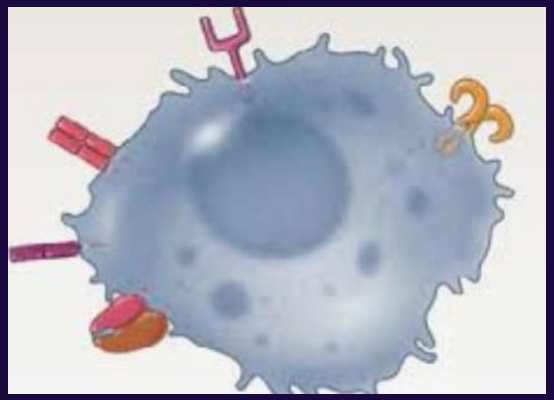
In the name of GOD

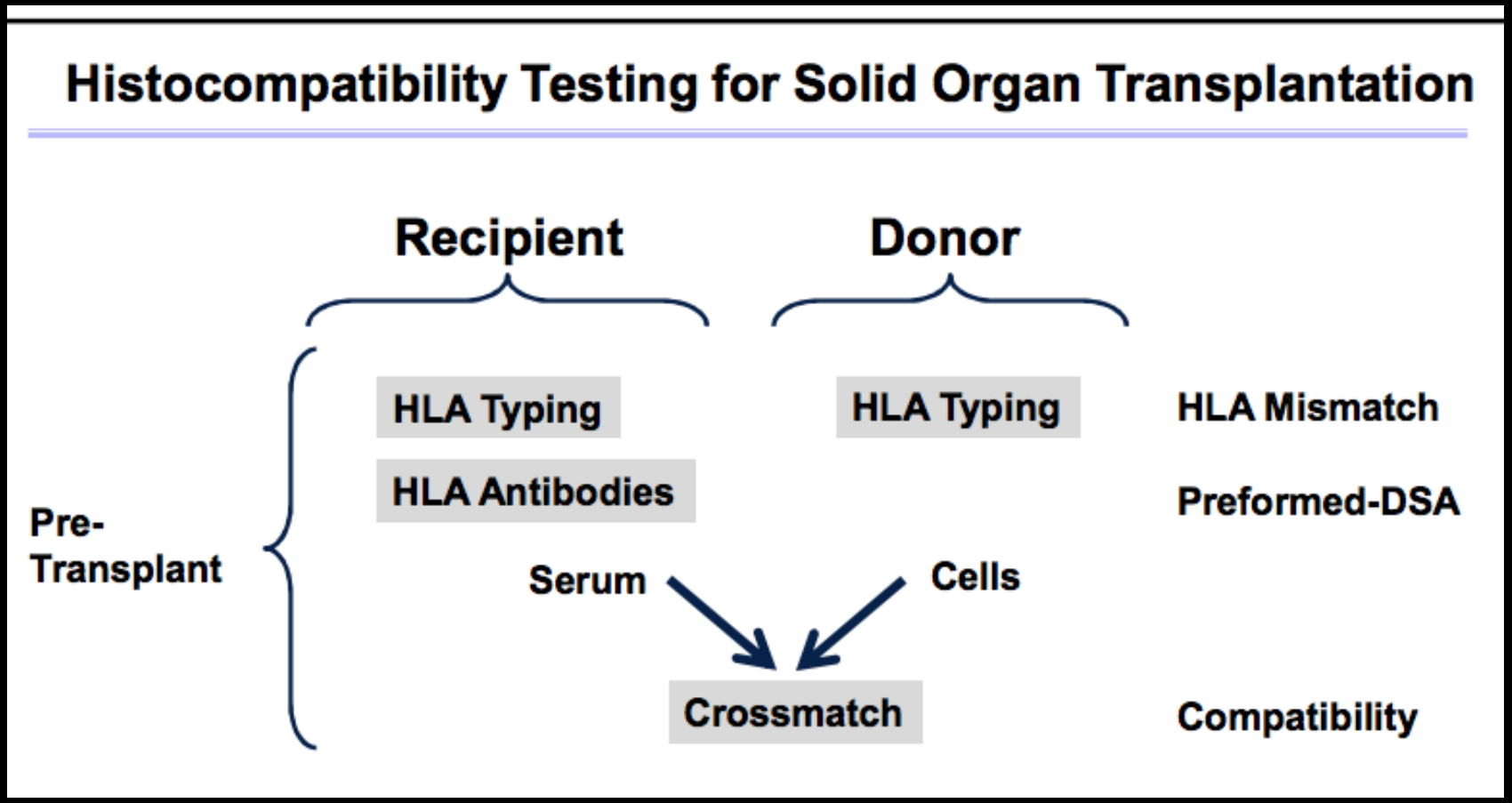
Immunologic risk assesment of kidney recipient



F.Samadian

Shaheed behesti university of medical science

ABO blood group determination

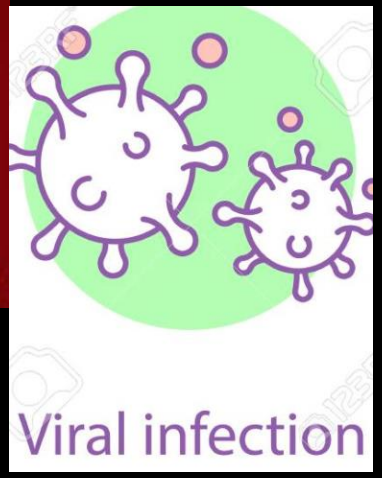


Recipient blood groups, their relative frequencies in the population, and compatible blood group donors

Recipient blood group	Percent of population (%)	Donor blood group compatible with recipient
A	42	A, O
B	10	B, O
AB	4	A, B, AB, O
O	44	O

- ABO blood group determination
- Serum screening for anti HLA antibody
- HLA typing
- Cross-matching

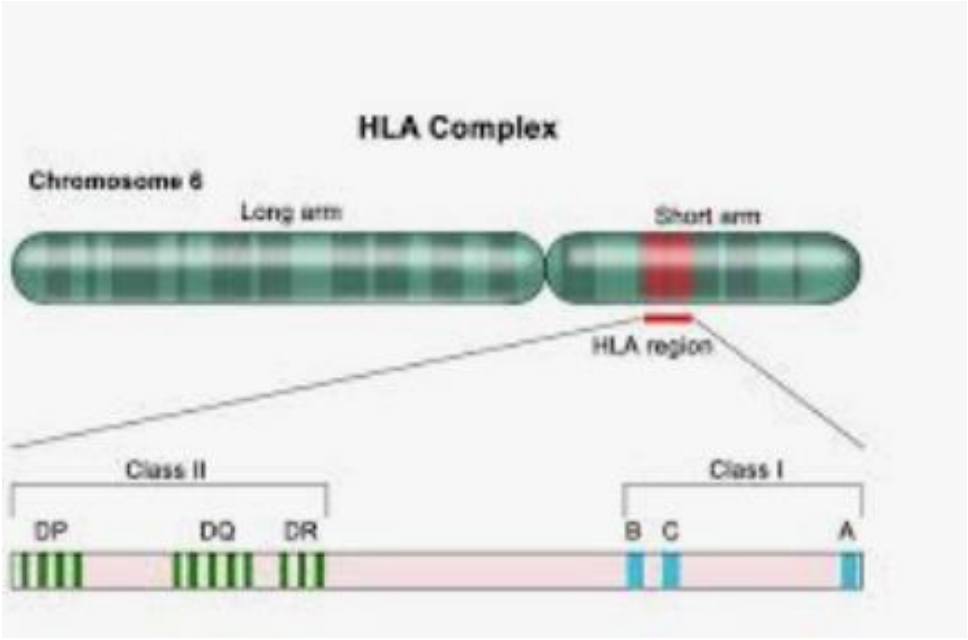
Transplant recipients can be sensitized against allo-HLA antigens by:



Immunological work up

- MHC ***class I*** molecules
  - HLA **A, B, C**
  - found on all nucleated cells

- MHC ***class II*** molecules
  - HLA **DP, DQ, DR**
  - Expressed on antigen presenting cells (and inducible)



CJASN™

Clin J Am Soc Nephrol. 2016 May 6; 11(5): 875–883.

HLA-DQ mismatches are associated with acute rejection, independent of HLA-ABDR mismatches and initial immunosuppression. Clinicians should be aware of the potential importance of HLA-DQ matching in the assessment of immunologic risk in kidney transplant recipients.

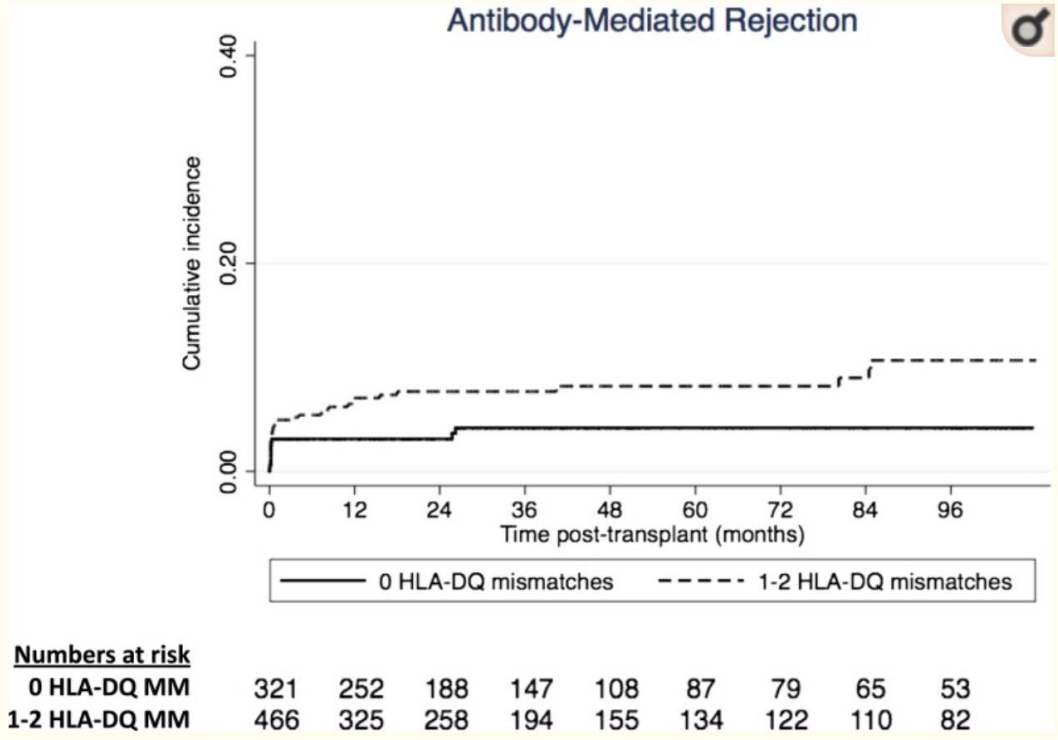
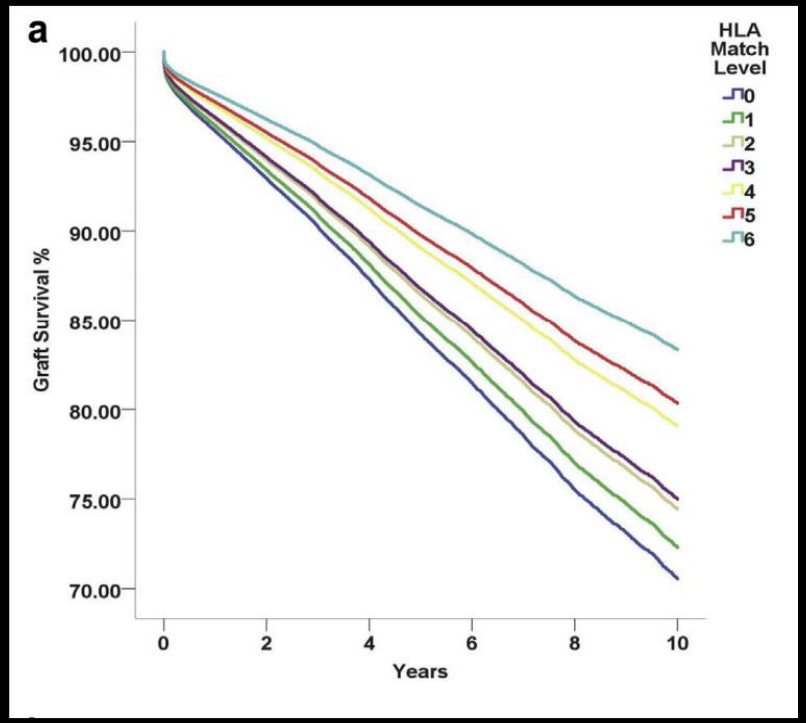


