



22-24
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2023

SOCIETAT
CATALANA DE
TRASPLANTAMENT

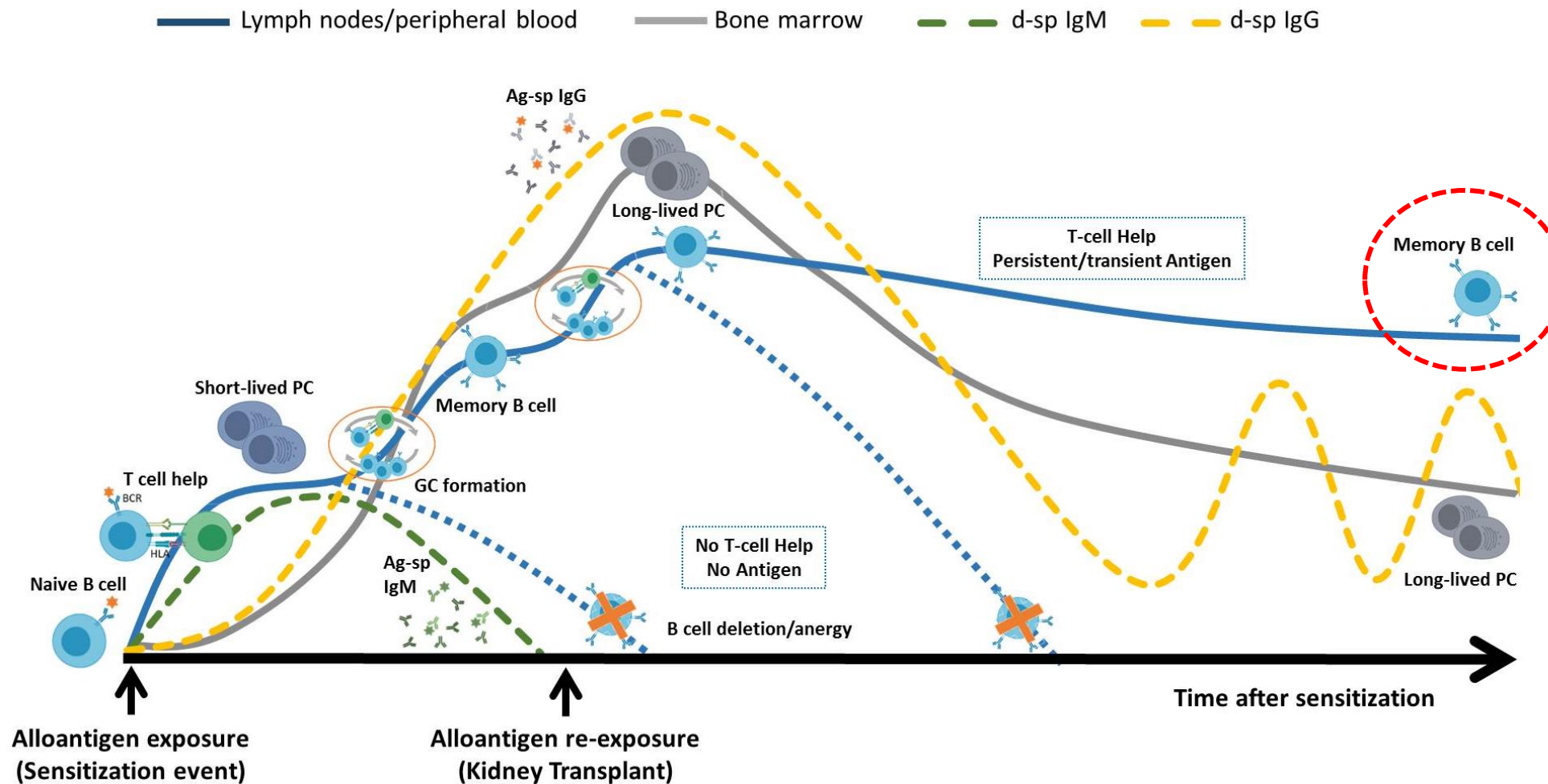
***IMPACT OF IMMUNOSUPPRESSION WITHDRAWAL IN DONOR(HLA)-
SPECIFIC MEMORY B CELL RESPONSES IN PEDIATRIC LIVER TRANSPLANT
RECIPIENTS***

