Educational Crossmatching Scheme

Dispatched on the 18th July 2023

Summary of Results

A total of 37 reports were received, but not all laboratories reported results for all tests.

Consensus HLA Type of whole blood donor sample EDXM 01/2023:

	A*	B*	C*	DRB1*	DRB3*	DRB5*	DQA1*	DQB1*	DPA1*	DPB1*
	02	08	05	03 (17)	01	01	01	02	01	04:01
	25	44	07	15			05	06	01	06:01
Number of reports	37	37	37	37	24	24	34	37	25	30
% Labs in consensus	95%	95%	95%	95%	100%	100%	94%	95%	92%	93%

There were a number of errors noted when defining the genotype. It appears that 2 laboratories reported the wrong HLA type. Interestingly, in both cases the discrepant HLA type corresponded to the HLA type of sample ED01/2023 from another NEQAS educational scheme which focuses on HLA Typing. The results from these laboratories were removed from the crossmatching analysis.

EDXM 01 Serum 1/2023 Results

HLA Antibody Detection and Definition
(Based on 75% Consensus)

		HLA Class I	No of labs	% consensus	HLA Class II	No of labs	% consensus
Detection	IgG	Positive	35/35	100%	Positive	34/35	97%
	IgM	Negative	3/3	100%	Negative	3/3	100%
Definition[1]	Total Number of Specificities Reported (by ≥ 1 lab, >1,000 MFI)	25			26		
	Number of Specificities Absent (reported by < 5% labs)	64			19		
	Number of Specificities Present (reported by ≥ 75% labs)	9			19		
	MFI >10000	A2 A68 A69	35	100%	DR15 DR16 DR51	35	100%
	MFI 5000 - 9999	A23 A24		94-97%	DR9 DP1 DP3 DP5 DP6 DP9 DP10 DP11 DP13 DP14 DP17 DP19 DP20		80-100%
	MFI 2000 - 4999	B49 B50 B57 B58		86-97%	DR1 DR103 DR7		100%
	MFI 1000-1999	N/A		N/A	N/A		N/A

[1] 75% consensus 'present' specificities are displayed within the MFI value range reported by the **majority** of participants. Class I specificities n=89, Class II specificities n=46.

Crossmatching
(Based on 75% Consensus)

	CDC						Flow Cytometry	
	PBL		T Cells		B Cells		T Cells	B Cells
	Without DTT	With DTT	Without DTT	With DTT	Without DTT	With DTT		
	Positive	Positive	*No Consensus*	*No Consensus*	Positive	Positive	Positive	Positive
Number of reports	3/3	4/4	*7/11 Pos*	*7/11Pos*	9/9	8/9	32/32	29/32
% Labs in consensus	100%	100%	*64%*	*64%*	100%	89%	100%	91%

Interpretation

Identification of Donor Specific Antibodies:

Specificity	No of Participants (n=35)	MFI Range Reported
A2	35 (100%)	4300-23836
DR15	35 (100%)	8323-21408
DR51	28 (80%)	6886-22844
DPB1*06:01	27 (77%)	6378-16422
B44	5 (14%)	565-898
DR52	2 (6%)	1750-2497
DQ6	2 (6%)	1016-8000
DPB1*04	1 (3%)	1010
DQ2	1 (3%)	1406

Crossmatch interpretation:

	The most common responses included:
Interpretation based on results	• CDC crossmatch positive • Flow cytometry crossmatch positive • Patient has Class I and II donor specific antibodies
Assigned risk	High n = 7 (20%) Contraindication n = 28 (80%)
Immunological advice	• Not suitable for direct transplantation • High levels of circulating IgG donor specific antibodies • Risk of hyperacute rejection
If advice is not to transplant, recommendations for future transplants	• Seek alternative donor (live or deceased) or a kidney sharing scheme • Consider Imlifidase enabled transplant • Consider desensitisation strategy • De-listing low level antibodies • Perform additional testing such as autologous crossmatching or antibody testing using additional kits

EDXM 01 Serum 2/2023 Results

HLA Antibody Detection and Definition

(Based on 75% Consensus)

		HLA Class I	No of labs	% consensus	HLA Class II	No of labs	% consensus
Detection	IgG	*No Consensus*	*24/35 Neg*	*69%*	Positive	33/35	94%
	IgM	Negative	3/3	100%	Negative	3/3	100%
Definition [1]	Total Number of Specificities Reported (by ≥ 1 lab, >1,000 MFI)	5			17		
	Number of Specificities Absent (reported by < 5% labs)	84			29		
	Number of Specificities Present (reported by ≥ 75% labs)	0			3		
	MFI >10000	N/A	35	N/A	N/A	33	N/A
	MFI 5000 - 9999	N/A		N/A	N/A		N/A
	MFI 2000 - 4999	N/A		N/A	DR15 DR16 DR51		83-94%
	MFI 1000-1999	N/A		N/A	N/A		N/A

[1] 75% consensus 'present' specificities are displayed within the MFI value range reported by the **majority** of participants. Class I specificities n=89, Class II specificities n=46.