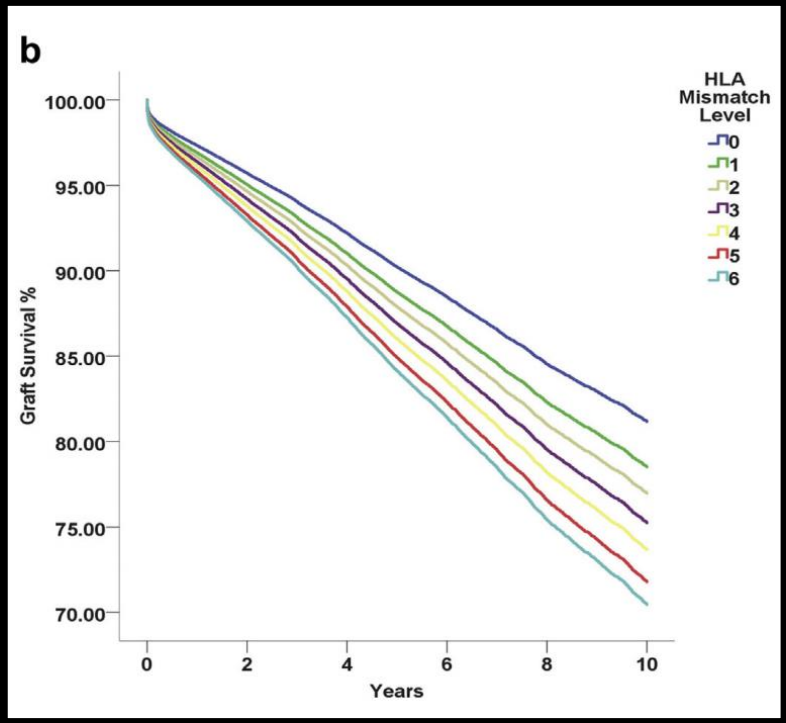
Figure 3.

Adjusted cumulative incidence curves for antibody-mediated rejection after kidney transplantation according to HLA-DQ matched and mismatched kidney transplants (log rank *P* value <0.01). MM, mismatched.

ISN kidney INTERNATIONAL 2018

OPTN/UNOS registry





Influence of Mismatched HLA Antigens on Graft survival

kidney INTERNATIONAL 2018
OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY

Analysis of OPTN/UNOS registry suggests the number of HLA matches and not mismatches is a stronger independent predictor of kidney transplant survival

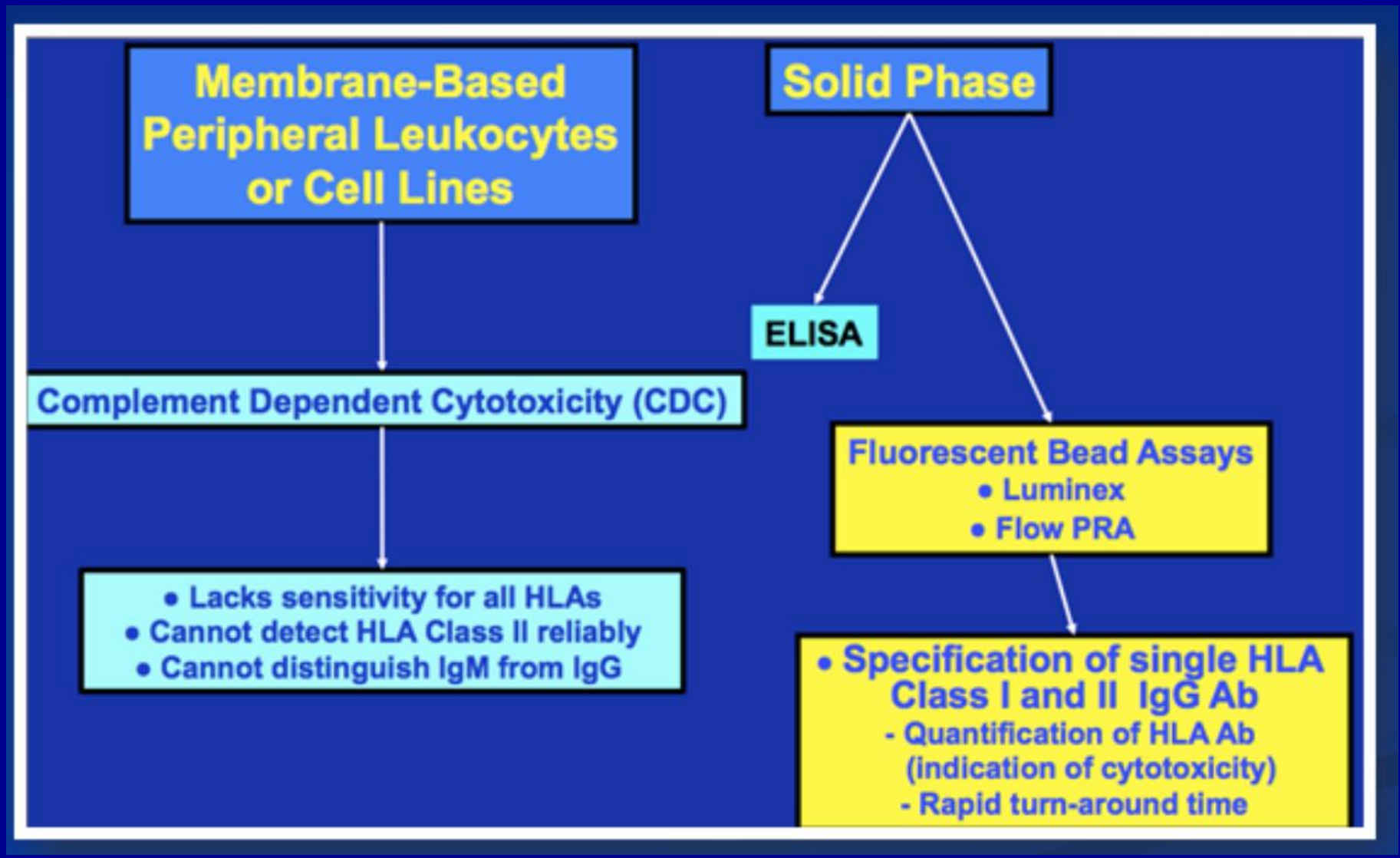
Rabi Yacoub[4], Girish N. Nadkarni[4], Paolo Cravedi, John Cijiang He, Veronica B. Delaney, Rebecca Kent, Kinsuk N. Chauhan, Steven G. Coca, Sander S. Florman, Peter S. Heeger, Barbara Murphy, Madhav C.

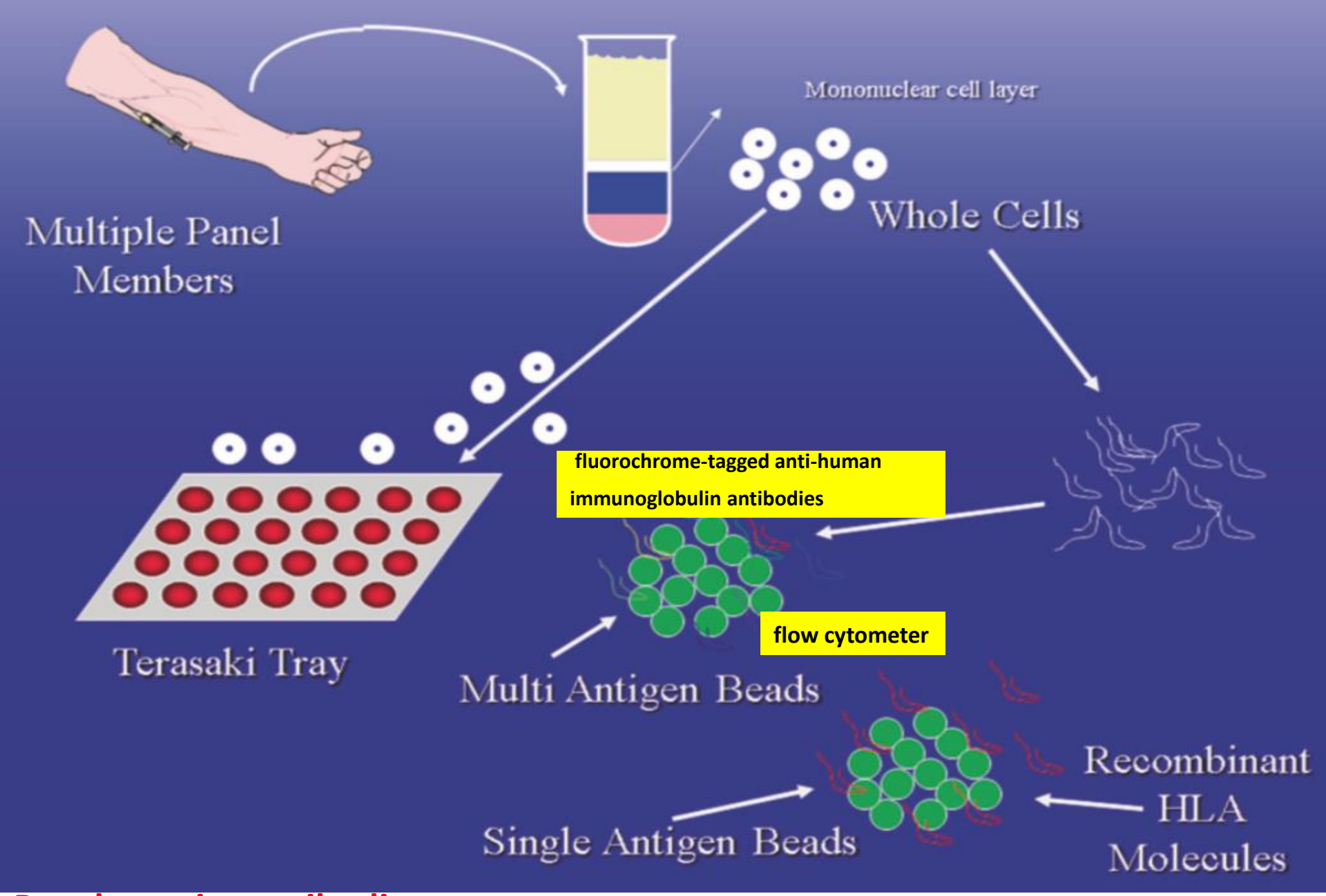
both matching and mismatching simultaneously, the degree of HLA mismatching lost significance while matching continued to have a significant prediction for delayed graft function, the one-year acute rejection rate, and graft survival. Sensitivity analyses and bootstrapping showed similar results for all studied outcomes. Thus, analysis of this large cohort demonstrates the apparent greater association of HLA matching over HLA mismatching on both early allograft events as well as graft survival.