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London, ⁴ Mount Sinai Hospital, ⁵ University of California San Francisco*

BACKGROUND

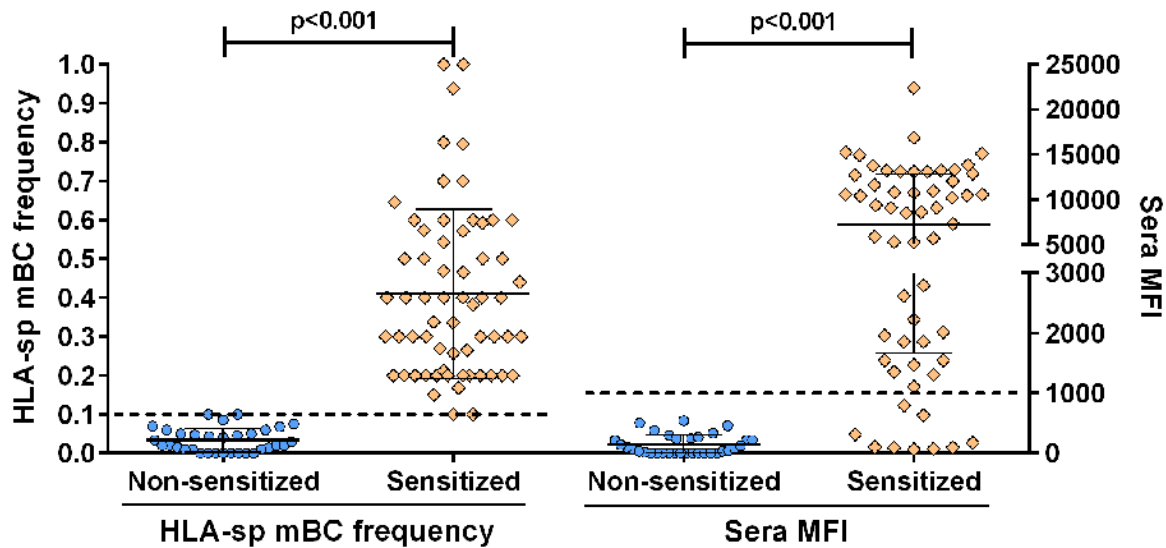
Compartmentalized biology of humoral memory



BACKGROUND

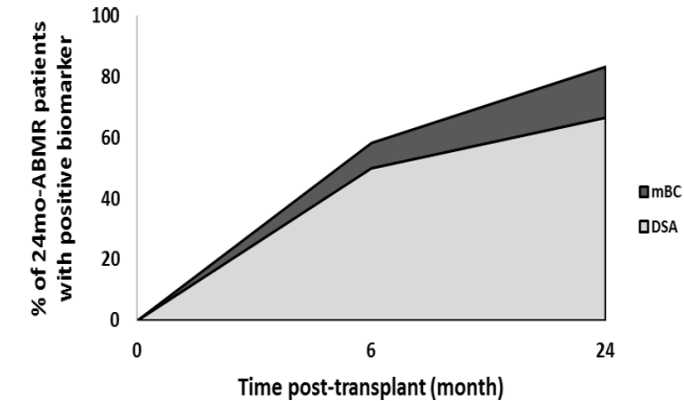
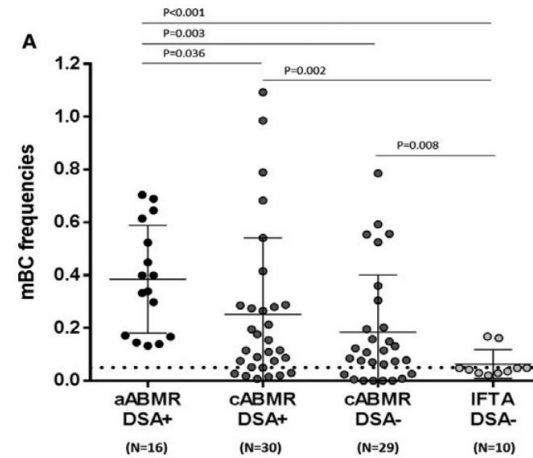
Monitoring circulating HLA-sp mBCs in organ transplantation

