

### Disclosure conflicts of interests speaker

Potential conflict of interest	None
Potentially relevant relationships with companies	Company names
<ul style="list-style-type: none"><li>• Sponsorship or grant for research</li><li>• Other relationship, .....</li></ul>	<ul style="list-style-type: none"><li>• Bavarian-Nordic (Rabipur™)</li><li>• U-Needle micro-needles</li><li>• MyLife Technologies nanoporous micro-needle array</li></ul>

## Modern concepts to improve immunisation response, with focus on germinal center response

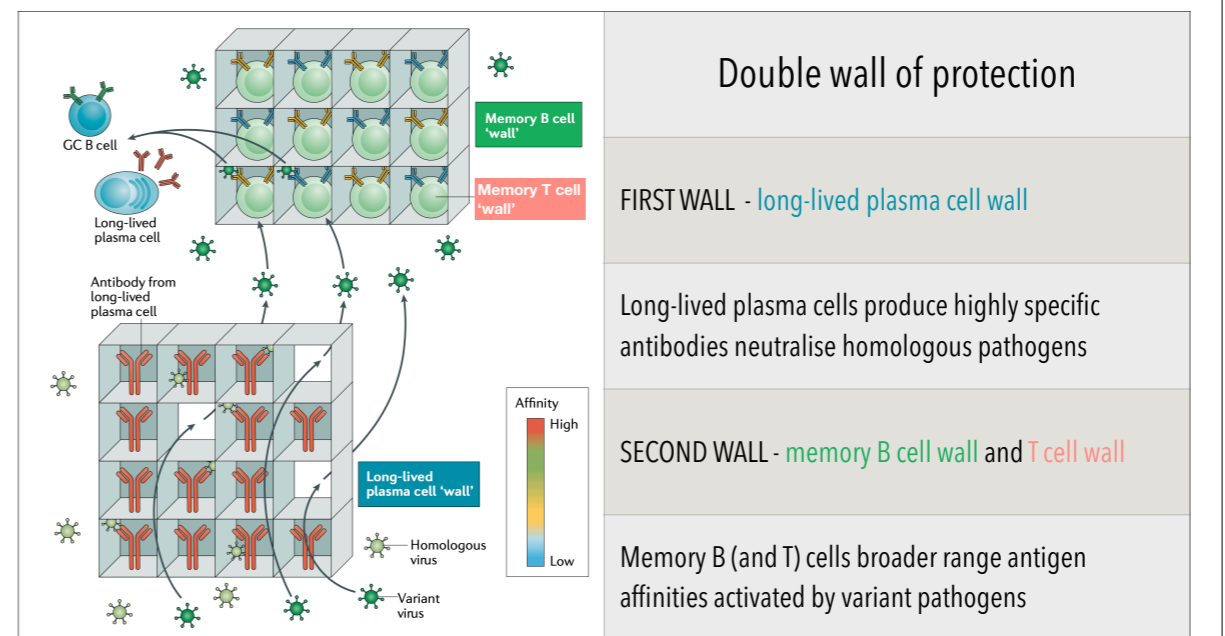


Quest of the B-cell and its deadly journey through the germinal center

Long-term antigen persistence in the germinal center is driving antibody affinity and diversity

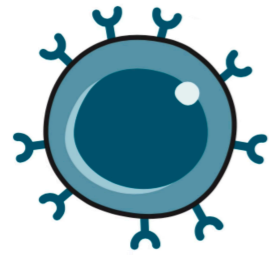
Pre-existing antibodies modulate recall GC specific for escape epitopes

Immunosuppression affects levels, affinity and diversity of antibodies and memory B-cells





## The quest of the B-cell



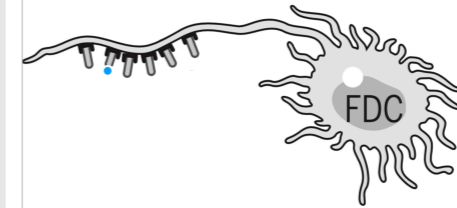
Challenge	Long-lived plasmacell memory B-cell
Weapons	Tweek antigen binding domain Somatic hypermutation
Adversaries	Fellow B-cells

## Meet the main characters



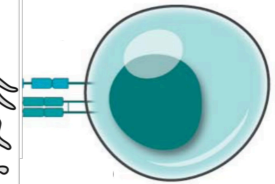
Subcapsular sinus  
macrophage

Sentinel  
Lymphnode



Follicular dendritic cell  
(FDC)

