Ragon Institute
Collaborate. Research. Cure.

Antigen specific memory B cells of extrafollicular origin may contribute to ART-free HIV control

296

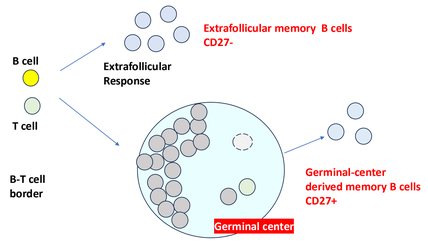
hhmi Howard Hughes Medical Institute

Elif Çakan[1], Essi Logan[1], Nicole Ingram[1], Daniel Lingwood[1], Shiv Pillai[1*], Bruce Walker[1,2*]

1- Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, USA.
2- Howard Hughes Medical Institute, Chevy Chase, MD, USA. * Indicates co-corresponding.

Key message: HIV-envelope-specific extrafollicular memory B cells are a durable population with a diverse and unique BCR repertoire, which is significantly enriched in ART-free HIV-controllers and associated with the durability of viremic control.

BACKGROUND

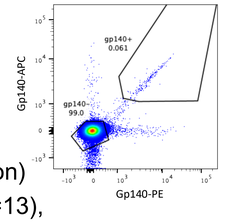


While an atypical B cell population, resembling transient activated B cells, has been reported in peripheral blood samples from persons living with HIV (PLWH), the functional contribution of these or other B cell subsets to spontaneous control of viremia remains unclear.

HYPOTHESIS

Virus specific extrafollicular memory (EFM) B cells contribute to ART-free HIV control.

METHODOLOGY



- This study utilizes the PBMC samples of;

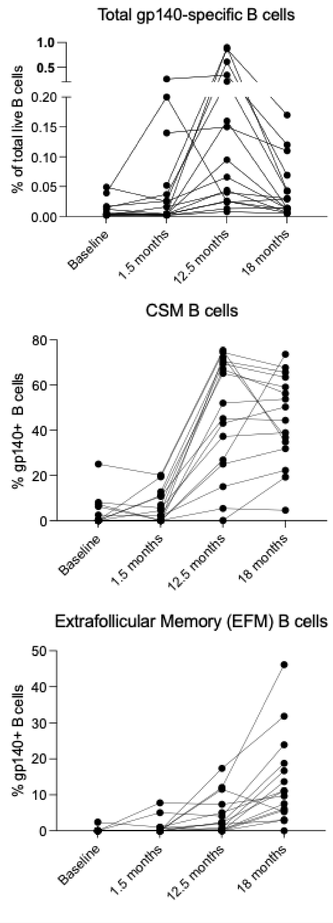
1- Longitudinal samples (before immunization and 1.5, 12.5 and 18 months following the first immunization) of vaccinated HVTN 100 subjects (n=13),
2- PLWH cohort of elite controllers (n=15), viremic controllers (n=9), chronic progressors under ART (n=12),
3- Aborted Control Cohort of PLWH including persons with durable ART-free control (n=7) and aborted control (n=6).

- Virus-specific B cells are mapped using fluorophore-labeled gp140 protein as flow-cytometry probe.

- BCR sequencing and monoclonal antibody cloning is performed from single-cell sorted gp140-specific GC-derived and extrafollicular memory B cells.

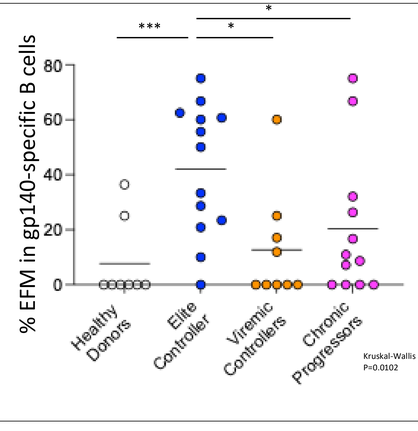
RESULTS

1- Gp140-specific durable extrafollicular memory B cells persisted 6 months after the final immunization in peripheral blood samples of the HVTN-100 cohort.

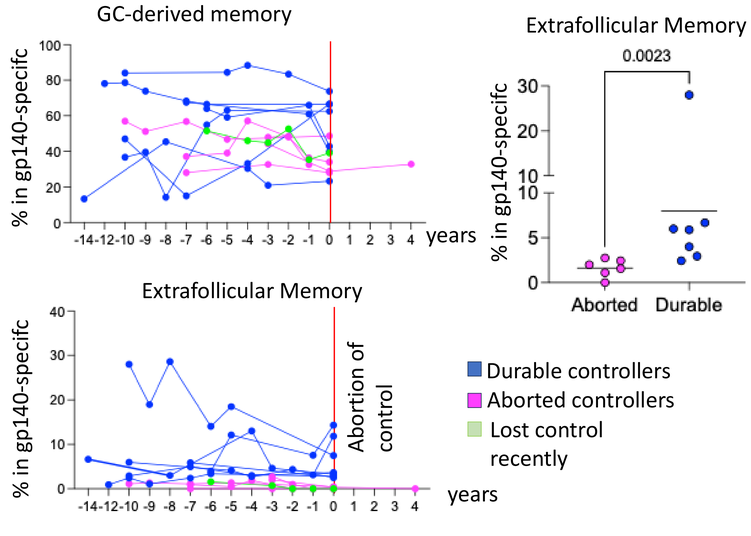


RESULTS

2- In the PLWH cohort, all antigen-specific B cell populations were increased compared to healthy individuals, but only antigen-specific extrafollicular memory B cells were significantly associated with ART-free HIV control (p= 0.01).

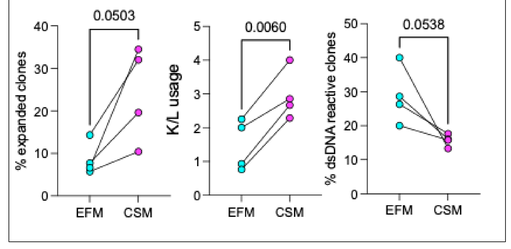


3- Gp140-specific extrafollicular memory B cells were significantly decreased in aborted controllers (p=0.014), and the loss of this population preceded the re-emergence of viremia.



RESULTS

4- Gp140-specific extrafollicular memory B cells have a more diverse repertoire with increased lambda chain usage (p = 0.02) and dsDNA reactivity (p=0.0536) compared to germinal center-derived memory B cells.



CONCLUSIONS

- Gp140-specific EFM B cells are durable 6 months post-immunization (18 months after baseline)
- Gp140-specific EFM B cells are increased in elite controllers in PLWH cohort and durable controllers compared to aborted controllers.
- Gp140-specific EFM B cells have increased Kappa usage with more dsDNA-reactive and less expanded clones.

PLAIN LANGUAGE SUMMARY

A virus specific durable B cell population that derives independent of germinal centers may contribute to ART-free HIV control.

Author contact : ecakan@mgh.harvard.edu