Detection of HLA-sp mBCs in highly sensitized kidney transplant patients



Lúcia, Marc, et al. *Kidney international* 88.4 (2015)

Donor(HLA)-sp mBCs precede subsequent Ab-mediated graft lesions

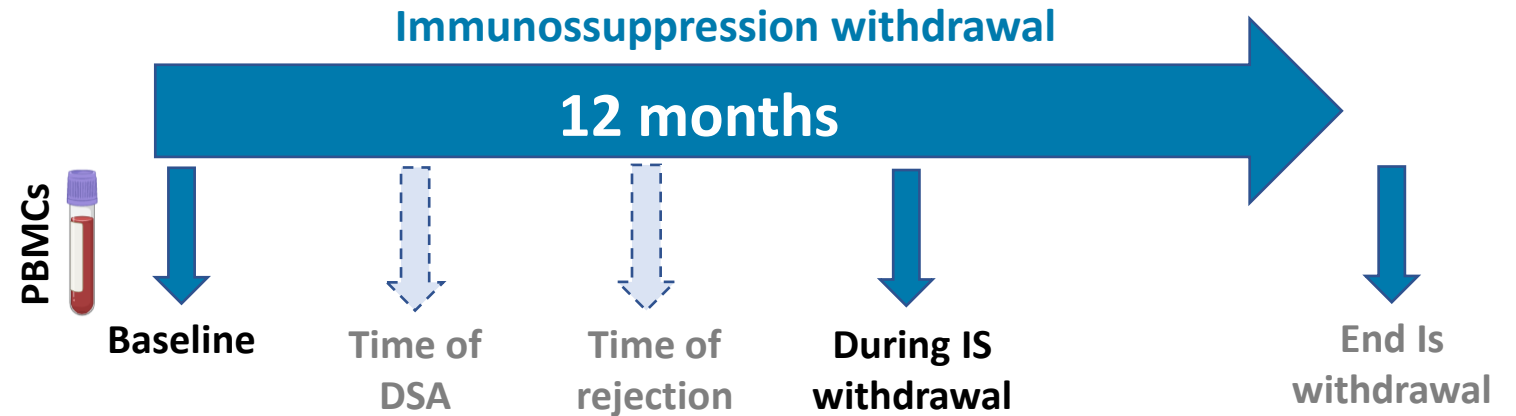
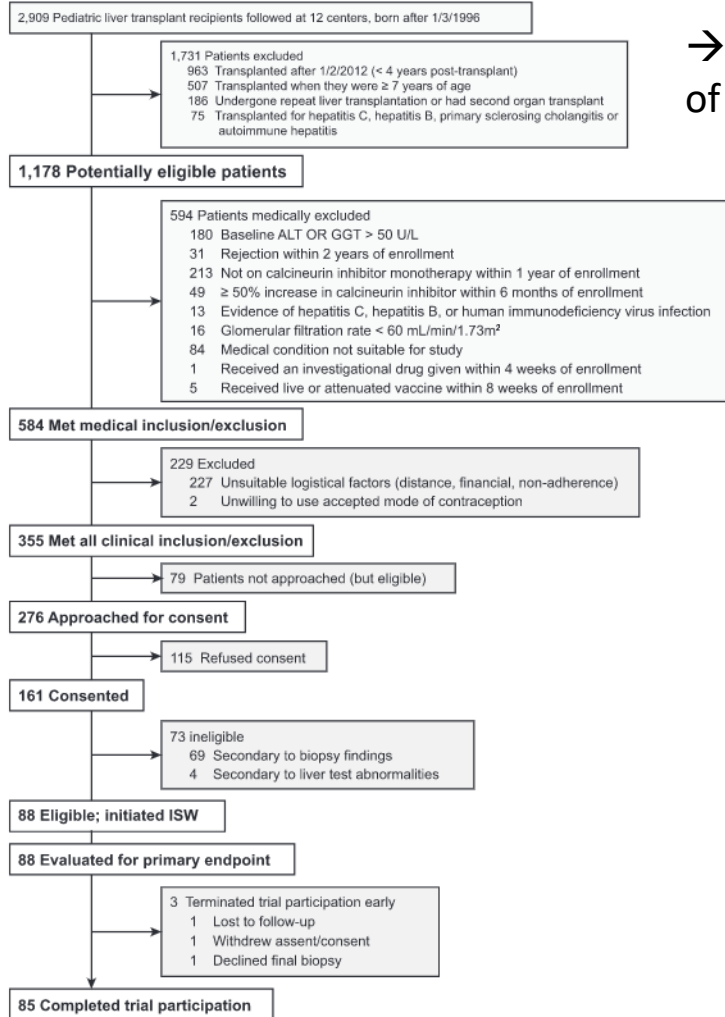