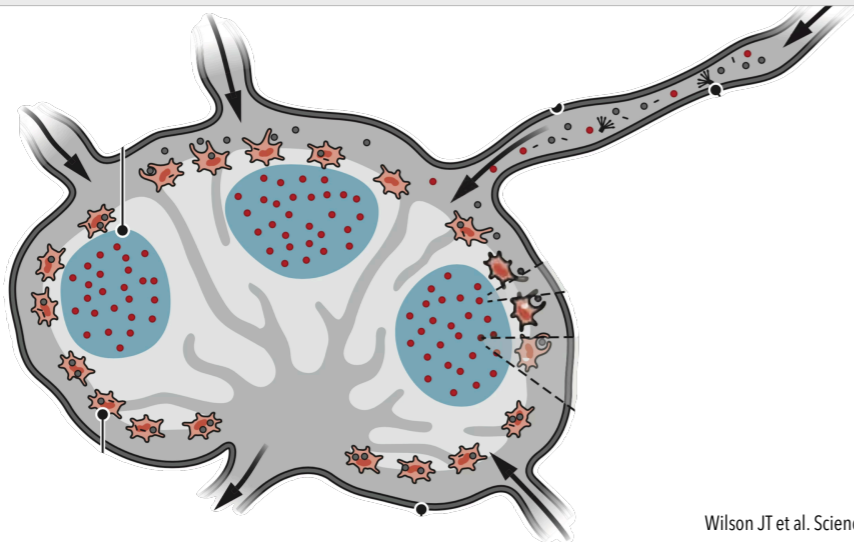
Spider man cell



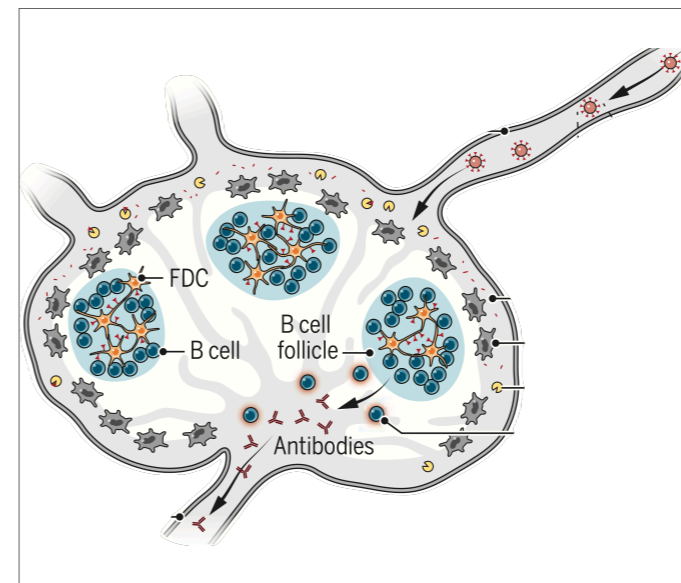
T follicular helper cell  
(TFHC)

