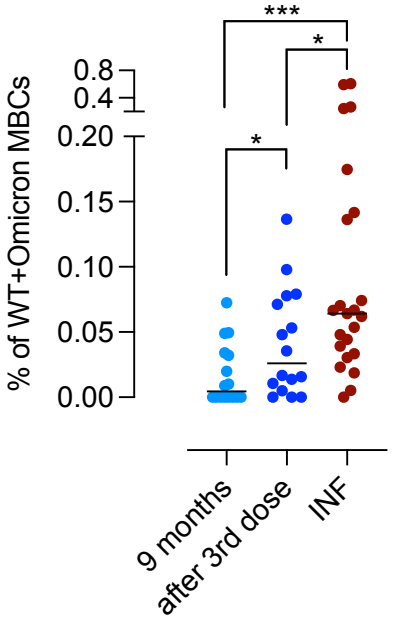


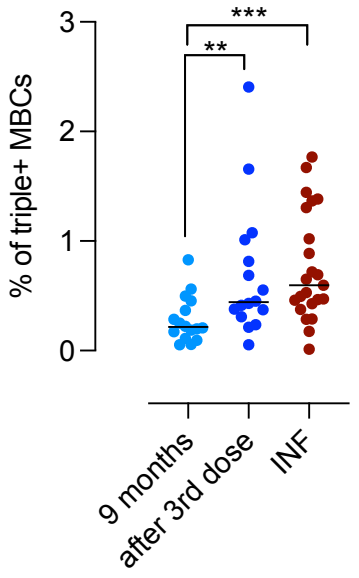

9 months after 2nd dose
10 days after 3rd dose
9 months after 2nd dose
10 days after 3rd dose
Spike WT
WT total
WT neg
CD27
WT total
WT+Omicron
Triple pos
WT only
WT+Delta
Spike Omicron
Spike Delta
WT neg
Omicron only
Delta only
Spike Omicron
Spike Delta

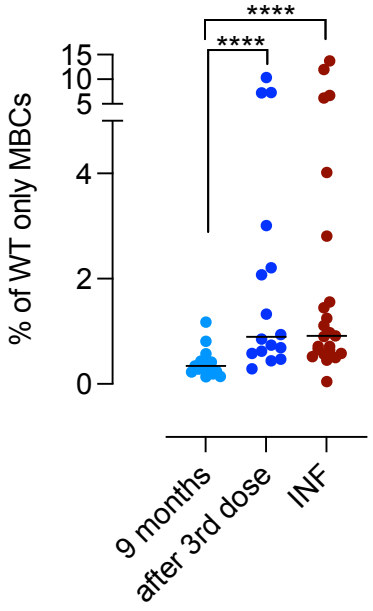

Breakthrough infection
Pt1
Pt2
Pt3
Spike WT
WT total
WT neg
CD27
WT total
WT+Omicron
Triple pos
WT only
WT+Delta
Spike Omicron
Spike Delta
WT neg
Omicron only
Delta only
Spike Omicron
Spike Delta

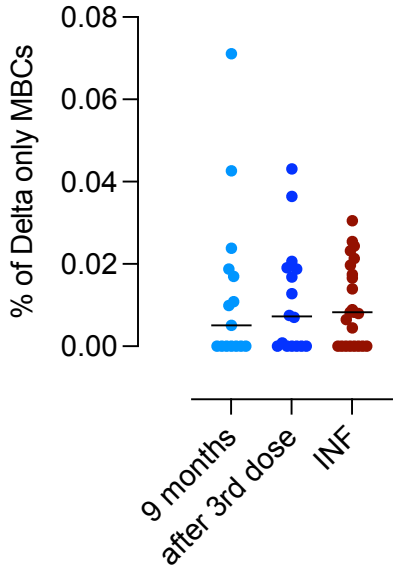

% of WT MCBs
20
10
10
8
6
4
2
0
****
***
9 months
after 3rd dose
INF

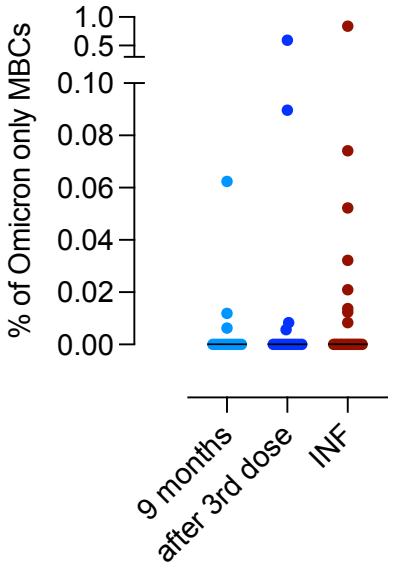

% of WT+Delta MBCs
4
1.0
0.5
0.0
*
**
9 months
after 3rd dose
INF


% of WT+Omicron MBCs
0.8
0.4
0.20
0.15
0.10
0.05
0.00
***
*
*
9 months
after 3rd dose
INF