Luque S et al *Am J Transplant* 2018

BACKGROUND

Immunosuppression Withdrawal for Stable Pediatric Liver Transplant Recipients (iWITH, NCT01638559)

→ determine, among stable long-term pediatric liver transplant recipients, the efficacy and safety of immunosuppression withdrawal to identify operational tolerance.



Study groups

Presence of DSA		Rejection	
DSA baseline	No DSA baseline	Tolerant	Non-tolerant
	De novo DSA		None

HYPOTHESIS

Describe donor(HLA)-reactive mBCs prior to and during IS withdrawal in pediatric liver transplant recipients



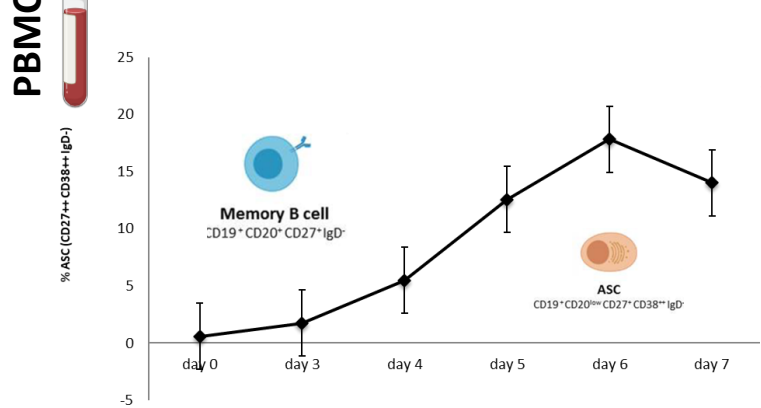
- Identify donor(HLA)-specific mBCs in pediatric liver transplant recipients with DSA at baseline
- Monitor donor(HLA)-specific mBC responses during IS withdrawal
- Track donor(HLA)-specific mBCs at time of rejection

Methodology

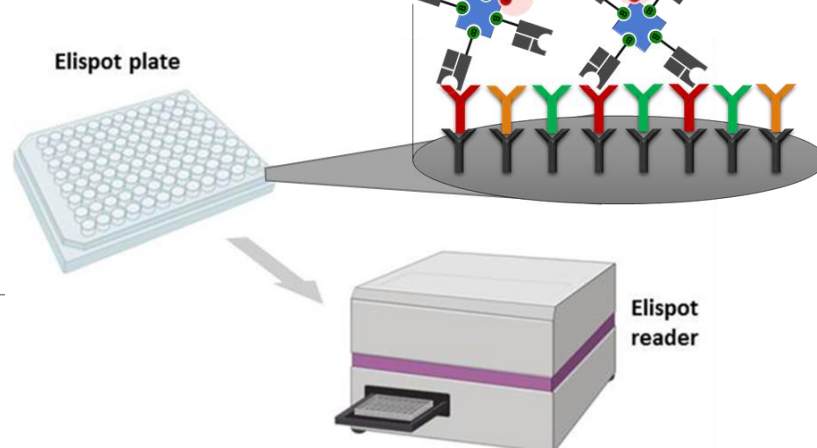
Assessment of HLA-specific ASCs by ELISPOT or fluorospot assay

In vitro differentiation of mBc into ASCs

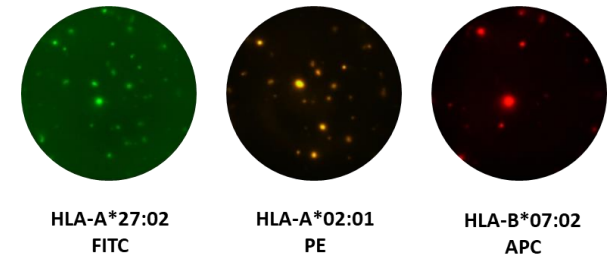
PBMCS 6-day Polyclonal mBc stimulation to obtain Ag-sp ASC