Wizard cell  
longevity potion

## The arena - the lymphnode where it all starts



Wilson JT et al. Science 2019;363:584



Subcapsular sinus macrophage

'Fly paper' for particles > 200 nm

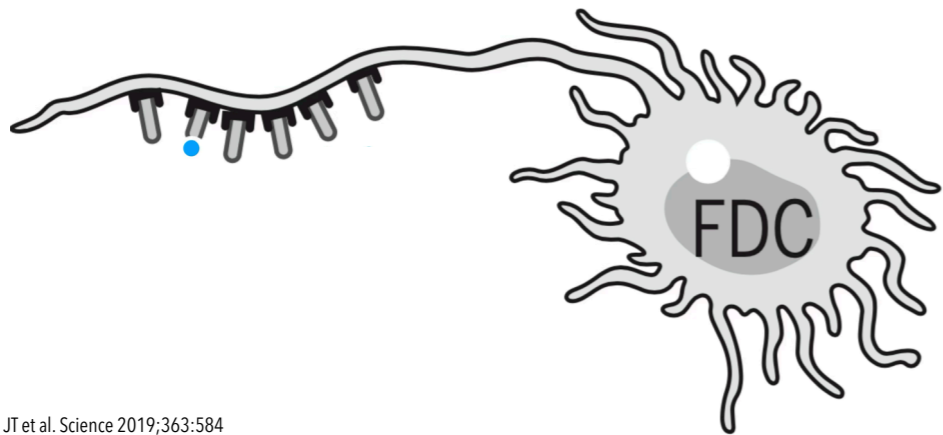
Shields LN against pathogens

Present processed antigens to B-cells

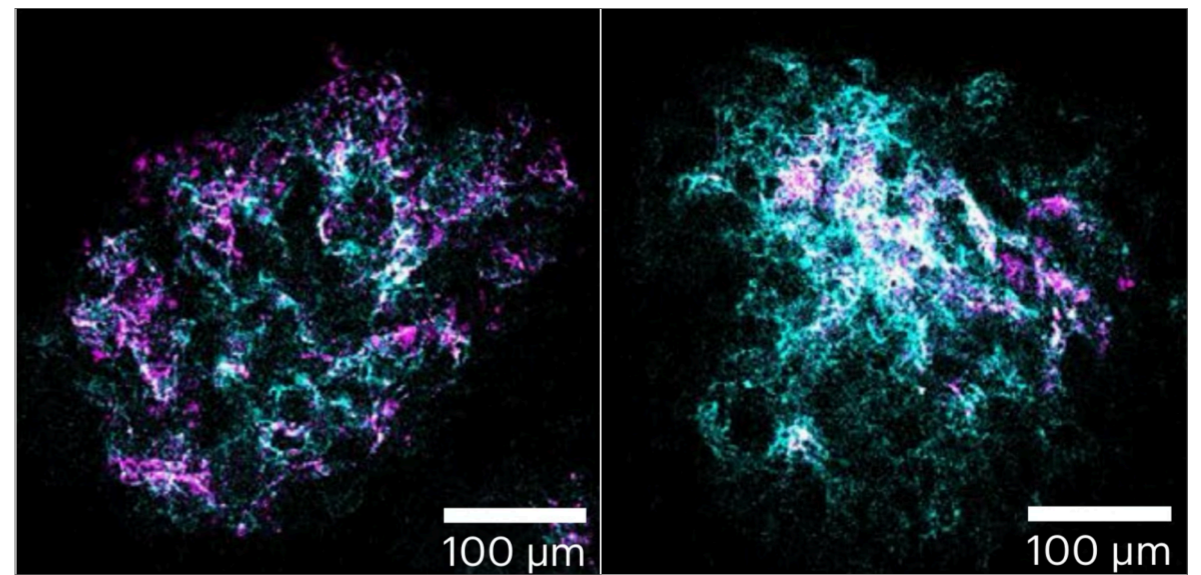
Transfers antigens to FDC

Kalia A et al. Science 2023;379:332

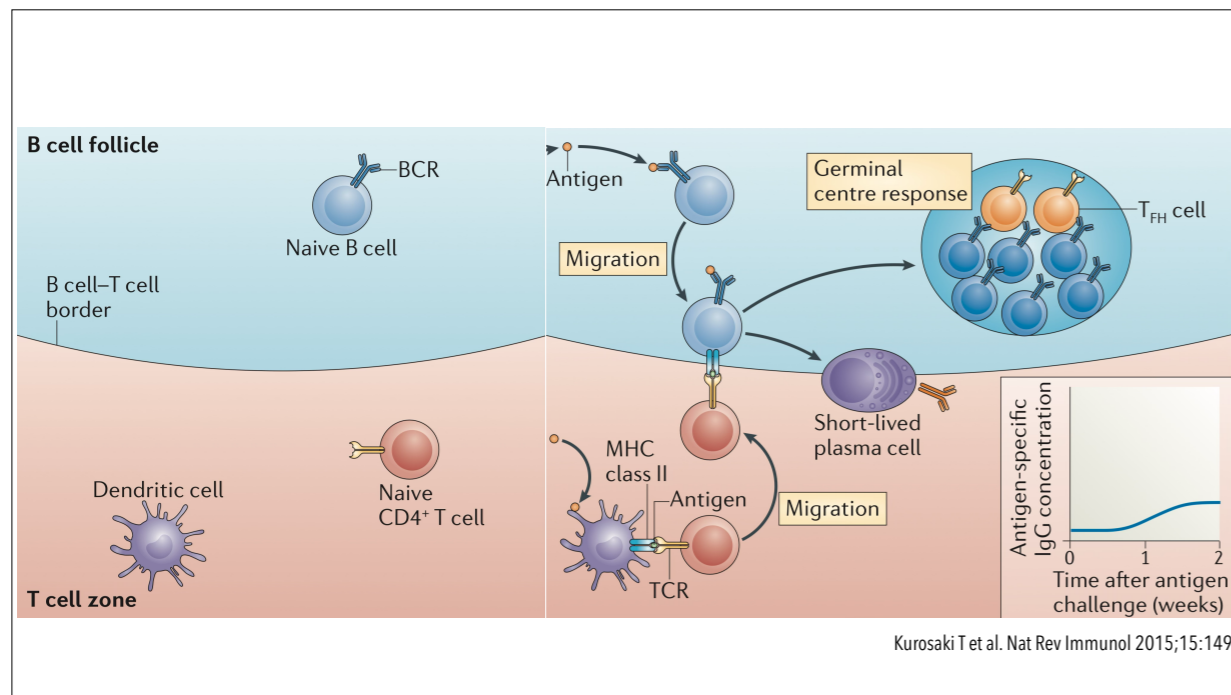
Long-term retention of antigens in germinal centers is controlled by the spatial organization of the follicular dendritic cell network

