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The Fundamental Concepts of Virtual Cross-matching in Kidney Transplantation

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TEHRAN 2023

Introduction

- ✓Human leukocyte antigens (HLAs) are the primary determinants of alloimmunity.

- ✓A crossmatch test is a test that determines the immunologic risk of a recipient with a potential donor by ensuring that there are no transplant-relevant circulating antibodies in the recipient against donor antigens.

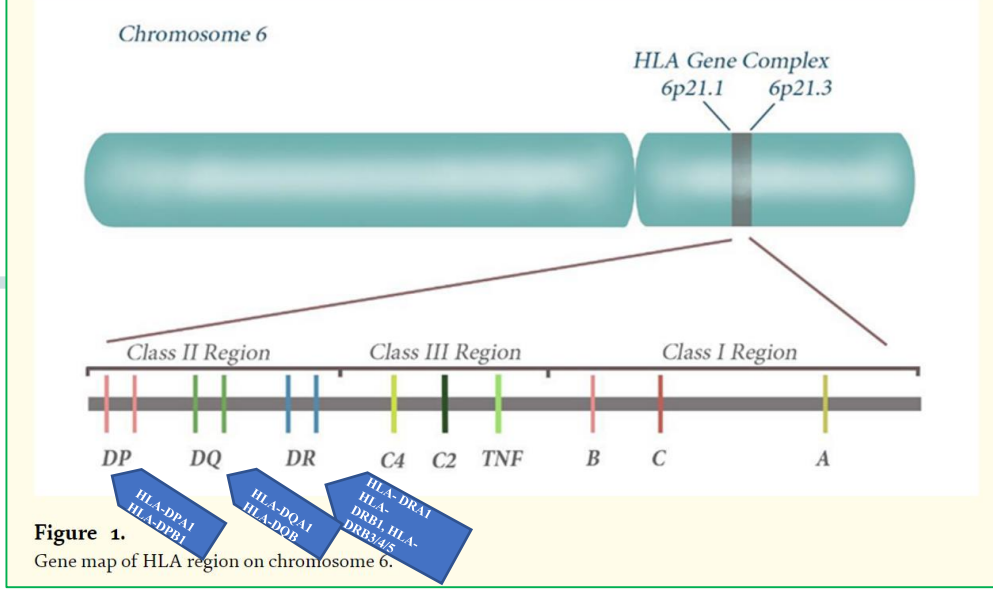


Figure 1.
Gene map of HLA region on chromosome 6.

