

# Dynamics of Pre-formed Donor-Specific HLA Antibodies After Liver Transplantation

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## Introduction

It is known that the levels of pre-formed donor-specific antibodies (DSAs) typically trend down after liver or multi-organ transplant involving liver. Several studies have shown that HLA class I and class II DSAs may have distinct rates and extents of decline post-liver transplant. The aim of the current study is to investigate whether DSAs at individual HLA loci show differential dynamics after liver transplantation.

## Objectives

- Verify the differential dynamics of class I vs. class II DSAs in this patient cohort.
- Understand how DSAs at individual HLA loci trend after liver transplantation.
- Assess the impact of pre-transplant levels on DSA persistence.

## Methods

A total of 144 pre-formed DSAs (26 HLA-A, 35 HLA-B, 20 HLA-C, 27 HLA-DR, 24 HLA-DQ, and 12 HLA-DP) from 36 liver transplant recipients (18 liver alone, 14 Kidney+Liver, and 4 Heart+Liver) who had at least 6 months post-transplant follow-up were included in this study. 1,000 MFI is used as the positive cutoff for DSAs. Only DSA data up to approximately 1-year post-transplant were collected for this study.

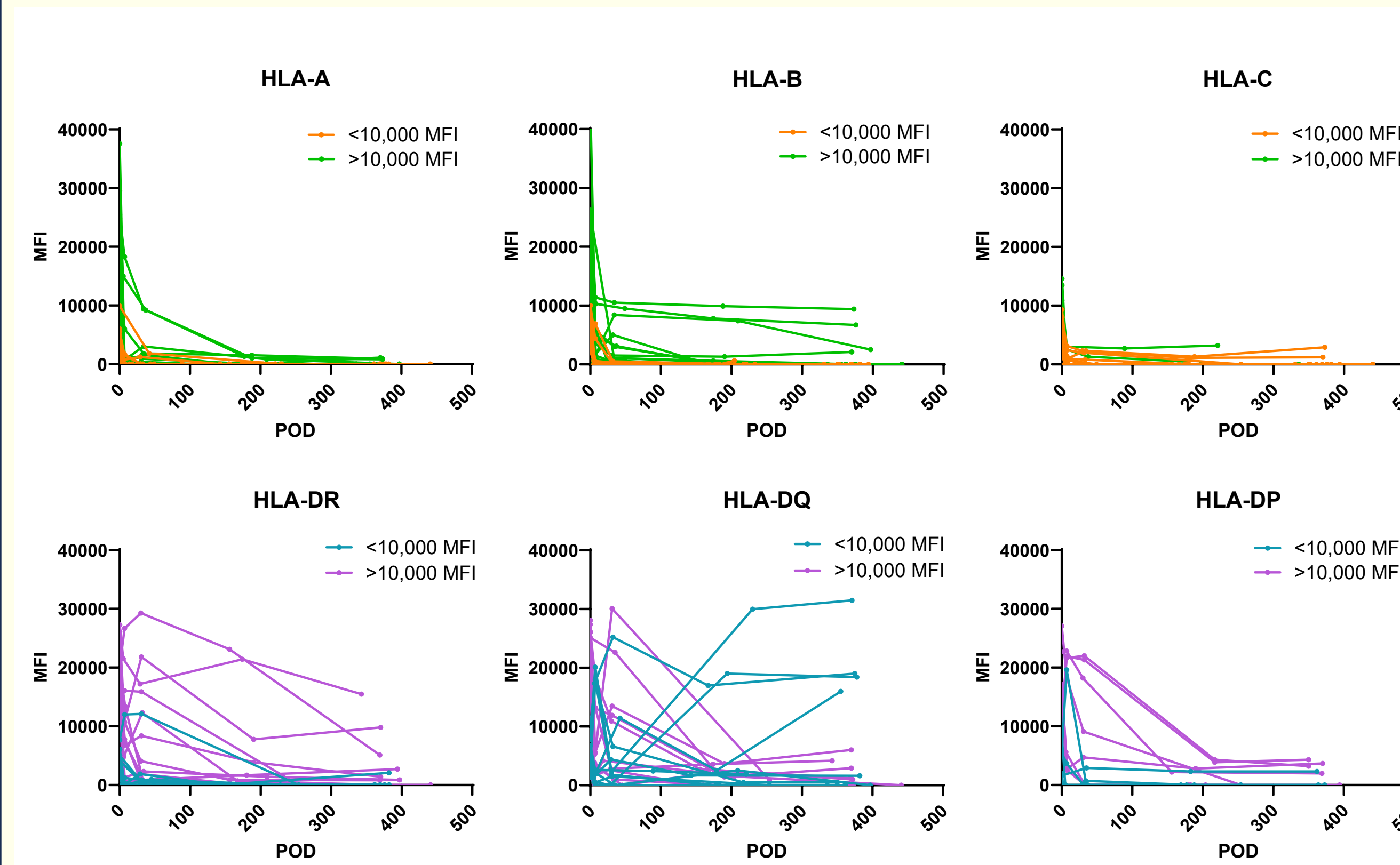
## Reference

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## Results

### Dynamics of Locus-Specific DSAs after Liver Transplant

In this cohort, nearly all of the DSAs at A and C loci became negative shortly after transplant and stayed absent during the study period. Four B locus DSAs remained positive 1-year post-transplant, but their MFIs were greatly reduced compared to pre-transplant levels. More DSA persistence and/or rebound were observed for class II loci.