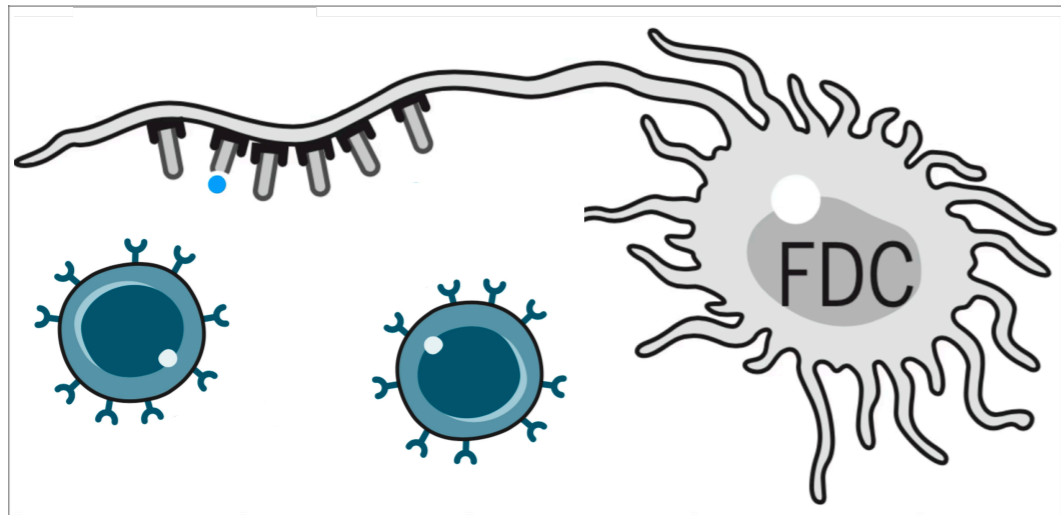


Wilson JT et al. Science 2019;363:584

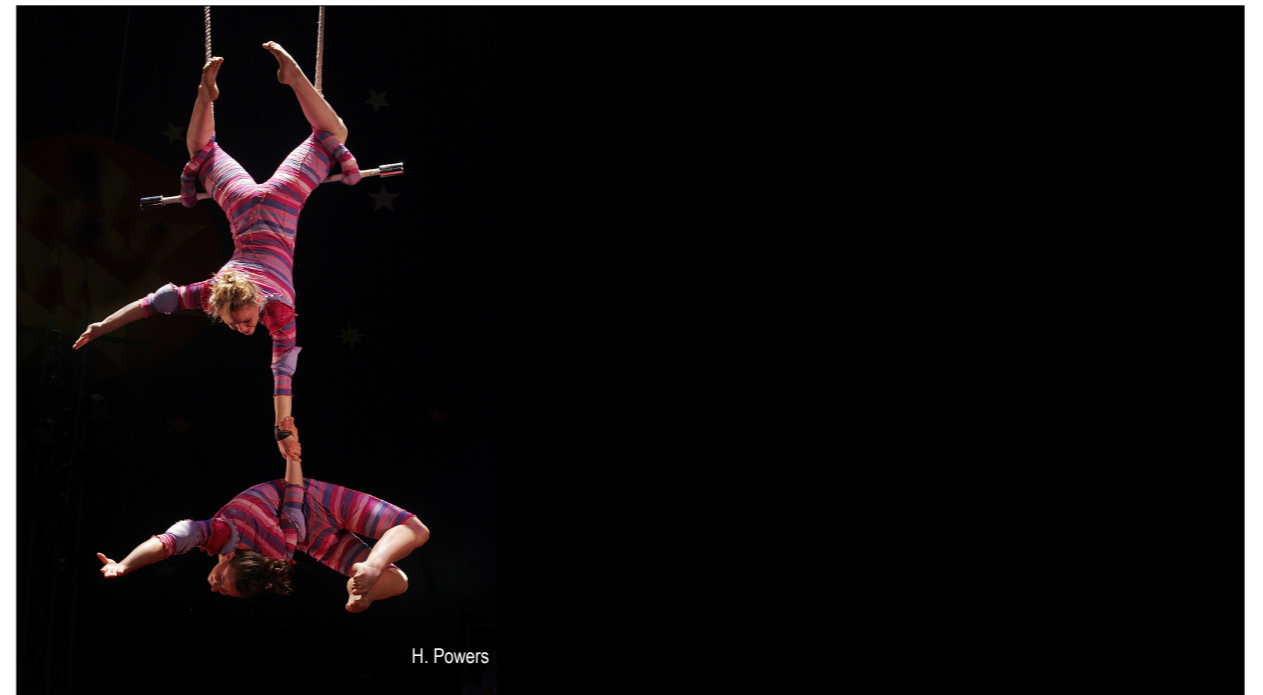


Martinez-Riano Nature Immunol 2023;24:1281

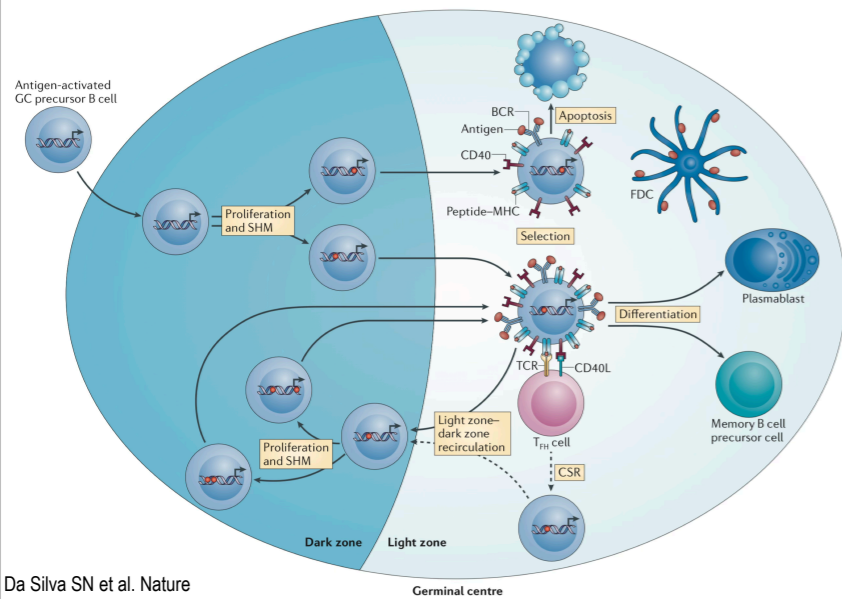




Wilson JT et al. Science 2019;363:584

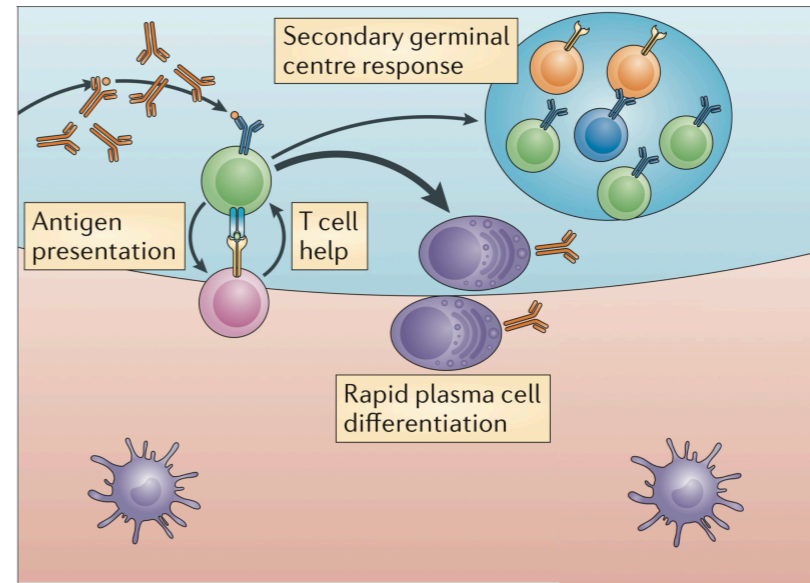