Pretransplant Assessment of Anti-HLA Antibody Status

determining the breadth and strength of anti-HLA antibodies that are present (PRA)

performing crossmatch prior to transplant to be certain that there are no DSAs


Membrane-Based Peripheral Leukocytes or Cell Lines
Solid Phase
ELISA
Complement Dependent Cytotoxicity (CDC)
Fluorescent Bead Assays
• Luminex
• Flow PRA
• Lacks sensitivity for all HLAs
• Cannot detect HLA Class II reliably
• Cannot distinguish IgM from IgG
• Specification of single HLA Class I and II IgG Ab
- Quantification of HLA Ab (indication of cytotoxicity)
- Rapid turn-around time



Panel reactive antibodies

Two different techniques: cytotoxic- ity method and bead-based method

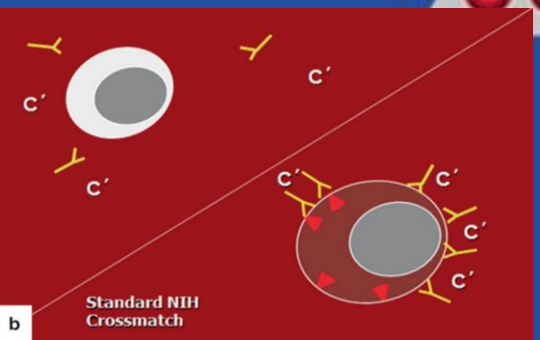
The Pretransplant Crossmatch

Standard Complement-Dependent Cytotoxicity or NIH Crossmatch

Anti-human Globulin-Enhanced Crossmatch

Flow Crossmatch Test

Luminex Crossmatch



Donor

Hanks

Mononuclear cell layer

Ficoll

ACD tube

Serum

Clot tube

Recipient

30′
23°C

C′
Rabbit complement

Eosin/ formalin

60′
23°C

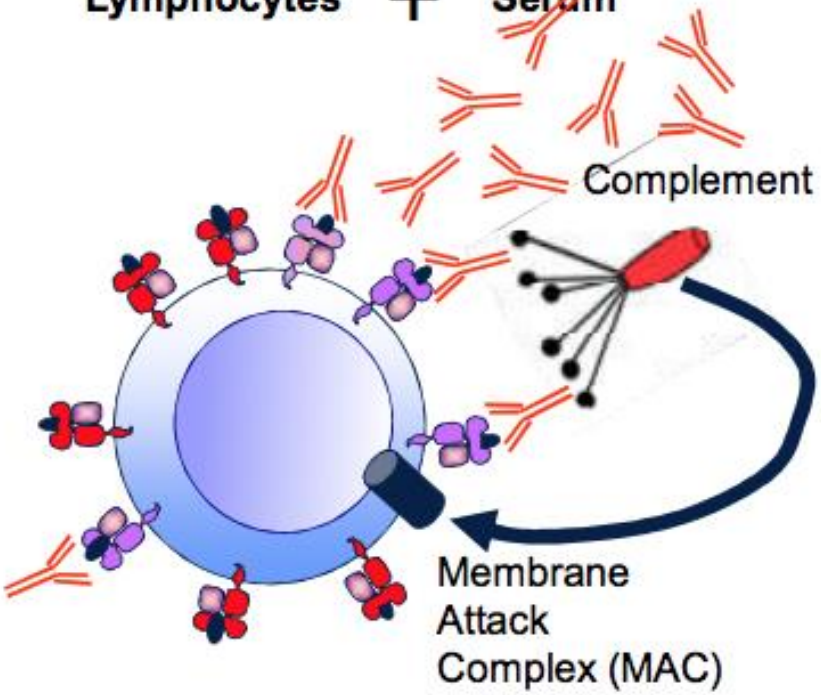
Standard NIH Crossmatch

Complement Dependent Cytotoxicity (CDC) Crossmatch

Donor

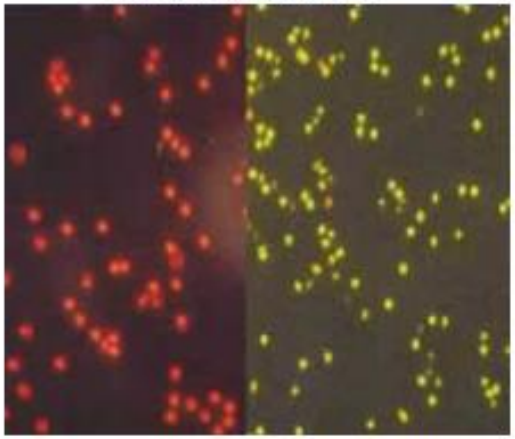
Recipient

Lymphocytes + Serum



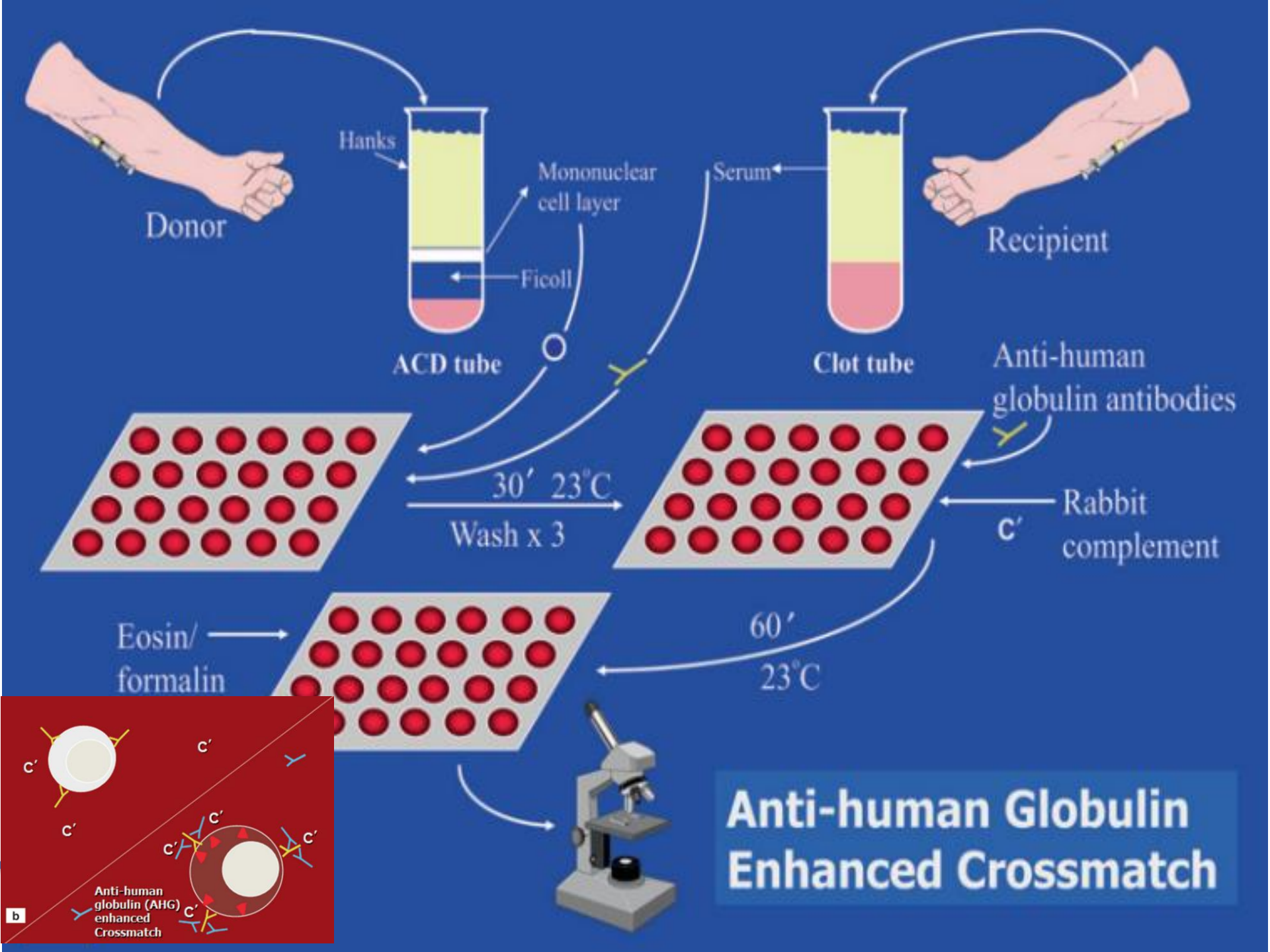
Paul Terasaki

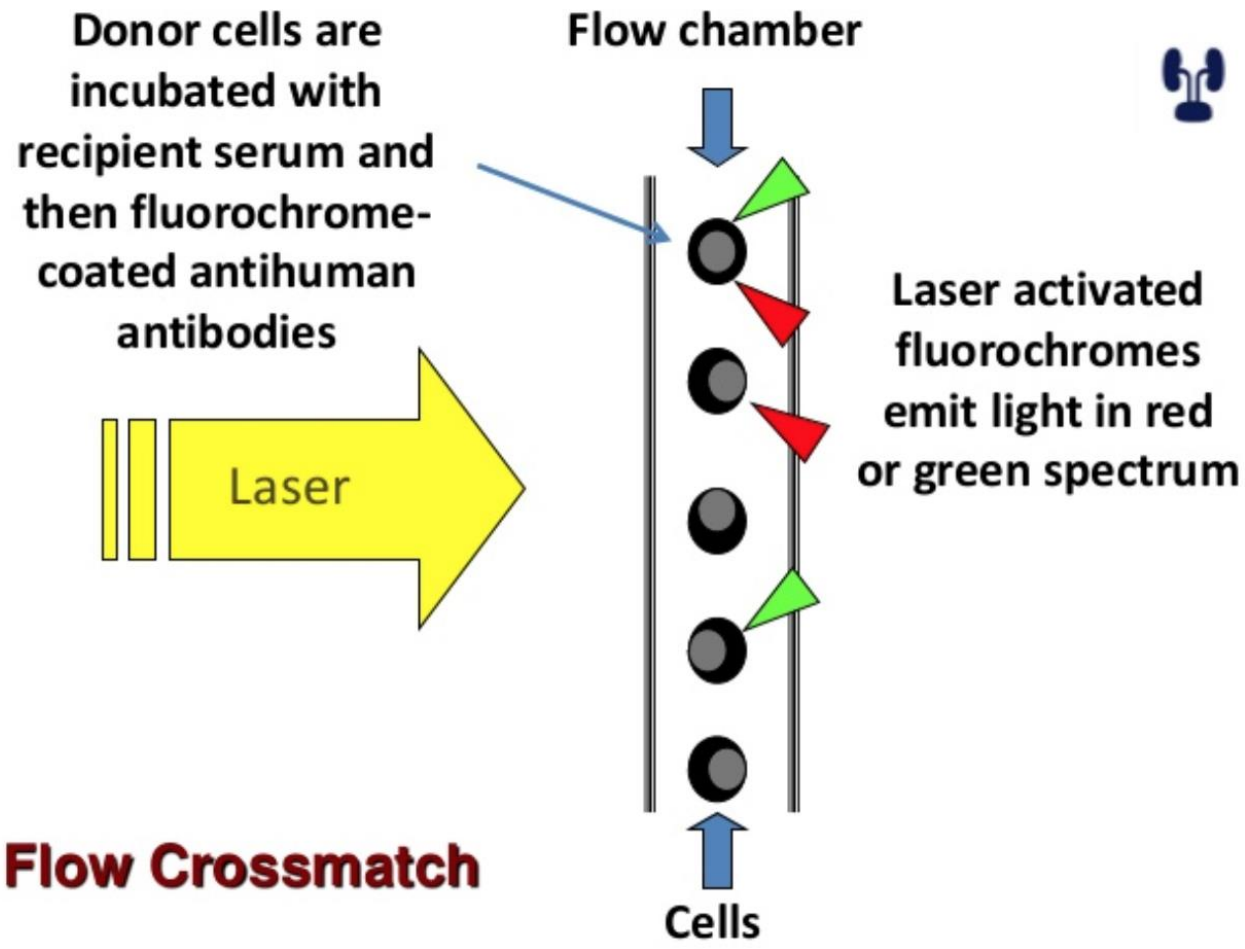
Fluorescein Diacetate +
Ethidium Bromide