Fluorophore-conjugated HLA tetramers

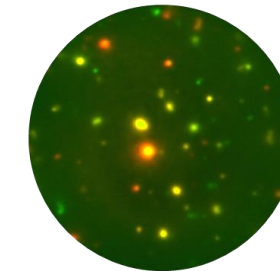


Detection of HLA-sp mBCs



Outputs

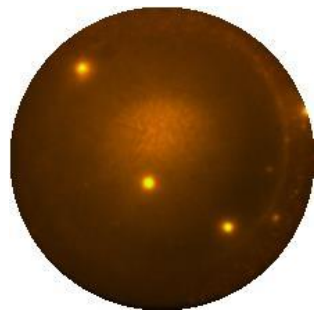
- HLA-sp IgG spots
- HLA-sp IgG MFI
- HLA-sp IgG activity



Simultaneous detection of different HLA-sp mBCs



5 spots
1948 activity

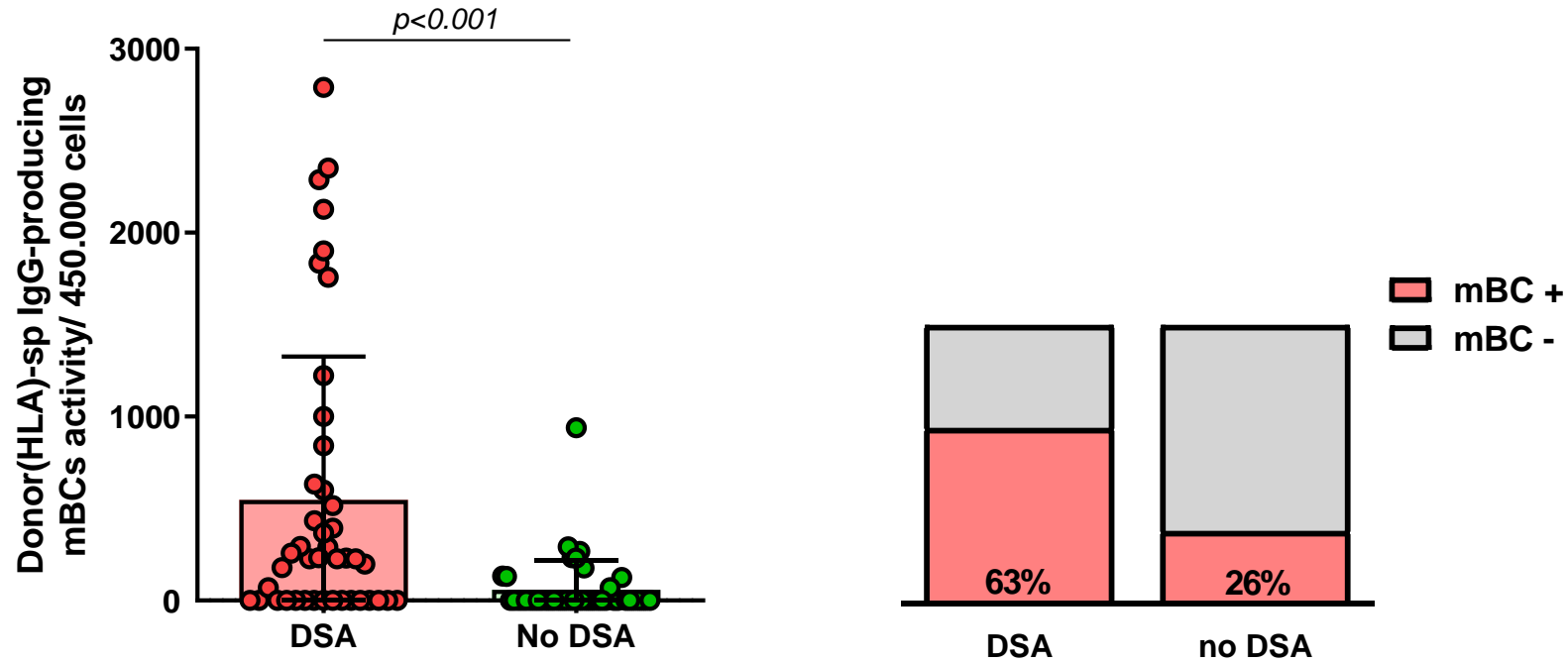


3 spots
1997 activity

$$\text{HLA-sp IgG activity} = (\text{Sum of Spot sizes multiplied on Spot intensities})/1000$$

