Are DQ8 and DQ9 an acceptable mismatch in transplantation?

CLINIMMUNE Cell & Gene Therapy

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Introduction

In the DQ3 serotype, there are three different alleles: DQ7, DQ8 and DQ9. DQB1*03:01 differs by five amino acids from DQB1*03:02 and by 6 amino acids from DQB1*03:03. DQ8 and DQ9 differ by only one amino acid. The purpose of this project was to investigate whether these two immune proteins are sufficiently similar that the immune system cannot recognize the difference. We hypothesized that one amino acid difference between DQ8 and DQ9 would not be alloreactive. If so, it may be possible to consider these two immune proteins functionally identical when considering them in transplantation.

A query was used to identify the number of patients who have both DQ typing and a PRA result. The number of patients with DQ7, DQ8, or DQ9 typing (either homozygous or heterozygous) was then calculated. Patients were then filtered for anti- DQ7, DQ8 or DQ9 antibody reactivity. In addition, DQ8 and DQ9 patients that had received a DQ9 or DQ8 transplant, respectively, were analyzed. Individual HLA-DQ molecules were cloned into T2 cells to test if anti-DQ antibodies detected in the HDPRA were functional.



- Data from consecutive samples starting Jan 1, 2018 through March 16, 2018
- Only looked at DQ3negative patients (n=609)
 Each dot represents a SAMPLE (but not

necessarily unique

patients)



Antibodies to DQ9 and Vice Versa?				
	Antibodies			
Patient typing	Anti-DQ8	Anti-DQ9		
DQ7 (n = 8218)	256 (3.12%)	246 (2.99%)		
DQ8 (n = 4796)		14 (0.29%)		
DQ9 (n = 1729)	20 (1.16%)			

Do DQ8⁺ Patients Ever Make

In our cohort, there are 14,743 patients typed as either DQ7, DQ8 or DQ9. Out of 4,796 DQ8⁺ patients, only 14 patients tested positive for anti-DQ9 antibody (0.29%). Of these 14 patients, 8 tested positive for an antibody which differs from the patient's α -chain. Out of 1,729 DQ9⁺ patients, 20 patients tested positive for anti-DQ8 antibody (1.16%). Out of these 20 patients there were 18 which differed from the patient's α -chain.

Antibodies are present when the α -chain differs

DQ8⁺ patients

Sample ID	Patient's DQ8	Antibody reactivity to DQ9	anti-DQ9 MFI in HDPRA
2022-14538	DQA1*03:01/DQB1*03:02	DQA1*03:01/DQB1*03:03	2532
2020-03217	DQA1*03:01/DQB1*03:02	DQA1*03/DQB1*03:03 DQA1*02:01/DQB1*03:03	2531, 3551 2847
2021-20627	DQA1*03:01/DQB1*03:02	DQA1*02:01/DQB1*03:03	12623





DQ9 Graft into DQ8⁺ Recipient (n = 65)

- One patient made anti-DQ9 antibody.
- This reactivity is against the DQ9 allele that contains a different α-chain from the patient.

DQ8 Graft into DQ9⁺ Recipient (n = 58)

- · One patient made anti-DQ8 antibody.
- This reactivity is against the DQ8 allele that contains a different α -chain from the patient.

Conclusions

- The frequency of DQ8 patients producing DQ9 antibodies and vice versa is significantly lower than the frequency of DQ7 patients producing DQ8 or DQ9 antibodies.
- The frequency of patients testing positive for antibodies with an identical α -chain to self are exceedingly rare.
- Only two patients made a response suggesting these two immune proteins could be considered functionally identical which would broaden the donor pool for patients that need a transplant.
- Due to this, we conclude that DQ8 and DQ9 are permissively mismatched for development of de novo DSA and could be an acceptable mismatch for transplant.