https://www.intechopen.com/chapters/50878

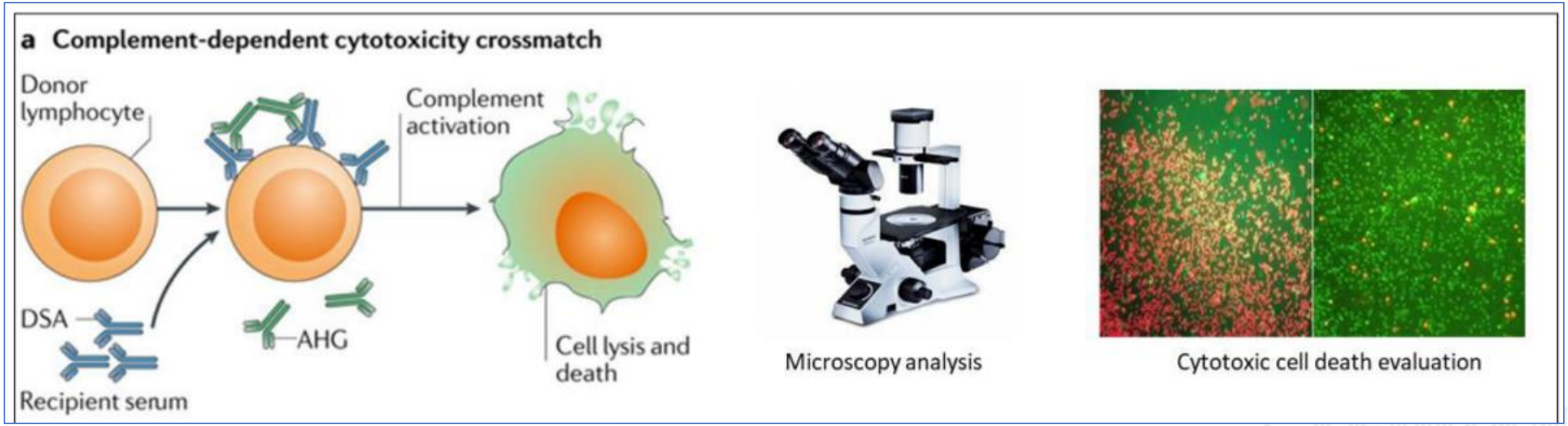
Physical Cross-match tests

1. Complement-dependent cytotoxicity crossmatch (CDCXM)
   Cell-based cytotoxicity assays (live cells)

2. Flow cytometry crossmatch (FCXM),
   Solid phase assays

Virtual Cross-match

Virtual Crossmatch is the process of assessing the results of solid phase and cell-based HLA antibody identification assays to predict, or correlate to, the results of a physical crossmatch



Montgomery, Nature Rer Neph, 2018

Major limitations:

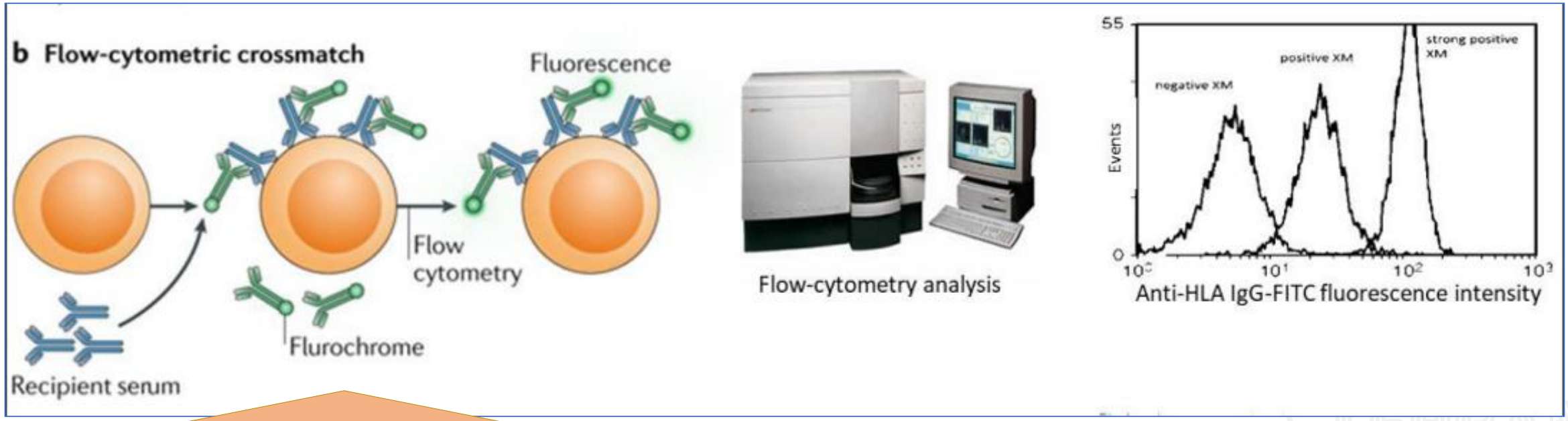
- The difficulty in defining the specificity of the anti-HLA antibody
- Broadly reactive antibodies against non-HLA antigens can make analysis impossible.
- False-positive results could arise from the presence of non-HLA antibodies and IgM HLA and non-HLA antibodies.
- False-negative results can occur with low titer antibody.
- Panels should contain cells from volunteers that are representative of the donor pool but often include only the most common phenotypes

UpToDate, 2023, Kidney transplantation in adults: Overview of HLA sensitization and crossmatch testing
https://www-uptodate-com.proxybibl.vgregion.se/contents/kidney-transplantation-in-adults-overview-of-hla-sensitization-and-crossmatch-testing?search=virtual%20cross%20match&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H1256329285

- ✓Most HLA laboratories worldwide have moved to using newer technologies for antibody screening.