H. Powers



Da Silva SN et al. Nature Rev Immunol 2015;15:137

Higher BCR affinity is directly associated with greater antigen capture and higher density of peptide-MHC complexes on the surface of the B cell. This results in the greatest share of TFH cell help



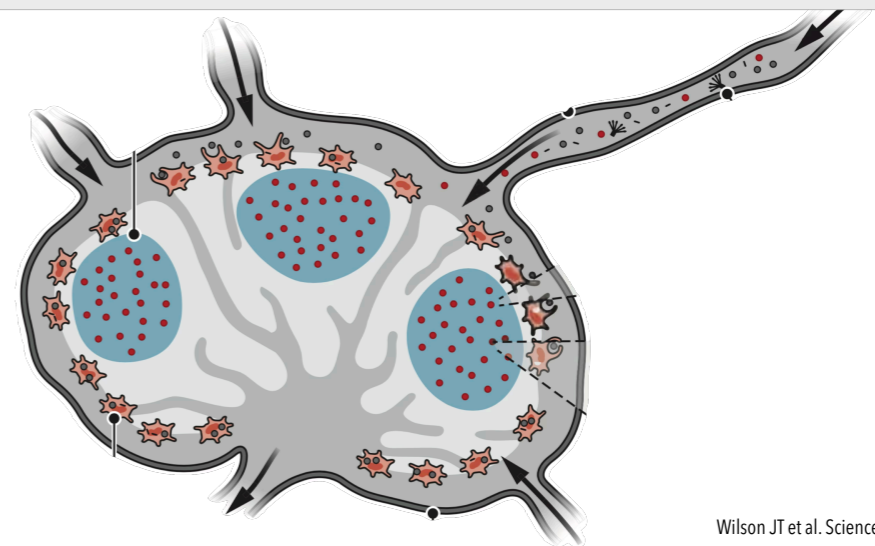