Dead cells — Live cells

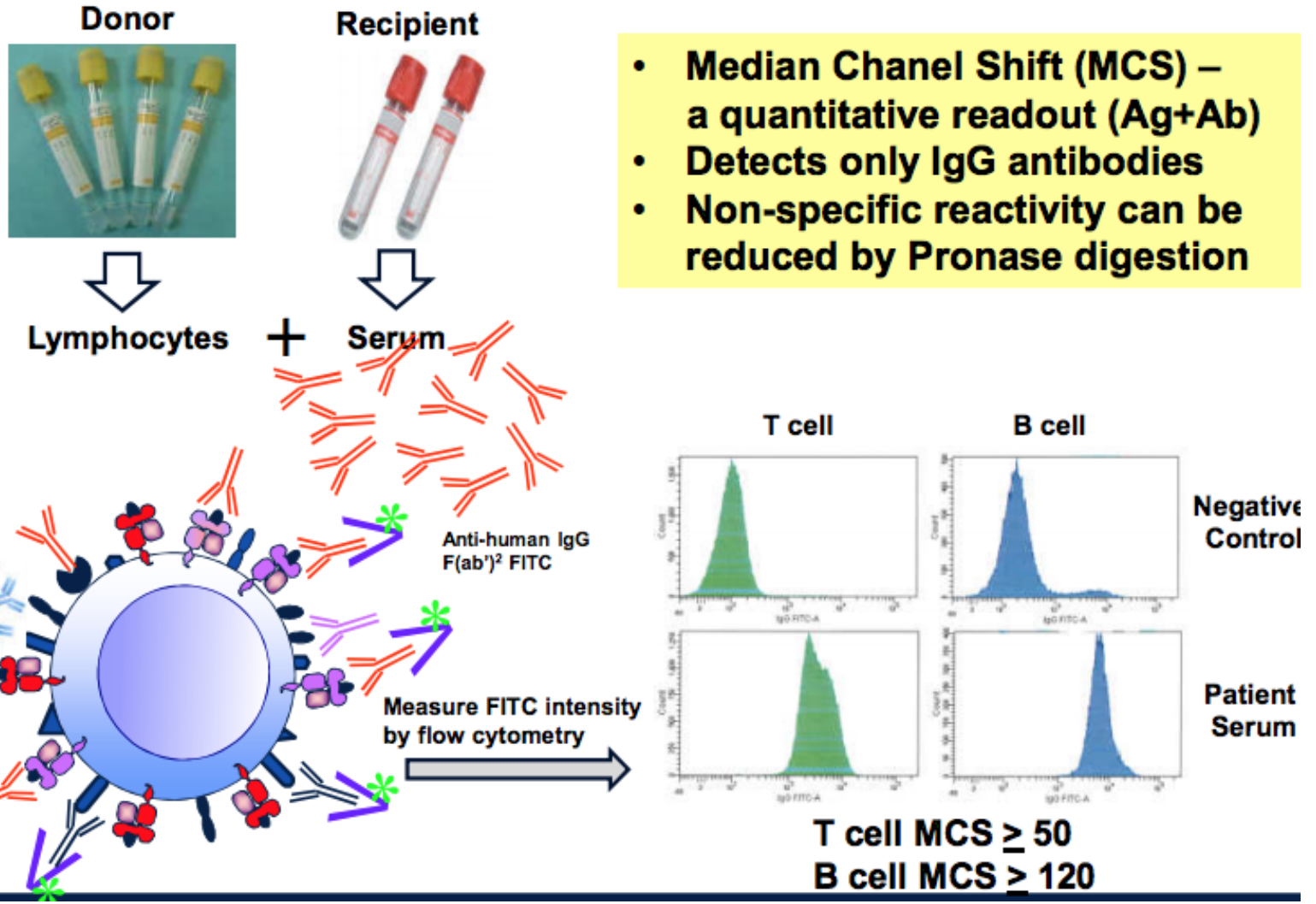
Positive — Negative


Donor
Hanks
Mononuclear cell layer
Ficoll
ACD tube
Serum
Clot tube
Recipient
Anti-human globulin antibodies
30′ 23°C
Wash x 3
Rabbit complement
C′
Eosin/ formalin
60′
23°C
Anti-human Globulin Enhanced Crossmatch
b
Anti-human globulin (AHG) enhanced Crossmatch



Flow Crossmatch

Flow Cytometry Crossmatch



- Median Chanel Shift (MCS) – a quantitative readout (Ag+Ab)
- Detects only IgG antibodies
- Non-specific reactivity can be reduced by Pronase digestion

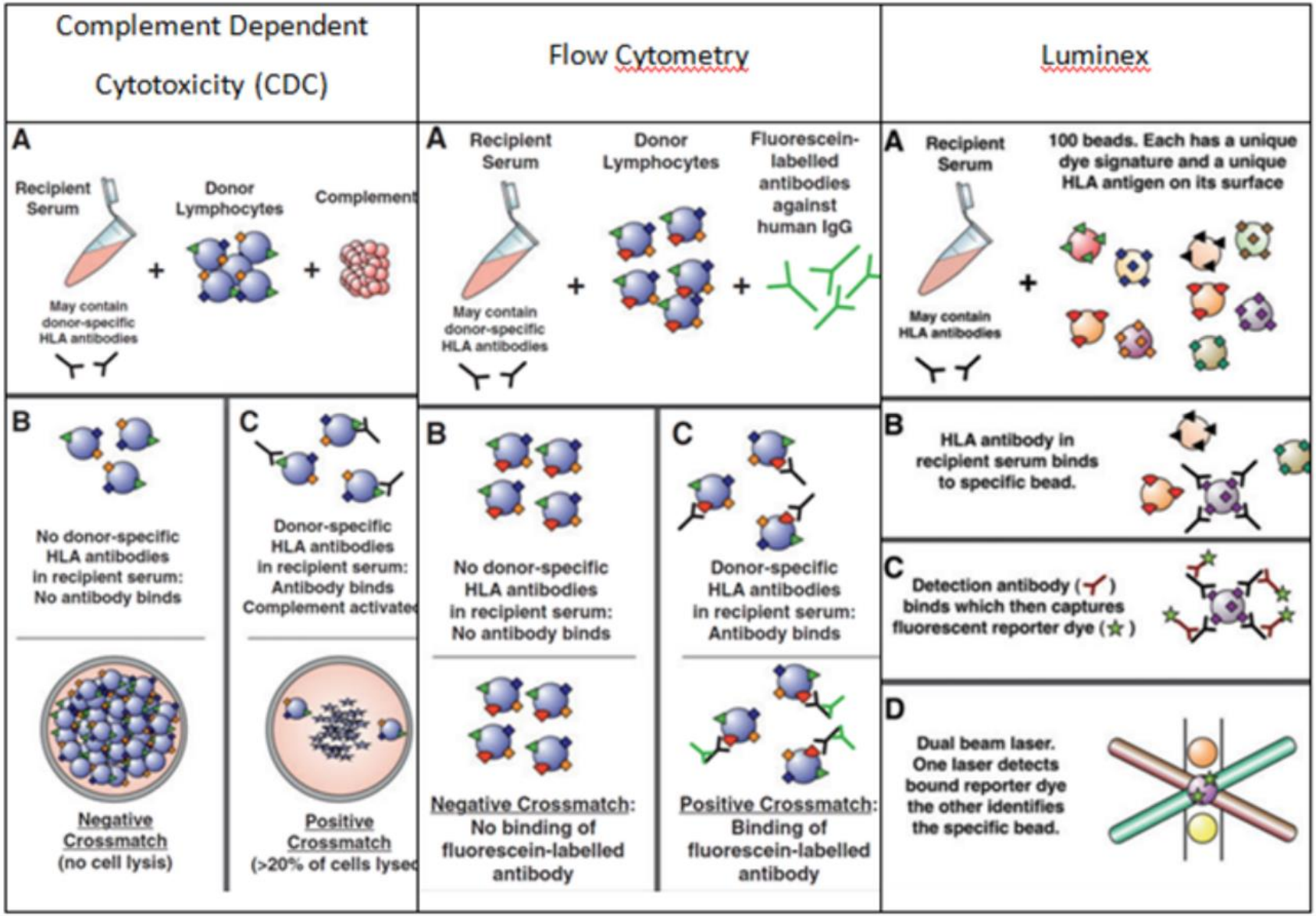
T cell MCS ≥ 50
B cell MCS ≥ 120

Flow Crossmatch Test

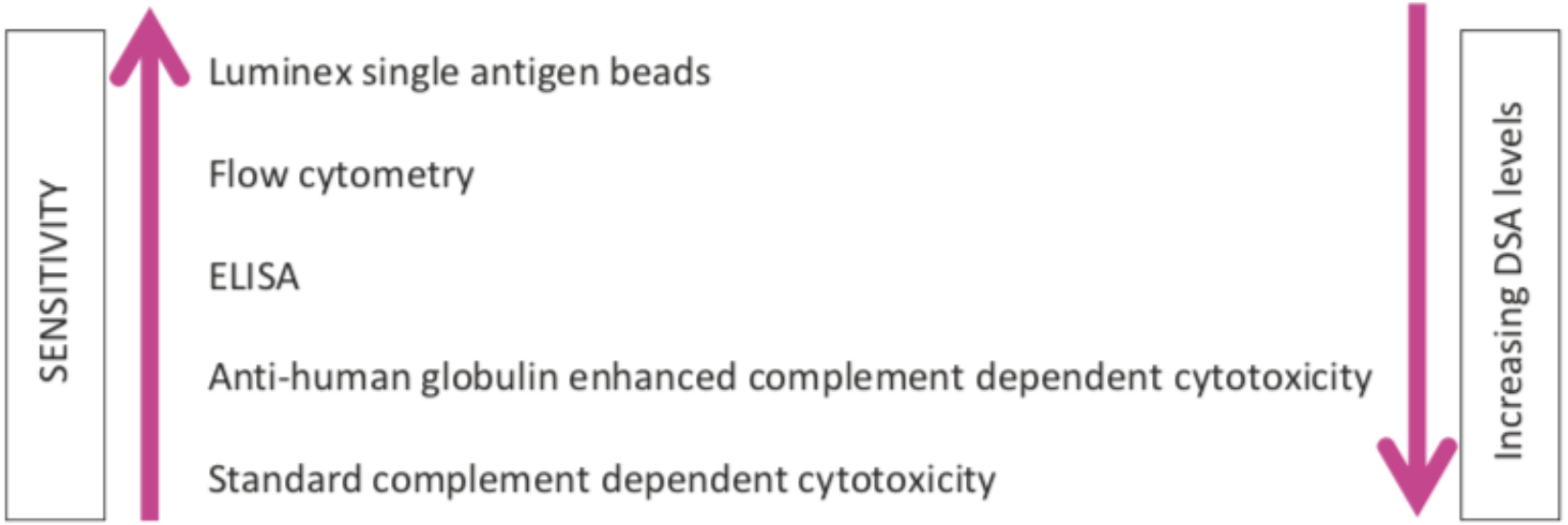
detection of very small amounts of DSAs

Can be done with donor cells that have been damaged and could not be used in a cytotoxic crossmatch which requires live cell.