- ✓Since 2009, the United Network for Organ Sharing (UNOS) has mandated the use of solid-phase assays to identify HLA antibodies in potential transplant recipients in the United States.

UpToDate, 2023, Kidney transplantation in adults: Overview of HLA sensitization and crossmatch testing
https://www-uptodate-com.proxybibl.vgregion.se/contents/kidney-transplantation-in-adults-overview-of-hla-sensitization-and-crossmatch-testing?search=virtual%20cross%20match&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H1256329285



Fluorescein- labeled Abs against human IgG

Montgomery, Nature Rer Neph, 2018

Flow PRA

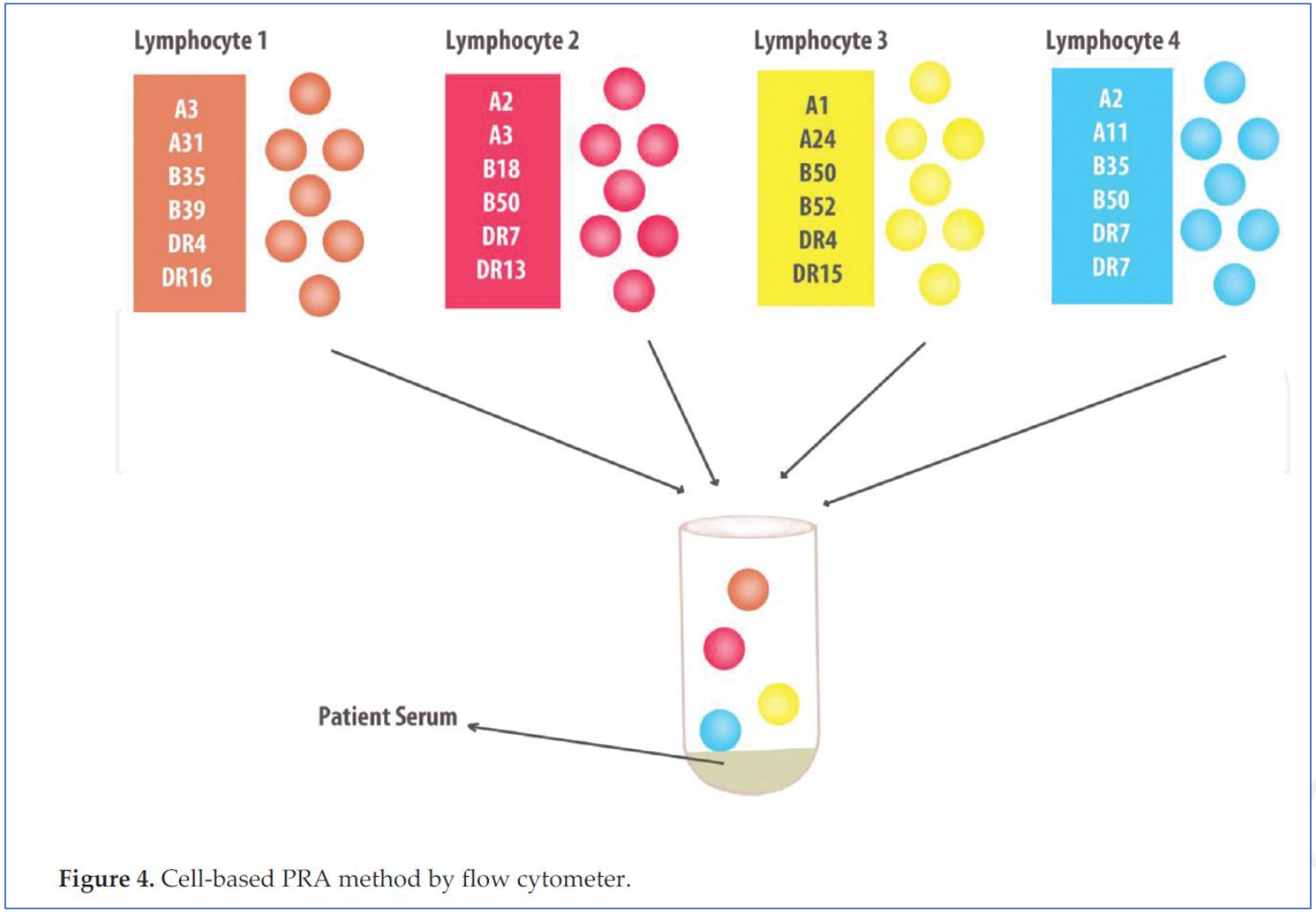


Figure 4. Cell-based PRA method by flow cytometer.

TK Anya. Detection of Anti-HLA Antibodies by Flow Cytometer. dx.doi.org/10.5772/62553