### The Impact of Pre-Transplant Levels on DSA Persistence

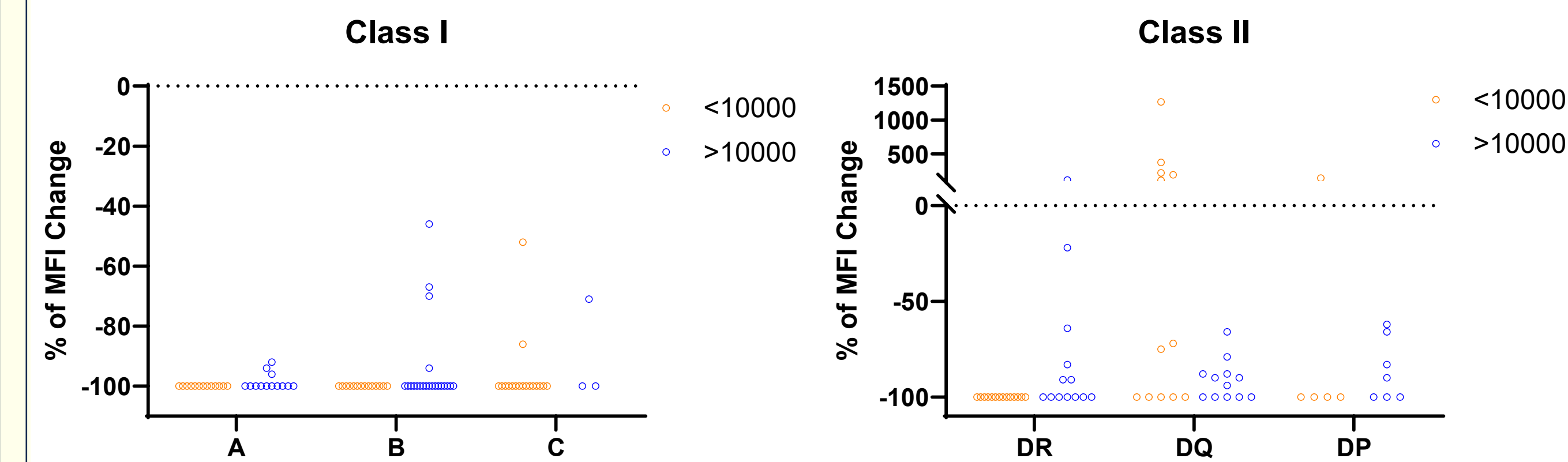
Pre-formed DSAs below 10,000 MFI against A, B, and DR loci (n=41) all decreased to negative level within 6 months post-transplant, except for one DR DSA rebounded at 1 year. In contrast, 13%, 45%, and 33% of the DSAs to the lower expressed C, DQ, and DP loci, respectively, were still positive 1-year post-transplant. As expected, DSAs that were greater than 10,000 MFI prior to transplant showed higher persistence after liver transplant, especially for DQ and DP loci where ≥50% of DSAs persisted at 1 year.

Locus	Pre-Txp MFI	Post-Txp			
		Total	30 days	6 months	1 yr
A	<10,000	13	2/13 (15%)	0/13 (0%)	0/10 (0%)
	>10,000	13	5/13 (38%)	3/13 (23%)	1/13 (8%)
B	<10,000	14	0/14 (0%)	0/14 (0%)	0/11 (0%)
	>10,000	21	9/21 (43%)	4/21 (19%)	4/18 (22%)
C	<10,000	17	3/17 (18%)	2/17 (12%)	2/15 (13%)
	>10,000	3	2/3 (67%)	1/3 (33%)	0/2 (0%)
DR	<10,000	14	3/14 (21%)	0/14 (0%)	1/10 (10%)
	>10,000	13	9/13 (69%)	6/13 (46%)	5/12 (42%)
DQ	<10,000	12	8/12 (67%)	7/12 (58%)	5/11 (45%)
	>10,000	12	9/12 (75%)	7/12 (58%)	5/10 (50%)
DP	<10,000	5	1/5 (20%)	1/5 (20%)	1/3 (33%)
	>10,000	7	5/7 (71%)	4/7 (57%)	4/7 (57%)

## Results-cont.

### Percent Changes of MFI at 6-Month Post-Transplant

All of the 81 class I DSAs showed a decline of MFI 6 months after liver transplant. Among which, 71 (88%) DSAs were negative at this time point, and 76 (94%) had a ≥80% reduction in MFI. On the other hand, 60% (38/63) of class II DSAs became negative at 6-month. One DR, five DQ, and one DP DSAs rebounded to MFIs greater than the pre-transplant levels. Despite more persistence and rebound post-transplant, the majority of class II DSAs (89% DR, 63% DQ, and 75% DP) showed a ≥80% MFI reduction 6-month post-transplant.



Locus	Total (n)	>80% Reduction n (%)
A	26	26 (100%)
B	35	32 (91%)
C	20	18 (90%)
<b>Class I</b>	<b>81</b>	<b>76 (94%)</b>

Locus	Total (n)	>80% Reduction n (%)
DR	27	24 (89%)
DQ	24	15 (63%)
DP	12	9 (75%)
<b>Class II</b>	<b>63</b>	<b>48 (76%)</b>

## Conclusions

- DSAs against HLA class II loci showed more persistence and rebound after liver transplantation, compared to class I DSAs.
- Higher expressed loci, A, B, and DR, had a more profound reduction of DSAs than low expressed C, DQ, and DP loci.
- Despite more persistence and rebound post-transplant, the majority of class II DSAs showed a significant reduction in MFI 6-month post-transplant.