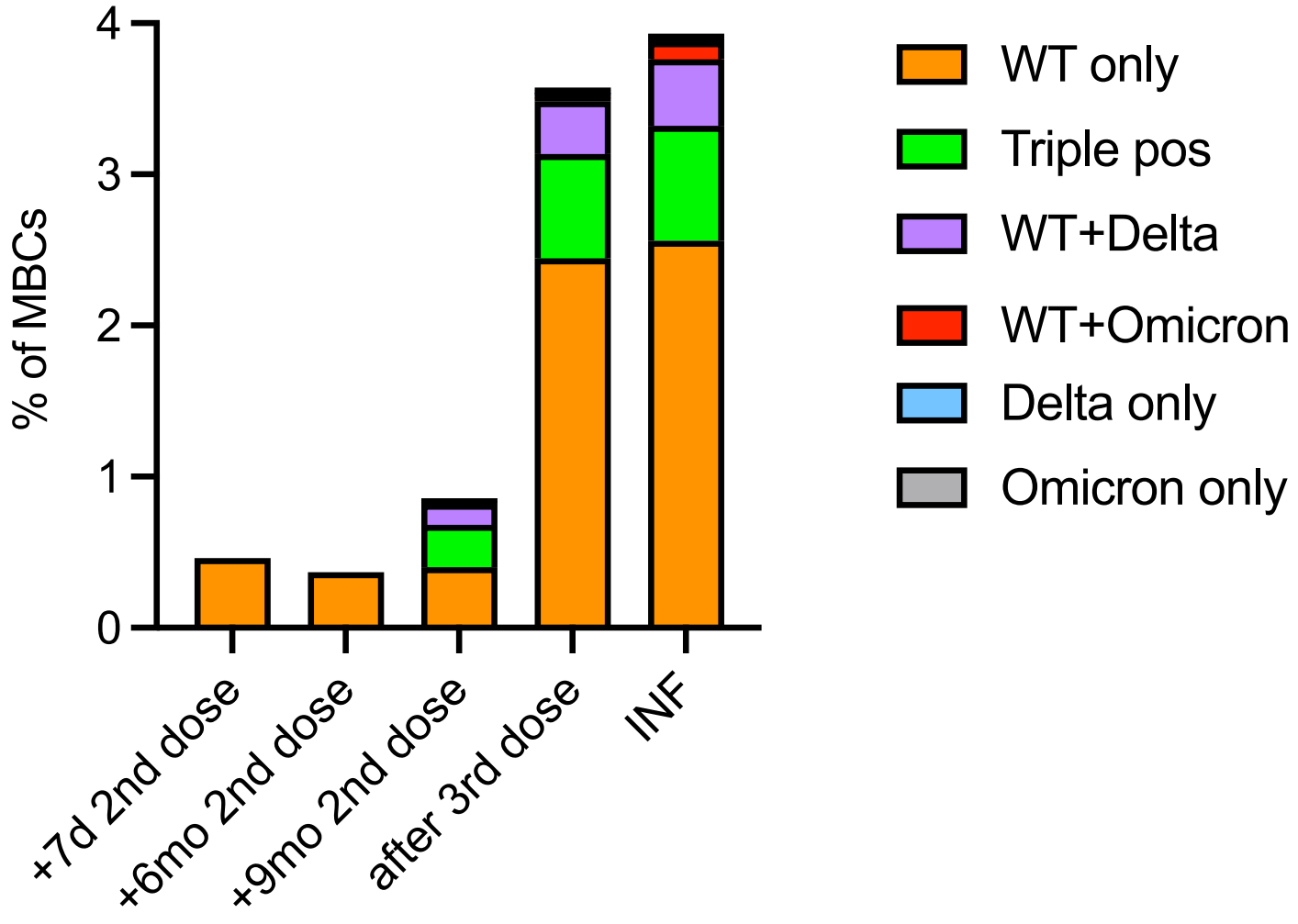

% of triple+ MBCs
3
2
1
0
***
**
9 months
after 3rd dose
INF


% of WT only MBCs
15
10
5
4
2
0
****
****
9 months
after 3rd dose
INF


% of Delta only MBCs
0.08
0.06
0.04
0.02
0.00
9 months
after 3rd dose
INF


% of Omicron only MBCs
1.0
0.5
0.10
0.08
0.06
0.04
0.02
0.00
9 months
after 3rd dose
INF