Binding properties of B cells in recall GCs are shaped by the opposing forces of antibody-mediated feedback and T helper cell memory

Schiepers A et al. Biorxiv 2024



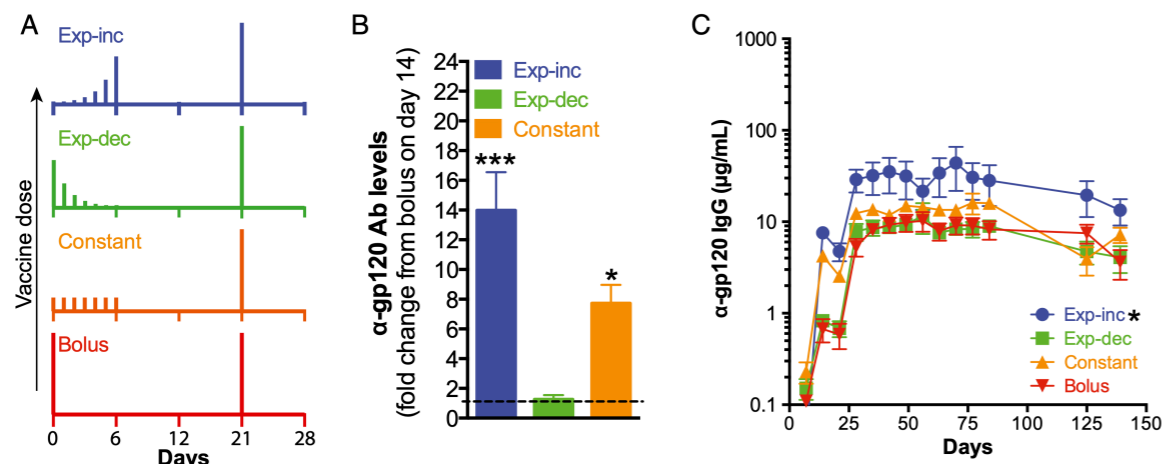
So what can we learn  
from this story for our  
daily practice?