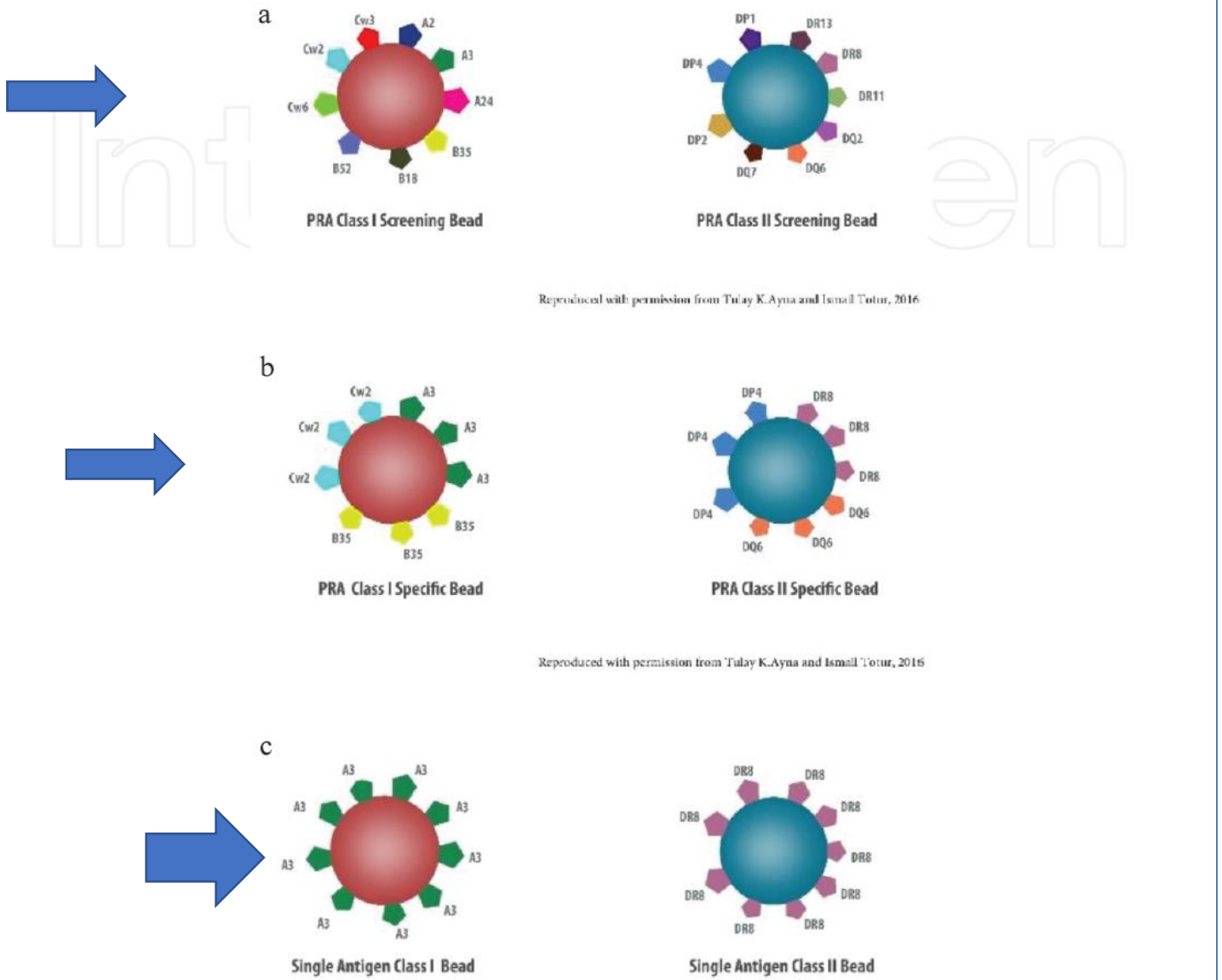