Vaccination boost and expand WT Spike specific MBCs inside WT → CROSS REACTIVE MBCs

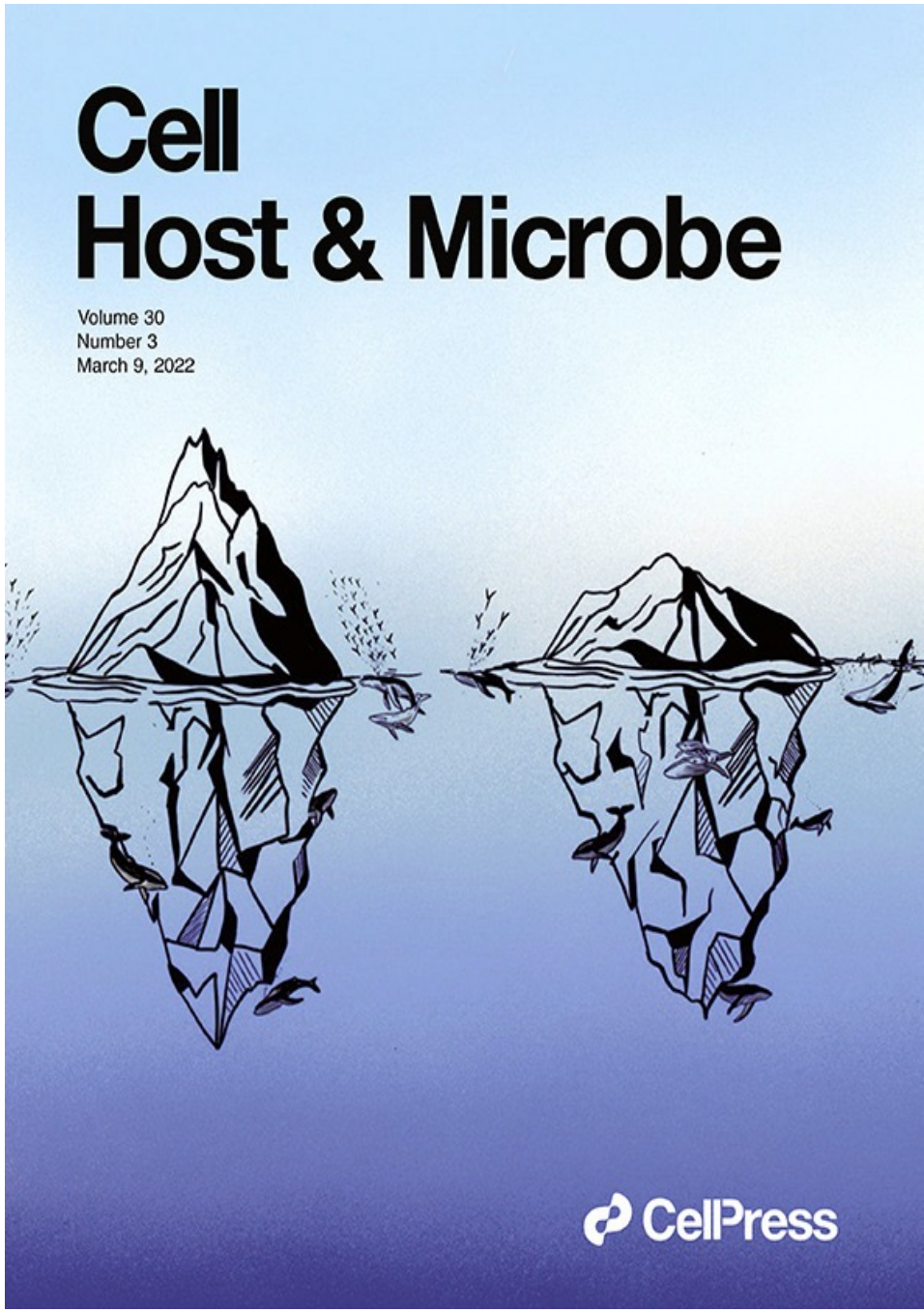


MBCs display a diverse repertoire, allowing for an adaptive response upon re-exposure to the pathogen, especially in case of VOC.

Boosting with a 3rd dose of ancestral vaccine increases variant neutralizing antibody, highliting the importance of vaccine-induced memory B cells that also expand

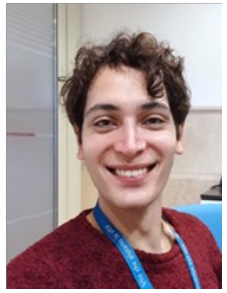
Breakthrough infections are not associated with waning immunity

Parenterally administered vaccines do not generate mucosal immunity



Acknowledgement

Head of the Research B cell Unit Rita Carsetti

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