RESULTS

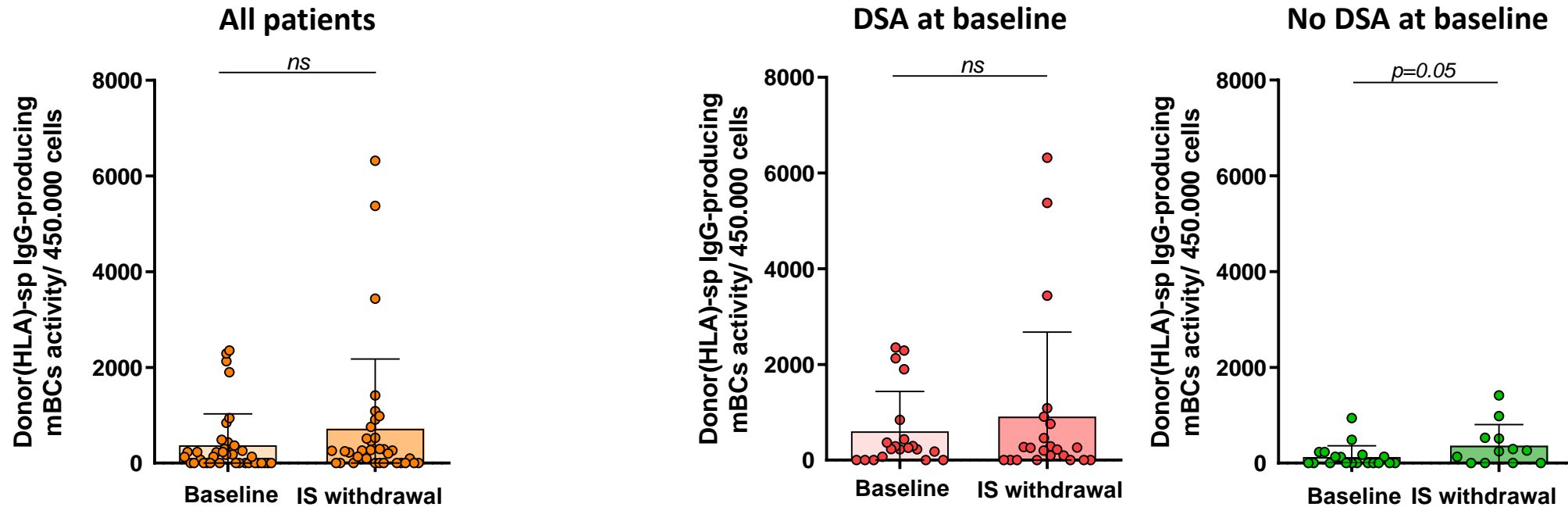
Detection of donor(HLA)-sp mBCs before IS withdrawal



Patients with circulating anti-HLA antibodies show higher numbers of circulating HLA-sp mBCs