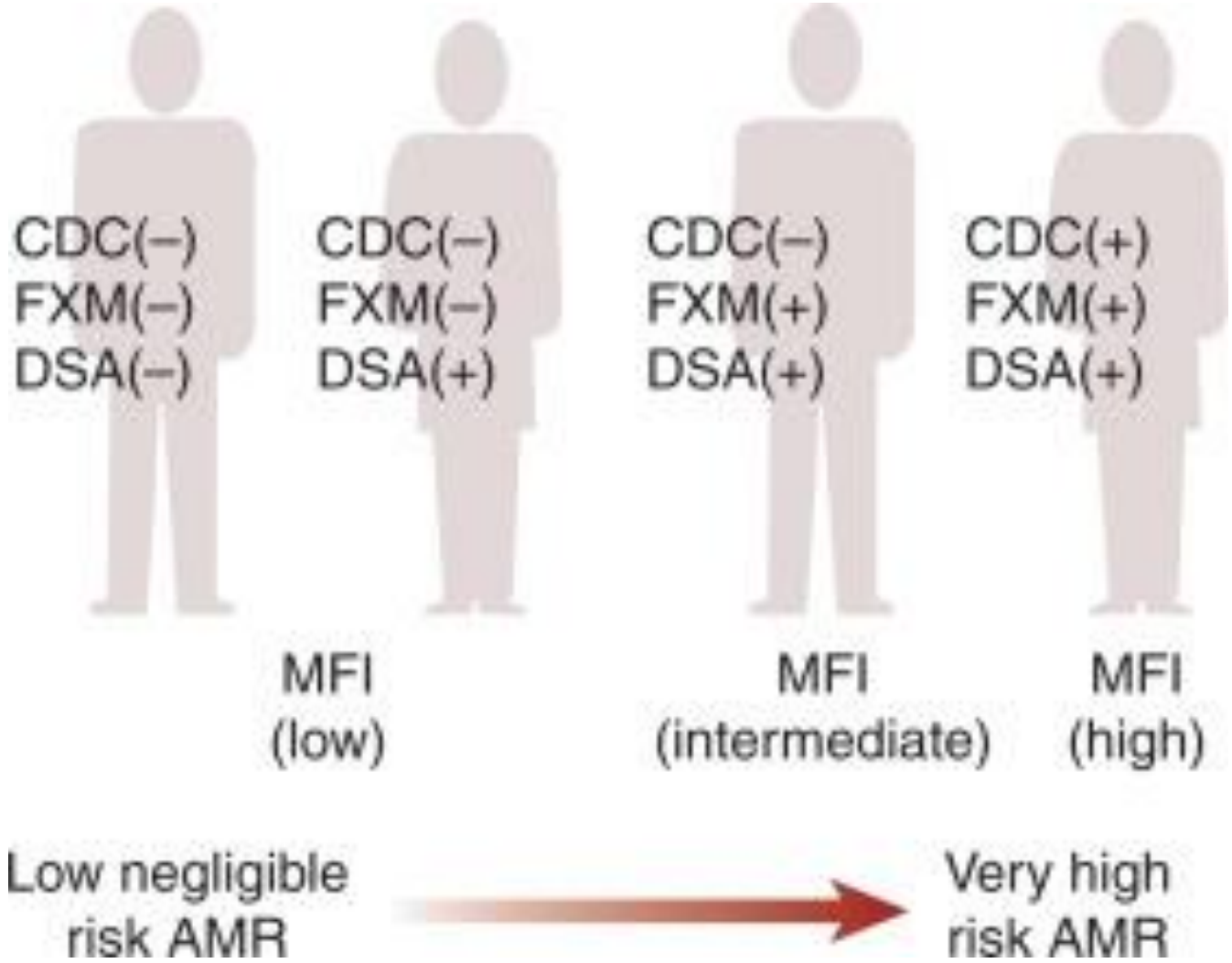
differentiate between T and B cells and between IgM and IgG antibodies



Antibody testing and cross match techniques [31].



This figure illustrates the increasing sensitivity of immuno- logic evaluation tests for (DSA) in the recipient serum. The most sensitive is the single antigen beads, while the least sensitive is the standard complement-dependent cyto- toxicity test



Risk stratification

Comparison between antibody testing methods

	Complement Dependent Cytotoxicity	Solid Phase Assays		
		Elisa	Flow Cytometry	Luminex
Sensitivity and Specificity	Low (may be improved with AHG)	High		
Depends on cell viability	Yes	No		
Quantification of antibodies	No	Yes		
Detects IgM antibodies	Yes (may be negated)	No		
Detects complement fixing antibodies	Yes	No (Only IgG)		
Detects non-HLA antibodies	Yes	No, but may be detected using specific assays e.g., MICA		
Cost	Low	High		
Availability	High	Low		

Various combinations of immunologic tests and possible interpretations

Cytotoxic crossmatch			Flow crossmatch		
Standard	AHG	B cell	T cell	B cell	Interpretation of crossmatch results
+	+	+	+	+	Serum contains significant amount of antibodies to the donor HLA. High risk for hyperacute rejection. Transplantation contraindicated
+	+	0	+	0	Probably not anti-Class I antibodies as B cell crossmatch should also be positive. Perform further antibody testing for antibody specificity
0	0	0	+	+	Probably with a low titer of anti-Class I antibodies and requires further testing. Some risk of hyperacute rejection likely
0	0	+	0	+	Anti-Class II antibody present, or low titer anti-Class I antibody. Check for titer for anti-Class II as this may lead to hyperacute rejection
0	0/+	+	0	0	There is likely an autoantibody, IgM, which is low risk for rejection. Treat with DTT or auto-absorb to remove IgM antibody. May be early sensitizing event prior to class switch from IgM to IgG. If class switch occurs, will be at risk for rejection
0	0	0	0	0	No anti-HLA antibodies present. Low risk for hyperacute rejection

The cytotoxic crossmatch tests include the standard CDC, AHG, and B cell. The flow crossmatch includes the T cell and B cell
AHG anti-human globulin, *0* negative reaction, + positive reaction

Diagnostic

HLA PCR TYPING REPORT

Physician: Dr. Nafar	Test code: H-97-03-30	Reception code: 03-234

Name	Rel.	Class I PCR	Class II PCR
ابراهیم ابهری	Recipient کلیه	A*23 B*49 C*07	DPB1*02 DQB1*03 DRB1*11 DRB3

DNA has been extracted with column based DNA extraction kit. Then HLA class I and class II alleles amplified with sequence specific primer (SSP) method. The number of used primers is as follows:

24 primers mix for identification of HLA-A
48 primers mix for identification of HLA-B
24 primers mix for identification of HLA-C
31 primers mix for identification of HLA-DRB1
13 primers mix for identification of HLA-DQB1

Diagnostics

Flow Panel Reactive Antibody (PRA) screening test

Physician: Dr. Pourreza Gholi	**Sample ID: 02-1576**	**Test date: 97/02/17**
Name: Zahra Azhdari	**Sex/age: F/48**	**Dialysis Status: Positive**
Previous transplant: Positive	**Blood transfusion: Positive**	**Number of pregnancy: 2 Abortion:3**

Method: **Flow Cytometry**

A pooled panel of different microparticles coated with different purified HLA Class I and II antigens were used to detect anti HLA IgG antibodies by flow Cytometry.

Results:

Anti HLA class I antibody:	Anti HLA class II antibody
8%	95%

Sensitized patient due to previous transplant.

Recommendations:

1- **Anti HLA class I and II antibody single antigen assay for determination of donor specific antibodies.**

Flow Panel Reactive Antibody (PRA) single antigen HLA Class I

Physician: Dr. Shakiba	**Sample ID: 11-2211**	**Test date: 96/11/26**
Name: Zahra Azhdari	**Sex/age: F/47**	**Dialysis Status: Positive**
Previous transplant: Positive	**Blood transfusion: Positive**	**Number of pregnancy: 5**

Method: **Flow Cytometry**

A panel of 36 different microparticles coated with purified HLA Class I antigens was used to detect anti HLA class I IgG antibodies by flow Cytometry. Median fluorescence intensity calculated and reported for each antigen separately.

For MFI of each antigen please refer to the second page. **Results:**

Reactive Antigens	
High Risk Antigens (MFI >1000)	
Moderate Risk Antigens (MFI 500-1000)	
Low Titer Antibodies	A*24:02- A*33:01- B*08:01- B*15:01- B*45:01- B*49:01
Donor HLA typing results: (Javad Ghomshe) **A*02-A*24-B*38-B*51-C*12- C*15- DRB1*13-DRB1*14-DRB3- DQB1*05- DQB1*06**	
Recipient HLA typing results:	
Donor HLA specific antibody (DSA): None	
CREG Specific antibody:	

Flow Panel Reactive Antibody (PRA) single antigen HLA Class II

Physician: Dr. Shakiba	**Sample ID: 11-2211**	**Test date: 96/11/26**
Name: Zahra Azhdari	**Sex/age: F/47**	**Dialysis Status: Positive**
Previous transplant: Positive	**Blood transfusion: Positive**	**Number of pregnancy: 5**

Method: **Flow Cytometry**

A panel of 36 different microparticles coated with purified HLA Class II antigens was used to detect anti HLA class II IgG antibodies by flow Cytometry. Median fluorescence intensity calculated and reported for each antigen separately. **Results:**

Reactive Antigens	
High Risk Antigens (MFI >1000)	DRB1*01:01- DRB1*01:02- DRB1*01:03- DRB1*09:01- DRB1*10:01- DRB5*01:01- DQB1*03:01- DQB1*03:02- DQB1*03:03- DQB1*04:02-
Moderate Risk Antigens (MFI 500-1000)	DRB1*04:05- DQB1*05:01- DQB1*06:02
Donor HLA typing results: (Javad Ghomshe) **A*02-A*24-B*38-B*51-C*12- C*15- DRB1*13-DRB1*14-DRB3- DQB1*05- DQB1*06**	
Recipient HLA typing results:	
Donor HLA specific antibody (DSA): DQB1*05:01- DQB1*06:02	

Interpretation guide:

MFI	**Risk estimation**
>1000	High risk
500-1000	Moderate risk
<500	Low risk*

Anti HLA Class I antigens MFI

Group	Panel Typing								Results (MFI)	Antigen acceptance
	A		B		Bw		Cw			
1	A*01:01	X	X	X	X	X	X	X	0	Low Risk Antigen
	A*02:01	X	X	X	X	X	X	X	60	Low Risk Antigen
	A*03:01	X	X	X	X	X	X	X	0	Low Risk Antigen
	X	X	B*49:01	X	4	X	X	X	300	Low Risk Antigen
	A*25:01	X	X	X	X	X	X	X	0	Low Risk Antigen
	A*29:02	X	X	X	X	X	X	X	0	Low Risk Antigen
	A*30:01	X	X	X	X	X	X	X	0	Low Risk Antigen
	X	X	X	X	X	X	X	X	-	-
	A*26:01	X	X	X	X	X	X	X	0	Low Risk Antigen
2	A*68:01	X	X	X	X	X	X	X	0	Low Risk Antigen
	A*11:01	X	X	X	X	X	X	X	0	Low Risk Antigen
	A*34:01	X	X	X	X	X	X	X	0	Low Risk Antigen
	A*24:02	X	X	X	X	X	X	X	100	Low Risk Antigen
	A*32:01	X	X	X	X	X	X	X	0	Low Risk Antigen
	A*33:01	X	X	X	X	X	X	X	300	Low Risk Antigen
	A*31:01	X	X	X	X	X	X	X	0	Low Risk Antigen
	X	X	X	X	X	X	X	X	-	-
	A*23:01	X	X	X	X	X	X	X	0	Low Risk Antigen
3	X	X	B*51:01	X	4	X	X	X	0	Low Risk Antigen
	X	X	B*13:01	X	4	X	X	X	0	Low Risk Antigen
	X	X	B*18:01	X	6	X	X	X	0	Low Risk Antigen
	X	X	B*35:01	X	6	X	X	X	200	Low Risk Antigen
	X	X	B*15:01	X	6	X	X	X	300	Low Risk Antigen
	X	X	B*45:01	X	6	X	X	X	0	Low Risk Antigen
	X	X	B:40:01	X	6	X	X	X	-	-
	X	X	X	X	X	X	X	X	0	Low Risk Antigen
	X	X	B*44:02	X	4	X	X	X	0	Low Risk Antigen
4	X	X	B*38:01	X	4	X	X	X	0	Low Risk Antigen
	X	X	B*57:01	X	4	X	X	X	0	Low Risk Antigen
	X	X	B*07:02	X	6	X	X	X	0	Low Risk Antigen
	X	X	B*52:01	X	4	X	X	X	100	Low Risk Antigen
	X	X	B*27:05	X	4	X	X	X	200	Low Risk Antigen
	X	X	B*08:01	X	6	X	X	X	0	Low Risk Antigen
	X	X	B*14:02	X	6	X	X	X	-	-
	X	X	X	X	X	X	X	X	0	Low Risk Antigen
	X	X	B*55:01	X	6	X	X	X		

Interpretation guide:

MFI	Risk estimation
>1000	High risk
500-1000	Moderate risk
<500	Low risk*

Flow Panel Reactive Antibody (PRA) single antigen HLA Class I

Physician: Dr. Shakiba	**Sample ID: 11-2211**	**Test date: 96/11/26**
Name: Zahra Azhdari	**Sex/age: F/47**	**Dialysis Status: Positive**
Previous transplant: Positive	**Blood transfusion: Positive**	**Number of pregnancy: 5**

Method: **Flow Cytometry**

A panel of 36 different microparticles coated with purified HLA Class I antigens was used to detect anti HLA class I IgG antibodies by flow Cytometry. Median fluorescence intensity calculated and reported for each antigen separately.

For MFI of each antigen please refer to the second page. **Results:**

Reactive Antigens	
High Risk Antigens (MFI >1000)	
Moderate Risk Antigens (MFI 500-1000)	
Low Titer Antibodies	A*24:02- A*33:01- B*08:01- B*15:01- B*45:01- B*49:01
Donor HLA typing results: (Javad Ghomshe) **A*02-A*24-B*38-B*51-C*12- C*15- DRB1*13-DRB1*14-DRB3- DQB1*05- DQB1*06**	
Recipient HLA typing results:	
Donor HLA specific antibody (DSA): Non	
CREG Specific antibody:	

Flow Panel Reactive Antibody (PRA) single antigen HLA Class II

Physician: Dr. Shakiba	**Sample ID: 11-2211**	**Test date: 96/11/26**
Name: Zahra Azhdari	**Sex/age: F/47**	**Dialysis Status: Positive**
Previous transplant: Positive	**Blood transfusion: Positive**	**Number of pregnancy: 5**

Method: **Flow Cytometry**

A panel of 36 different microparticles coated with purified HLA Class II antigens was used to detect anti HLA class II IgG antibodies by flow Cytometry. Median fluorescence intensity calculated and reported for each antigen separately. **Results:**

Reactive Antigens	
High Risk Antigens (MFI >1000)	DRB1*01:01- DRB1*01:02- DRB1*01:03- DQB1*03:01- DQB1*03:02- DQB1*03:03-
Moderate Risk Antigens (MFI 500-1000)	DRB1*04:05- DQB1*05:01- DQB1*06:02
Donor HLA typing results: (Javad Ghomshe) **A*02-A*24-B*38-B*51-C*12- C*15- DRB1*13-DRB1*14-DRB3- DQB1*05- DQB1*06**	
Recipient HLA typing results:	

Class I PCR	**Class II PCR**
A*02	**DQB1*02- DQB1*03**
B*15-B*41	**DRB1*04- DRB1*07**
C*04- C*17	**DRB4**

Physician: Dr. Shakiba	**Sample ID: 11-133**	**Test date: 96/11/02**
Recipient Name: Zahra Azhdari	**Donor name: Seyed ghasem minaee**	**Relationship: Unrelated**
Recipient gender/age: F/46	**Donor gender/age: M/28**	**Recipient blood group: O+** **Donor blood group: O+**
Previous transplant: Positive	**Blood transfusion: Positive**	**Number of pregnancy: -**

Method: **Flow Cytometry**

Donor cells were incubated with recipient serum. Donor B and T cells were separated using specific fluorescent monoclonal antibodies. The presence of recipient IgG antibodies on donors B and T cells evaluated using monoclonal anti- IgG Fc antibody. Shift in median channel fluorescence compared to negative control calculated and reported.

Interpretation guide:

T-cells channel shift:
≤ 30 channels = NEGATIVE
≥ 30 but ≤ 45 channels = PROBABLE NEGATIVE
≥ 45 channels = LIKELY POSITIVE

B-cells channel shift:
≤ 60 channels = NEGATIVE
≥ 60 but ≤ 120 channels = PROBABLE NEGATIVE
≥ 120 channels = LIKELY POSITIVE

Results:

T cell Median Channel Shift: 20 channels

B cell Median Channel Shift: 145 channels

Negative T cell cross match. Positive B cell cross match.

CPRA

A higher cPRA reflects increased difficulty in finding a suitable donor.

- Calculated PRA (CPRA) is the percentage of donors expected to have HLA antigens listed as unacceptable for a candidate on the waiting list
- CPRA is calculated for kidney, kidney-pancreas and pancreas candidates on the waiting list
- If no unacceptable antigens are entered, CPRA value defaults to 0

Check all A unacceptable antigens:

☐ 1	☐ 2	☐ 0201	☐ 0202	☐ 0203	☐ 0205
☐ 0206	☐ 3	☐ 9	☐ 10	☐ 11	☐ 1101
☐ 1102	☐ 19	☐ 23	☐ 24	☑ 2402	☐ 2403
☐ 25	☐ 26	☐ 28	☐ 29	☐ 2901	☐ 2902
☐ 30	☐ 3001	☐ 3002	☐ 31	☐ 32	☐ 33
☑ 3301	☐ 3303	☐ 34	☐ 3401	☐ 3402	☐ 36
☐ 43	☐ 66	☐ 6601	☐ 6602	☐ 68	☐ 6801
☐ 6802	☐ 69	☐ 74	☐ 80		

Check all B unacceptable antigens:

☐ 5	☐ 7	☐ 0702	☐ 8	☑ 0801	☐ 0802
☐ 0803	☐ 0804	☐ 12	☐ 13	☐ 1301	☐ 1302
☐ 14	☐ 1401	☐ 1402	☐ 15	☑ 1501	☐ 1502
☐ 1503	☐ 1510	☐ 1511	☐ 1512	☐ 1513	☐ 1516
☐ 1517	☐ 16	☐ 17	☐ 18	☐ 21	☐ 22
☐ 27	☐ 2705	☐ 2708	☐ 35	☐ 37	☐ 38
☐ 39	☐ 3901	☐ 3902	☐ 3905	☐ 3913	☐ 40
☐ 4001	☐ 4002	☐ 4005	☐ 4006	☐ 41	☐ 42
☐ 44	☐ 4402	☐ 4403	☐ 4415	☑ 45	☐ 46
☐ 47	☐ 48	☑ 49	☐ 50	☐ 51	☐ 5101
☐ 5102	☐ 52	☐ 53	☐ 54	☐ 55	☐ 56
☐ 57	☐ 5701	☐ 5703	☐ 58	☐ 59	☐ 60
☐ 61	☐ 62	☐ 63	☐ 64	☐ 65	☐ 67
☐ 70	☐ 71	☐ 72	☐ 73	☐ 75	☐ 76
☐ 77	☐ 78	☐ 81	☐ 82		

CPRA

Check all BW unacceptable antigen:

☐ 4 ☐ 6

Check all C unacceptable antigens:

☐ 01	☐ 02	☐ 03	☐ 04	☐ 05	☐ 06
☐ 07	☐ 0701	☐ 0702	☐ 08	☐ 09	☐ 10
☐ 12	☐ 14	☐ 15	☐ 16	☐ 17	☐ 18

Check all DR unacceptab

☐ 1	☑ 0101
☐ 0301	☐ 0302
☐ 0404	☑ 0405
☐ 8	☐ 9
☐ 1101	☐ 1104
☐ 1301	☐ 1303
☐ 1404	☐ 1454
☐ 16	☐ 1601

Check all DR51 unaccept

☑ 51

Check all DR52 unaccept

☐ 52

Check all DR53 unaccept

☐ 53

ℹ The actual CPRA provided to a candidate is calculated by UNet based solely on the unacceptable antigens that are entered by the transplant center for that candidate. The value produced by the CPRA Calculator on this Web site is for your informational use only.

A:	2402, 3301
B:	0801, 1501, 45, 49
BW:	
C:	
DR:	0101, 0102, 103, 0405, 0901, 10
DR51:	51
DR52:	
DR53:	
DQB1:	0301, 0302, 0303, 0402, 0501, 0602

Back

CPRA value used for allocation per OPTN policy: 70

Detailed CPRA value: 70.47 %

Check all DQB1 unacceptable antigens:

☐ 1	☐ 2	☐ 0201	☐ 0202	☐ 3	☑ 0301
☑ 0302	☑ 0303	☐ 0319	☐ 4	☐ 0401	☑ 0402
☐ 5	☑ 0501	☐ 0502	☐ 6	☐ 0601	☑ 0602
☐ 0603	☐ 0604	☐ 0609	☐ 7	☐ 8	☐ 9

Table 4. Estimated number of match runs needed to have a 95% probability of finding an acceptable donor based on candidate cPRA

cPRA, %	Theoretical number of match runs to have a 95% chance of finding an acceptable donor
10	2
20	2
30	3
40	4
50	5
60	6
70	9
80	14
85	19
90	29
95	59
99	300
99.5	600
99.9	3000
99.99	30,000
99.999	300,000

cPRA, calculated panel-reactive antibody.