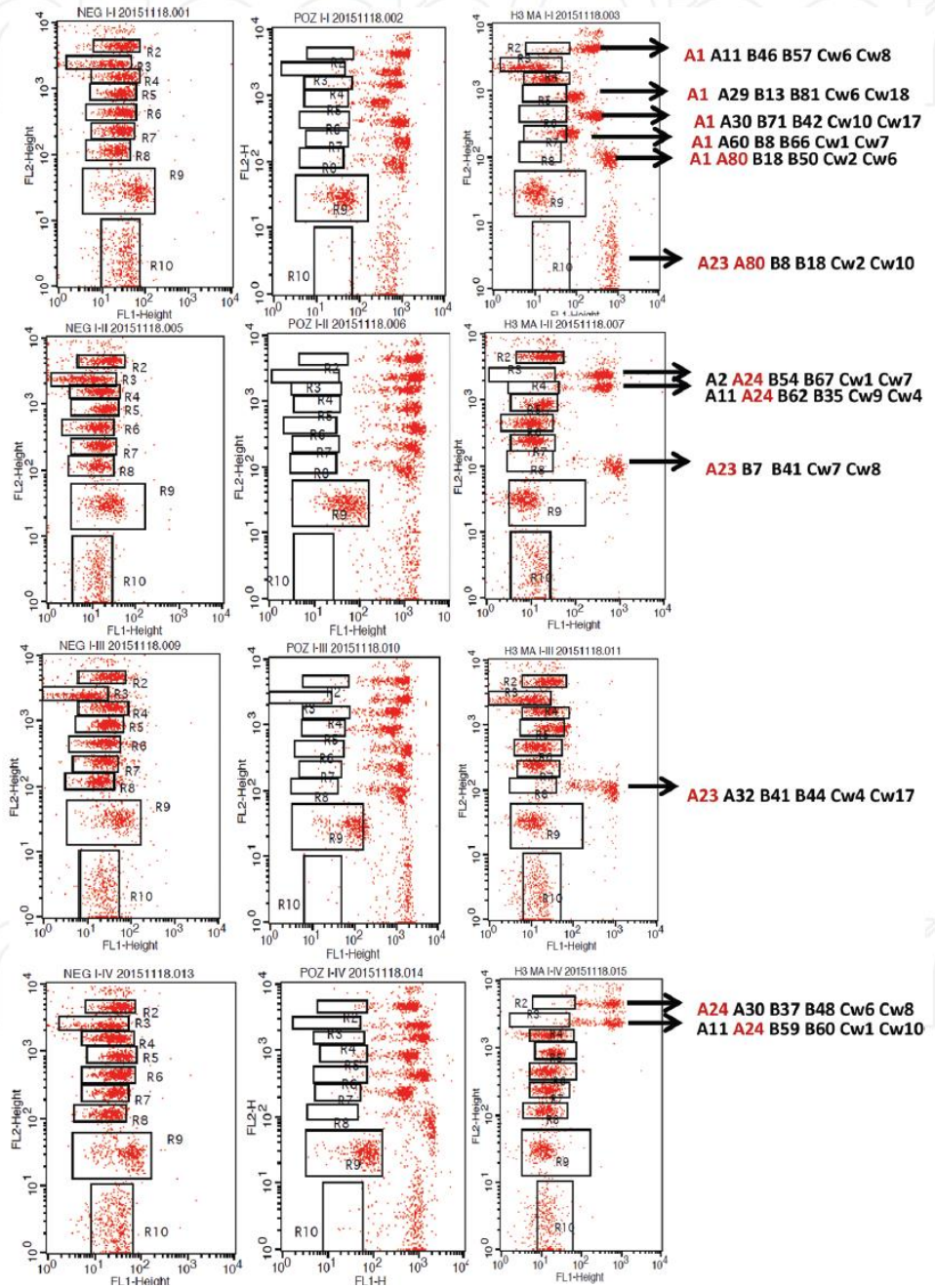