RESULTS

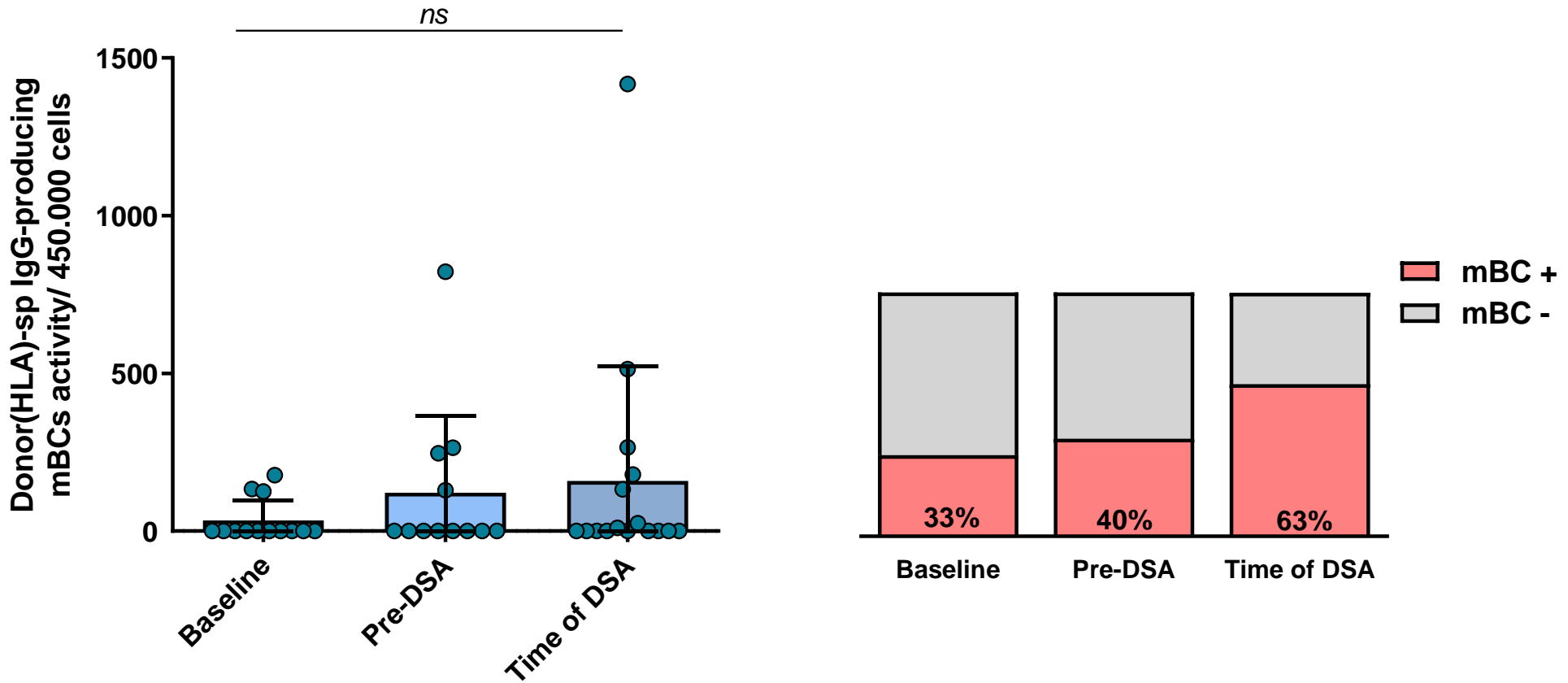
Evolution of donor(HLA)-sp mBCs during IS withdrawal



➔ Donor(HLA)-sp mBCs increase during IS withdrawal in all patients and significantly in those with no DSA at baseline

RESULTS

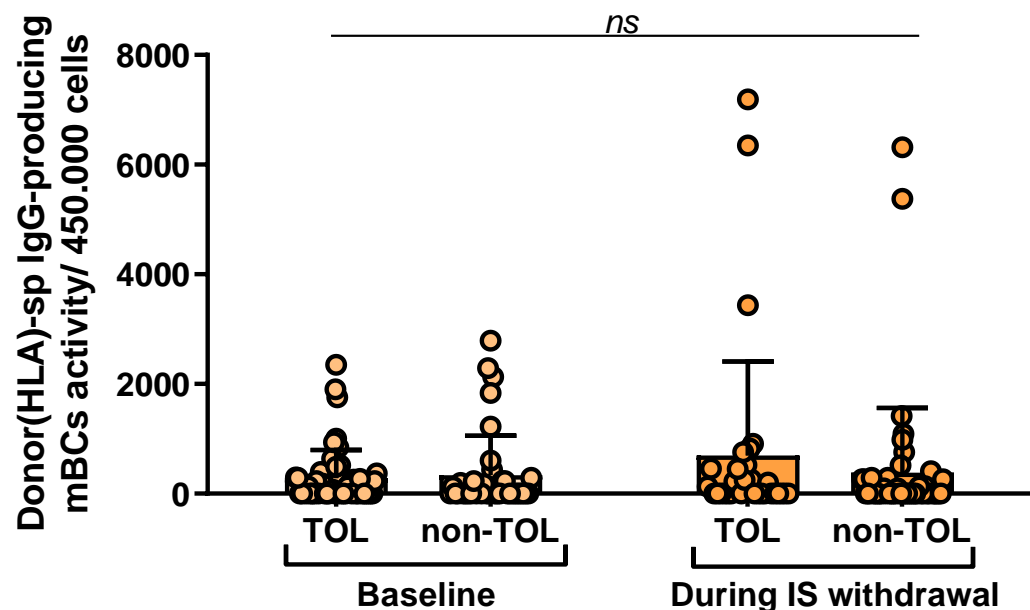
Donor(HLA)-sp mBCs in patients with de novo DSA appearance during IS withdrawal