Prolonged Antigen Retention in Lymph Nodes enhances Germinal Center  
Formation and Antibody Affinity and Diversity



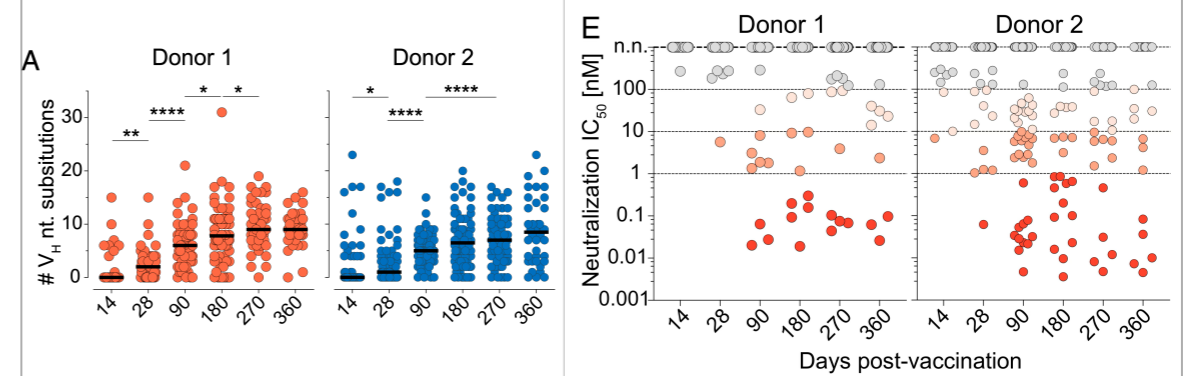
Wilson JT et al. Science 2019;363:584

### Sustained antigen availability during germinal center initiation enhances antibody responses to vaccination



PNAS 2016 October 4;113:E6639

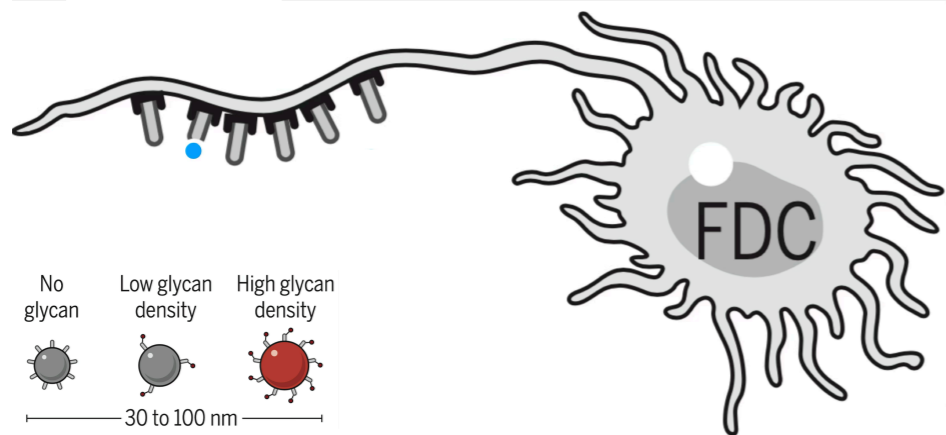
### Germinal center activity continues for many months after primary 17D-YF vaccination



PNAS 2020;117:6675



A sugary coat makes antigens more sticky for C2R and may ultimately be the sweeter approach for vaccine delivery'