Crossmatching Results

(Based on 75% Consensus)

	CDC						Flow Cytometry	
	PBL		T Cells		B Cells		T Cells	B Cells
	Without DTT	With DTT	Without DTT	With DTT	Without DTT	With DTT		
	Negative	Negative	Negative	Negative	Negative	Negative	Negative	*No Consensus*
Number of reports	3/3	4/4	11/11	11/11	8/9	8/9	32/32	*19/32 Pos*
% Labs in consensus	100%	100%	100%	100%	89%	89%	100%	*59%*

Interpretation

Identification of Donor Specific Antibodies:

Specificity	No of Participants (n=35)	MFI Range Reported
DR15	32 (91%)	1300-4647
DR51	25 (71%)	1100-3886
DP6	21 (60%)	970-2250
DQ6	7 (20%)	2000-13707
A2	3 (9%)	882-2359

Crossmatch interpretation:

	The most common responses included:
Interpretation based on results	• CDC crossmatch negative • Flow cytometry crossmatch T cell negative, B cell positive • Class II donor specific antibodies present
Assigned risk	Low n = 6 (17.2%) Medium n = 17 (48.6%) High n = 9 (25.7%) Contraindication n = 3 (8.6%)
Immunological advice	• Not suitable for direct transplantation • Patient at risk of antibody mediated rejection • Possible antibody removal pre-transplant • If transplant proceeds use enhanced immunosuppression and post-transplant monitoring • Test for presence of autologous and non-HLA antibodies
If advice is not to transplant, recommendations for future transplants	• Seek alternative donor (live or deceased) or via a kidney sharing scheme • Consider de-sensitisation • Investigate whether the patient is a suitable for a higher risk transplant • Perform additional testing such as autologous crossmatching or antibody testing using additional kits

EDXM 01 Serum 3/2023 Results

HLA Antibody Detection and Definition
(Based on 75% Consensus)

		HLA Class I	No of labs	% consensus	HLA Class II	No of labs	% consensus
Detection	IgG	Positive	34/35	97%	Positive	33/35	94%
	IgM	Negative	3/3	100%	Negative	3/3	100%
Definition[1]	Total Number of Specificities Reported (by ≥ 1 lab, >1,000 MFI)	17			21		
	Number of Specificities Absent (reported by < 5% labs)	72			25		
	Number of Specificities Present (reported by ≥ 75% labs)	3			6		
	MFI >10000	N/A	33	N/A	DQ6	33	100%
	MFI 5000 - 9999	B37		80%	DQ5		100%
	MFI 2000 - 4999	A2 B7		92-94%	DQ4 DQ8 DQ9 DP14		83-89%
	MFI 1000-1999	N/A		N/A	N/A		N/A

[1] 75% consensus 'present' specificities are displayed within the MFI value range reported by the **majority** of participants. Class I specificities n=89, Class II specificities n=46.

Crossmatching
(Based on 75% Consensus)

	CDC						Flow Cytometry	
	PBL		T Cells		B Cells		T Cells	B Cells
	Without DTT	With DTT	Without DTT	With DTT	Without DTT	With DTT		
	Negative	Negative	Negative	Negative	Negative	Negative	*No Consensus*	*No Consensus*
Number of reports	3/3	4/4	11/11	11/11	9/9	9/9	*21/32 Pos*	*23/32 Pos*
% Labs in consensus	100%	100%	100%	100%	100%	100%	*66%*	*72%*

Interpretation

Identification of Donor Specific Antibodies:

Specificity	No of Participants (n=35)	MFI Range Reported
DQ6	34 (97%)	2418-16500
A2	33 (94%)	1198-6286
DP6	17 (49%)	1029-2819
DR51	4 (11%)	508-1357
DQA1*01	2 (6%)	4516
DQ5[+]	*1 (3%)*	*1017*

[+]*Not donor specific*

Crossmatch interpretation:

	The most common responses included:
Interpretation based on results	• CDC crossmatch negative • Flow cytometry crossmatch positive • Class I and II donor specific antibodies detected • Possible autologous or non-HLA antibodies also present
Assigned risk	Medium n = 8 (24%) High n = 17 (50%) Contraindication n = 9 (26%)
Immunological advice	• Not suitable for direct transplantation • Patient at risk of antibody mediated rejection • Possible antibody removal pre-transplant • If transplant proceeds use enhanced immunosuppression and post-transplant monitoring • Test for presence of autologous and non-HLA antibodies
If advice is not to transplant, recommendations for future transplants	• Seek alternative donor (live or deceased) or via a kidney sharing scheme • Consider de-sensitisation • Investigate whether the patient is a suitable for a higher risk transplant • Perform additional testing such as autologous crossmatching or antibody testing using additional kits

UK NEQAS for H&I Comments

The same sample was used for both Serum 1 and Serum 2. The sample was provided at neat for Serum 1 and at a dilution of 1:16 for Serum 2. We thought it would be interesting to see how the dilution affected the detection of antibodies across different laboratories. The only antibodies reaching consensus present in Serum 2 were DR15, DR16 and DR51 detected at a range of 2000-4999 MFI by 83-94% of participants, by contrast these antibodies were detected at >10,000 MFI by 100% of participants at neat in Serum 1 in addition to other Class I and Class II antibodies.

Suggested Reading

Tambur AR, Schinstock C. Clinical utility of serial serum dilutions for HLA antibody interpretation. HLA. 2022 Nov;100(5):457-468. doi: 10.1111/tan.14781. Epub 2022 Aug 29. PMID: 35986896; PMCID: PMC9804468.