Probability of finding an acceptable match $= 1 - (\text{cPRA})^n$, where n = number of potential donors (23).

European Renal Best Practice Guideline on kidney donor and recipient evaluation and perioperative care

Chapter 2. Immunologic work-up of kidney donors and recipients

2.1. How should HLA typing be performed in renal transplant candidates and donors?

2.1.1. We suggest that at least one typing is performed by molecular human leucocyte antigen (HLA) typing of patients and donors to avoid mistakes in the classification of the HLA antigens. **(2D)**

2.1.4. For highly sensitized patients with allele-specific antibodies we suggest consideration of high resolution molecular typing in both recipients and donors. **(2D)**

European Renal Best Practice Guideline on kidney donor and recipient evaluation and perioperative care

2.2. In a renal transplant recipient, how should HLA matching be used to optimize outcome?

2.2.1. We suggest matching for human leucocyte antigen (HLA)-A, -B and -DR whenever possible. (**2C**)

2.2.4. We suggest giving more weight to HLA-DR matching than to HLA A and B matching. (**2C**)

2.2.5. We recommend giving more weight to HLA matching in younger patients, in order to avoid broad HLA sensitization which might impair re-transplantation. (**Ungraded Statement**)

ndt
Nephrology Dialysis Transplantation

European Renal Best Practice Guideline on kidney donor and recipient evaluation and perioperative care

2.3. In renal transplant candidates, what HLA antigens and non-HLA antigens should be defined in addition to HLA A, B and DR?

2.3.1. We recommend performing human leucocyte antigen (HLA) DQ, HLA DP and HLA C typing of the donor only when the intended recipient has HLA antibodies against those antigens. **(1D)**

2.3.1. We do not recommend routine typing for major histocompatibility complex class I related chain-A (MICA) and other non-HLA antigens in either the recipient or donor.

2.6. In renal transplant candidates, what technique of cross-match should be used to optimize outcomes?

We recommend a complement-dependent cytotoxic (CDC) cross-match be performed in HLA sensitized patients to prevent hyperacute rejection. (**1B**)

We suggest that in HLA antibody negative patients with negative regular quarterly screening samples a cross-match can be omitted, unless a potential HLA sensitizing event has occurred since last screening. **(2B)**

We do not recommend to perform Luminex cross match, or endothelial cell cross match because their additional value needs further evaluation. (**1D**)

We recommend a positive CDC cross-match should only be accepted as truly positive when donor specific antibodies are known to be present. (**1B**)

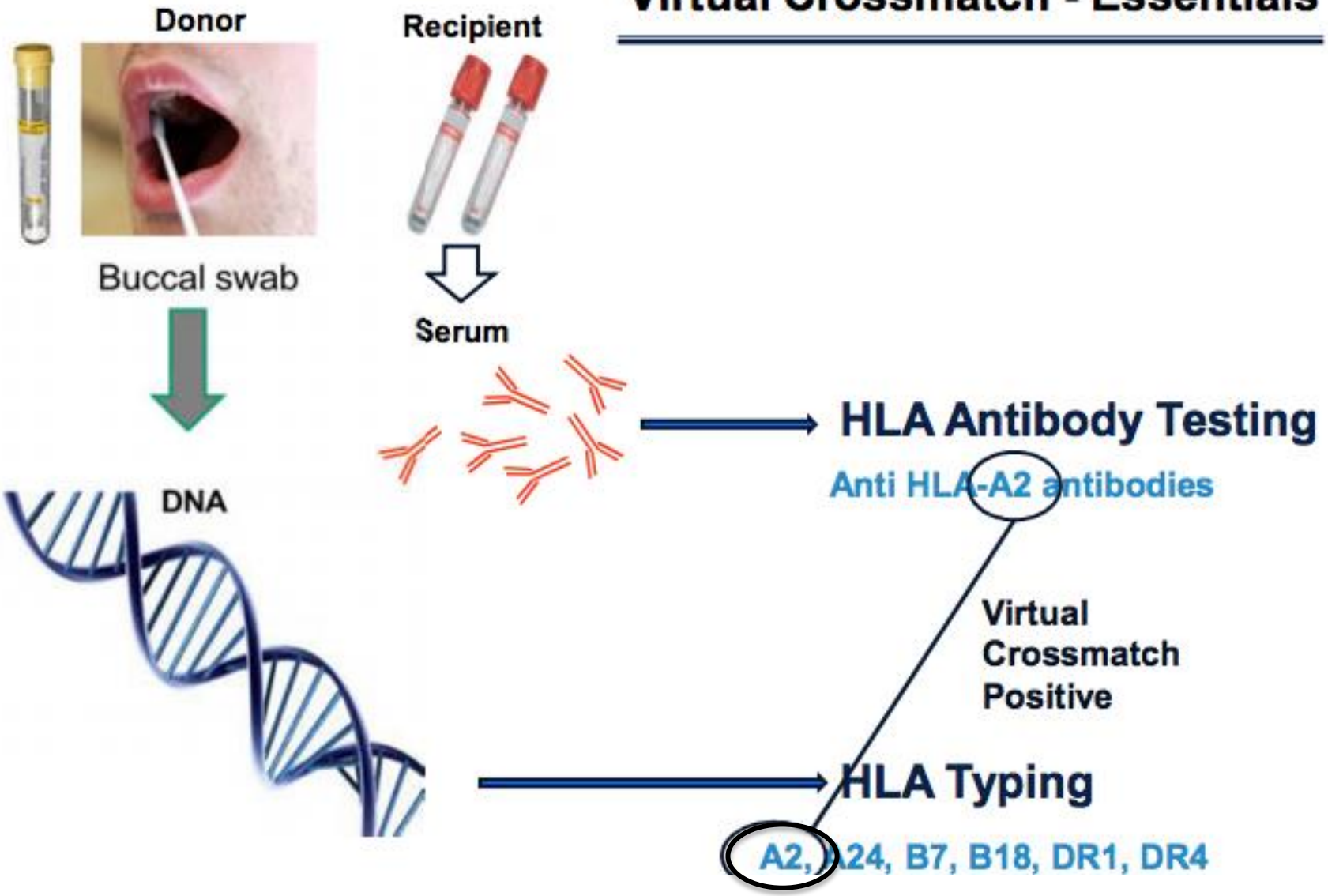
19.2: Perform HLA antibody testing at transplant evaluation, at regular intervals prior to transplantation and a minimum of 2 weeks after a sensitizing event or a clinical event that can impact PRA. *(Not Graded)*

19.3: We recommend that HLA antibody testing be performed using solid phase assays. *(1B)*

19.4: We recommend HLA typing of KTCs at evaluation using molecular methods, optimally at all loci. *(1D)*

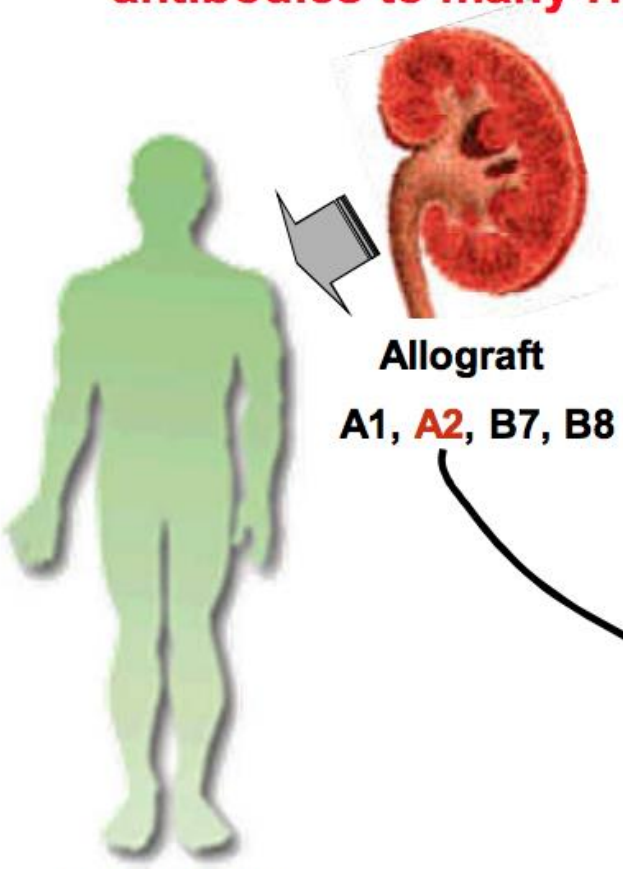
19.5: We suggest not routinely testing KTCs for non-HLA antibodies. *(2C)*

Virtual Crossmatch - Essentials



No antibodies to self-HLA are made.

Individuals alloimmunized by a specific HLA type can make antibodies to many HLA types.



Allograft

A1, A2, B7, B8

Recipient

A1, A1, B7, B8

Anti-A2

A28

A68

A23

A69

B57

A24

B58

Cross-REactive groups (CREG)

Cross-REactive Groups (CREG)

CREG	HLA Specificities	CPRA value
A1	A1,A3,A11,A29,A30,A31,A36,A80	65%
A2	A2,A23,A24,A68,A69,B57,B58	75%
A10	A25,A26,A32,A33,A34,A43,A66,A74	22%
Bw4	A23,A24,A25,A32,Bw4	74%
B5	B18,B35,B46,B49,B50,B51,B52,B53,B62,B63,B71,B72,B73,B75,B76,B77,B78	56%
Bw6	Bw6	85%
B7	B7,B8,B13,B27,B41,B42,B47,B48,B54,B55,B56,B59,B60,B61,B67,B81,B82	59%
B8	B8,B18,B38,B39,B59,B64,B65,B67	36%
B12	B13,B37,B41,B44,B45,B47,B49,B50,B60,B61	48%
C1	Cw1,Cw7,Cw8,Cw9,Cw10,Cw12,Cw14,Cw16,B46,B73	77%
C2	Cw2,Cw4,Cw5,Cw6,Cw15,Cw17,Cw18	66%
DR1	DR1,DR10,DR103	21%
DR51	DR51,DR15,DR16	29%
DR52	DR52,DR11,DR12,DR13,DR14,DR17,DR18	62%
DR53	DR53,DR4,DR7,DR9	50%
DQ1	DQ5,DQ6	64%
DQ2	DQ2	37%
DQ3	DQ7,DQ8,DQ9	56%
DQ4	DQ4	10%
DP1c	DP2,DP3,DP4,DP6,DP9,DP10,DP11,DP14,DP17,DP18.DP20,DP28	----
DP2c	DP1,DP5,DP13,DP15,DP19,DP23	----

frontiers in Immunology

PERSPECTIVE
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Check for updates

HLA-Epitope Matching or Eplet Risk Stratification: The Devil Is in the Details

"Epitope matching" became a trending topic in organ transplantation.

discussions on clinical implementation and utilization of this approach in organ allocation algorithms are currently on-going.