Figure 5. Bead-based PRA method by flow cytometer. (A) PRA screening beads. (B) PRA identification beads. (C) Single antigen beads.

>5% is considered as positive

TK Anya. Detection of Anti-HLA Antibodies by Flow Cytometer. dx.doi.org/10.5772/62553



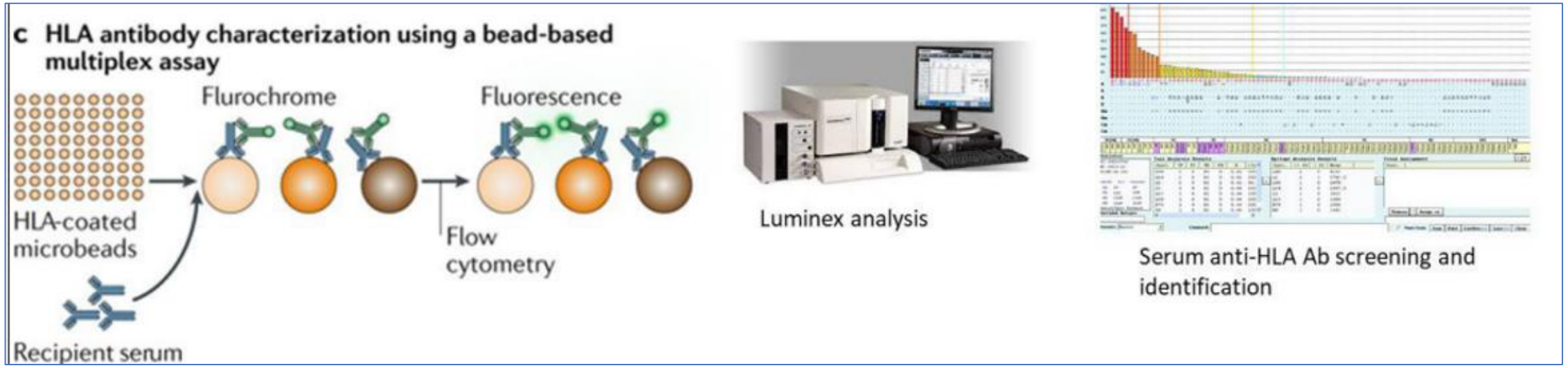
Evaluation of class I PRA identification tests (including negative, positive, and patient sera). PRA screening result is 31% positive.