➔ Donor(HLA)-sp mBCs can be detected circulating prior to DSA

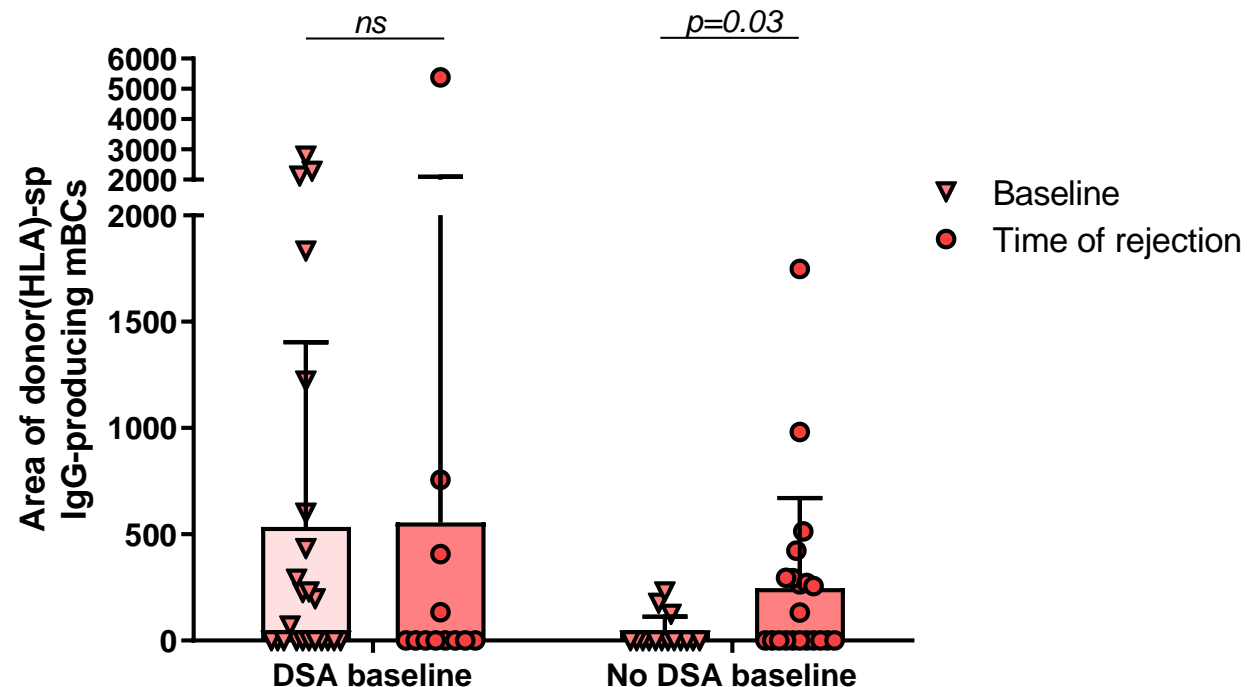
RESULTS

Donor(HLA)-sp mBCs and allograft tolerance



No differences in donor(HLA)-sp mBCs were observed between tolerant and non-tolerant recipients

Donor(HLA)-sp mBCs at time of rejection



Donor(HLA)-sp mBCs increase at time of rejection in patients without DSA at baseline

Conclusions

- HLA-sp mBCs can be detected circulating in pediatric liver transplant recipients with positive DSAs.
 - Those HLA-sp mBCs seem to appear over time and increase its frequencies during IS withdrawal.
 - HLA-sp mBCs can be detected in prior to DSA appearance.
 - HLA-sp mBCs frequencies increase at time of rejection and seem to play an active role in humoral immune activation
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- Oriol Bestard
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University of California San Francisco

- Sandy Feng

King's College London

- Alberto Sanchez-Fueyo