More recently, the term "eplet mismatch load" was introduced in publications

the field of "epitope matching" shows enormous promise, it

is still in its infancy

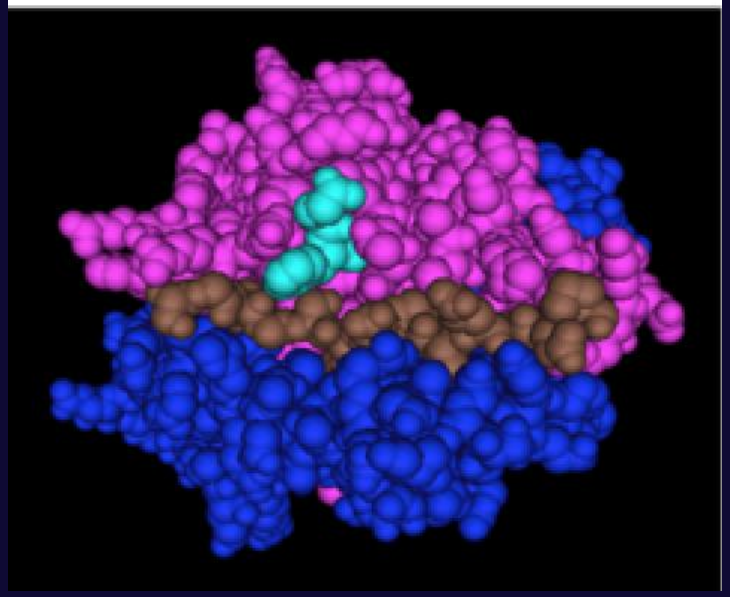
HLA Antibodies in Transplantation

- HLA antibodies cause allograft rejection and transplant failure
- HLA antibodies recognize epitopes

Therefore

HLA epitopes are important in transplantation

Eplet



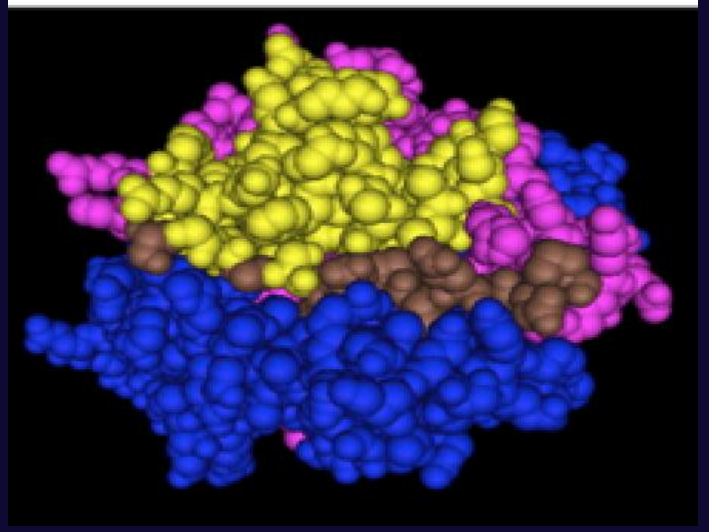
Eplets

Essential components of HLA epitopes recognized by antibody

Amino acid configurations within a 3 Angstrom radius of surface-exposed polymorphic residues

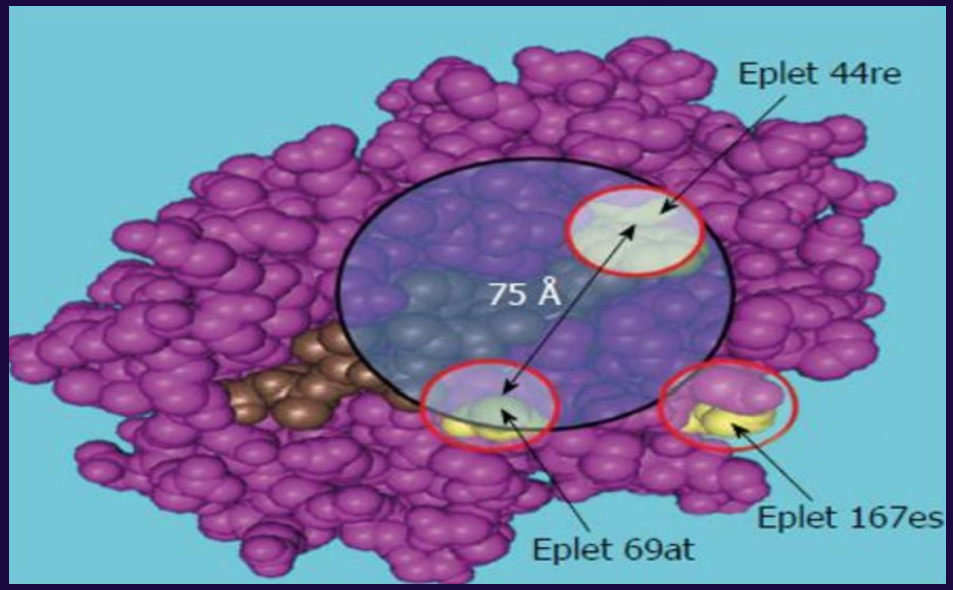
Parts of “structural” HLA epitopes that contact the CDRs of antibody

Epitope



HLA Epitopes

- HLAMatchmaker considers eplets as equivalents to functional epitopes
- Amino acid residues within a 15 Ångstrom radius of eplets can contribute structural HLA epitopes



- HLAMatchmaker Computerized program Estimate the eplet mismatches between R/D HLA
- 0-2 eplet MM VS > 20 MM= HR for rejection of 2.16
  - Nguyen,Transplant direct,2016

Journal of Immunology Research

Indexed in Science

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Journal of Immunology Research
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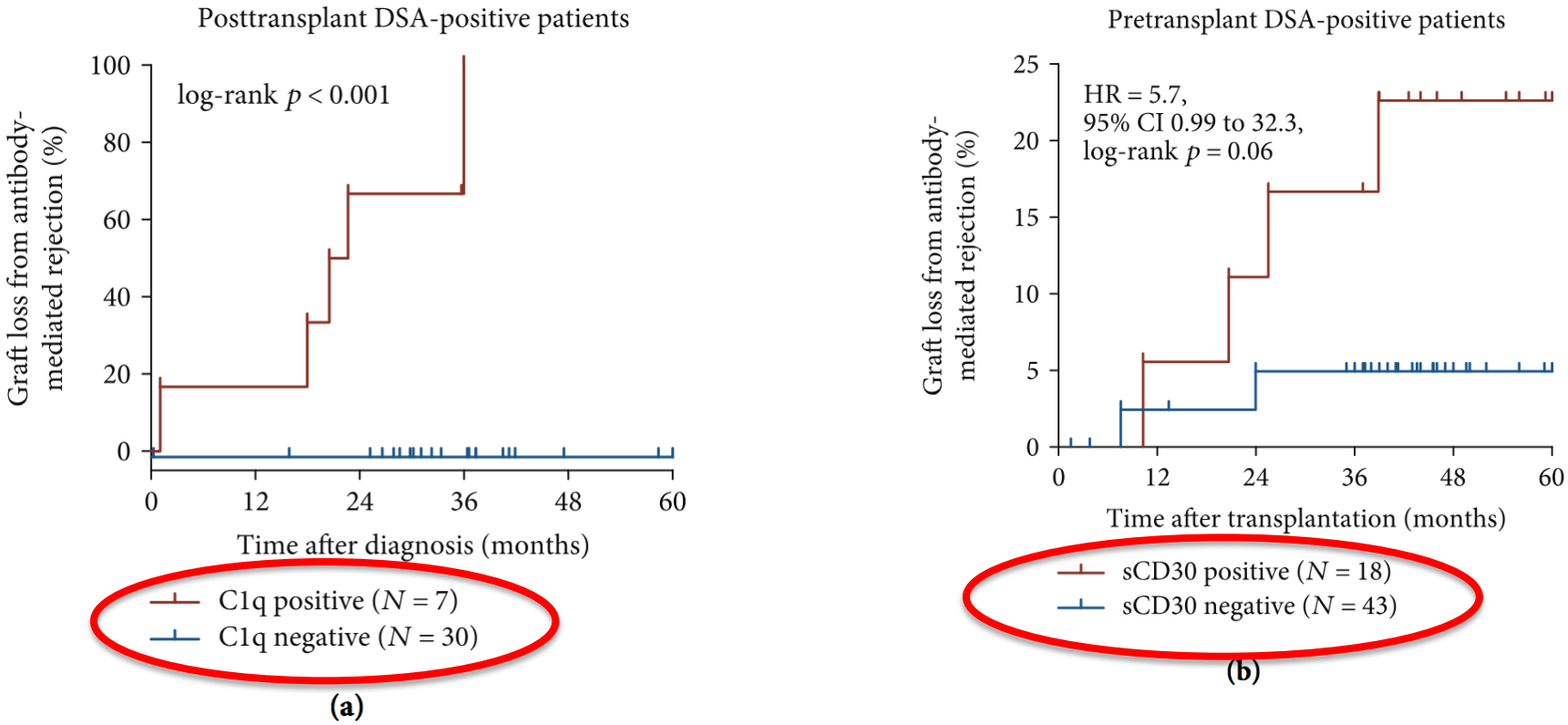
https://doi.org/10.1155/2017/5619402

Review Article

Clinical Relevance of HLA Antibodies in Kidney Transplantation: Recent Data from the Heidelberg Transplant Center and the Collaborative Transplant Study



Graft loss from antibody-mediated rejection in high-risk sensitized patients with and without C1q-binding posttransplant donor-specific HLA antibodies (DSA) (a) and in patients who in addition to pretransplant DSA positivity had also increased levels of the immune activation marker sCD30 before transplantation (b)

Transplant Proc. 2016 Apr;48(3):756-60. doi: 10.1016/j.transproceed.2015.12.116.

Role of Pretransplant Complement-fixing Donor-specific Antibodies Identified by C1q Assay in Kidney Transplantation.

Thammanichanond D[1], Wiwattanathum P[2], Mongkolsuk T[3], Kantachuvesiri S[2], Worawichawong S[4], Vallipakorn SA[5], Kitpoka P[3].

Author information

Abstract

BACKGROUND: Kidney transplant recipients who have pretransplant donor-specific human leukocyte antigen (HLA) antibodies have greater risk for developing allograft rejection and allograft loss. However, there is a varied effect of graft injury among patients with pretransplantation donor-specific antibodies (DSA). The difference of complement activating ability may be the reason why some DSA are detrimental to kidney allograft. This study aimed to investigate the association between pretransplantation C1q-binding DSA and clinical outcomes.

METHODS: This retrospective study included 48 pretransplant sera from kidney transplant recipients who had pretransplant DSA with negative complement-dependent cytotoxic (CDC) crossmatches. The IgG DSA testing and C1q testing were performed on a Luminex platform with single antigen bead assay. The clinical outcomes between C1q-positive and C1q-negative groups were compared.

RESULTS: C1q-positive DSA were detected in 12 out of 48 patients (25%). The incidences of antibody-mediated rejection (AMR) were higher among patients with C1q-positive DSA than patients with C1q-negative DSA (66.7% vs 41.7%). Nevertheless, there were no statistically significant associations between C1q-DSA and AMR (odds ratio 2.8, 95% CI 0.68-11.6, P = .13) and between C1q-DSA and graft loss (odds ratio 0.52, 95% CI 0.09-2.89, P = .44). The C1q-positive DSA group had significantly higher IgG DSA MFI than the C1q-negative DSA group (P < .001).

CONCLUSION: C1q-binding ability of DSA in pretransplant sera of kidney recipients was not associated with antibody-mediated rejection and graft loss post-transplantation. In contrast with the clinical relevance of C1q testing in the post-transplantation setting, C1q testing in pretransplant sera has limited use for immunological risk assessment.


Thank you