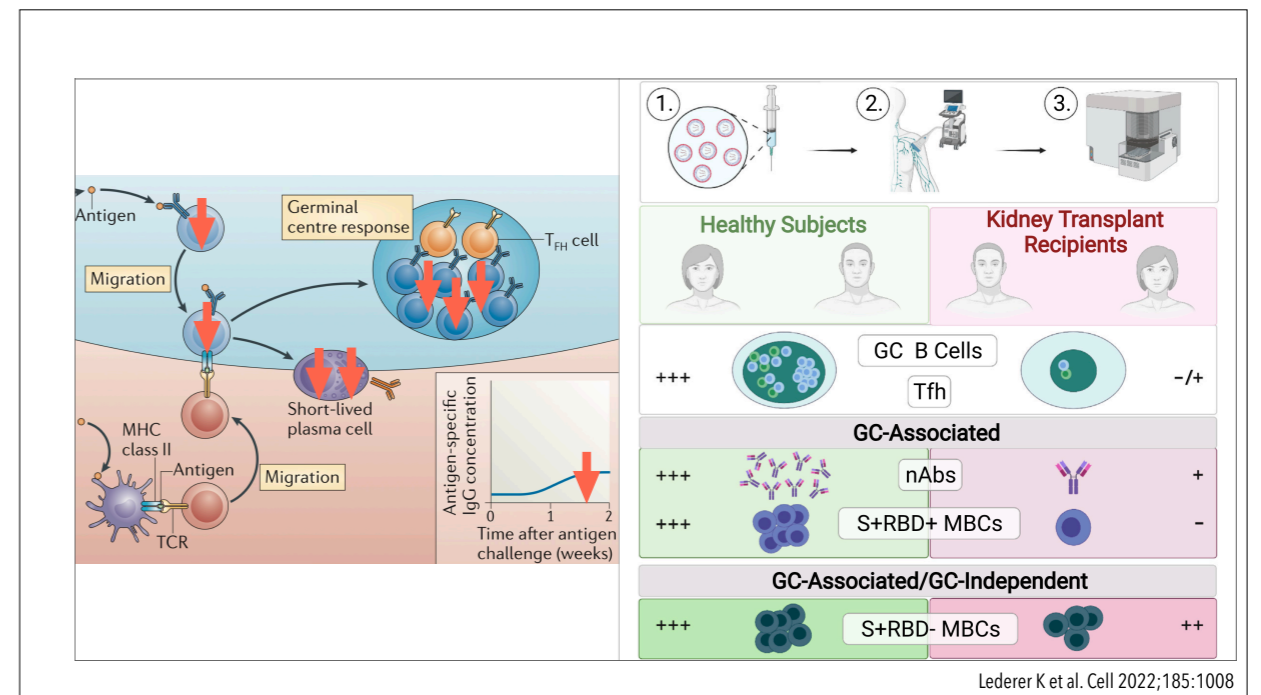
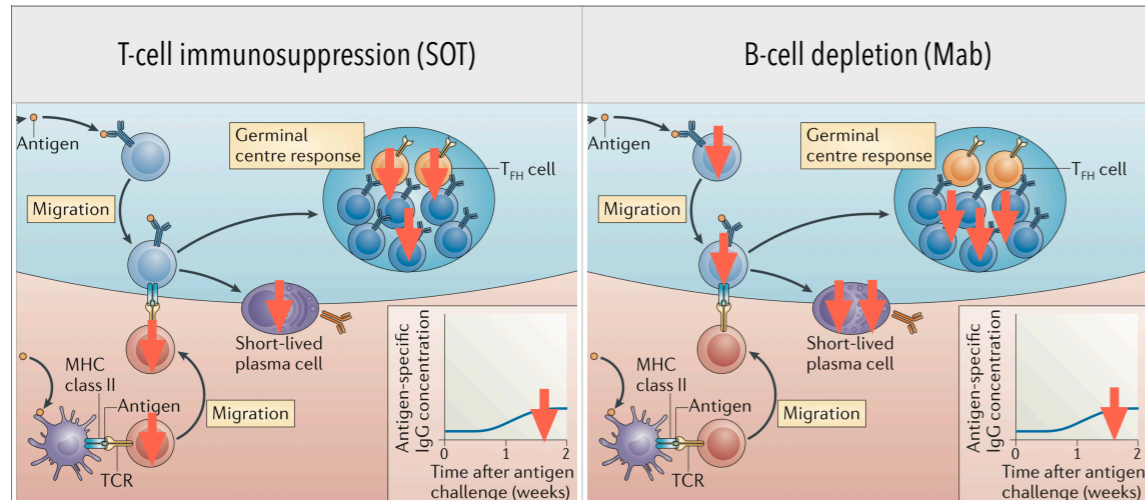


Wilson JT et al. Science 2019;363:584

### Challenges with fractional dosing and modified schedules

Fractional dosing	Shorter life span germinal center	Lower antibody levels Earlier waning Memory B-cells less affected
Shortened schedules	Memory cells with less somatic hypermutation cycles	Earlier seroconversion Lower antibody levels Earlier waning Fewer memory B-cells
Extended schedules	More cycles of SHM	More memory B-cells Higher antibody affinity and diversity

## The importance of immunization before immunosuppression (if possible)



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Long-term antigen persistence in the germinal center is driving antibody affinity and diversity

Pre-existing antibodies modulate recall GC specific for escape epitopes

Immunosuppression affects levels, affinity and diversity of antibodies and memory B-cells