Detection of Anti-HLA Antibodies by Flow Cytometer. http://dx.doi.org/10.5772/62553143

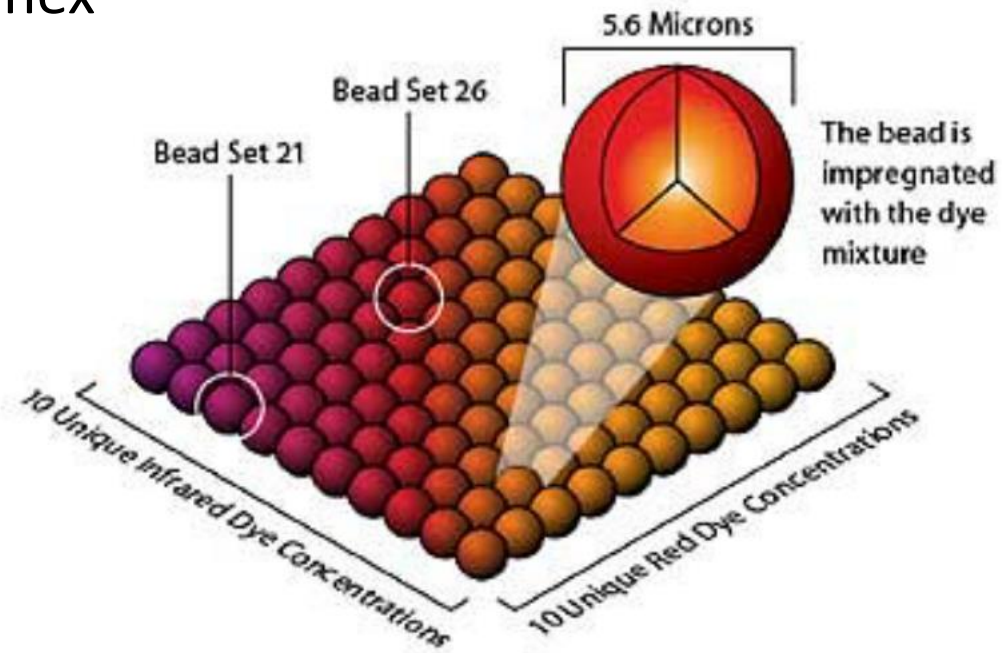
Single Antigen Bead Assay (Class I & Class II)

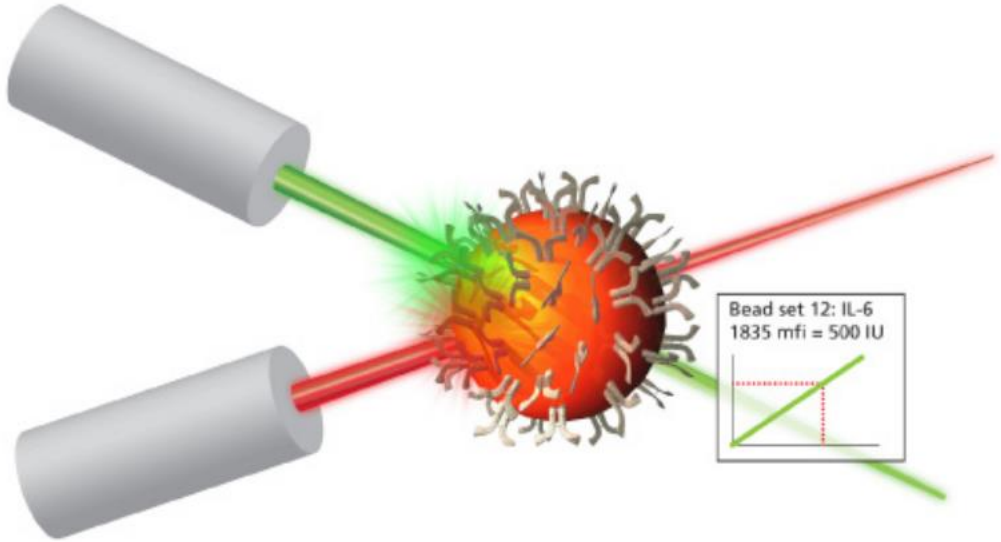
✓It is a test that utilizes bead-based technology to detect and quantify specific human leukocyte antigens (HLA) antibodies in a recipient's blood, both in Class I and Class II.

- ELISA
- Flow Cytometry
- Luminex



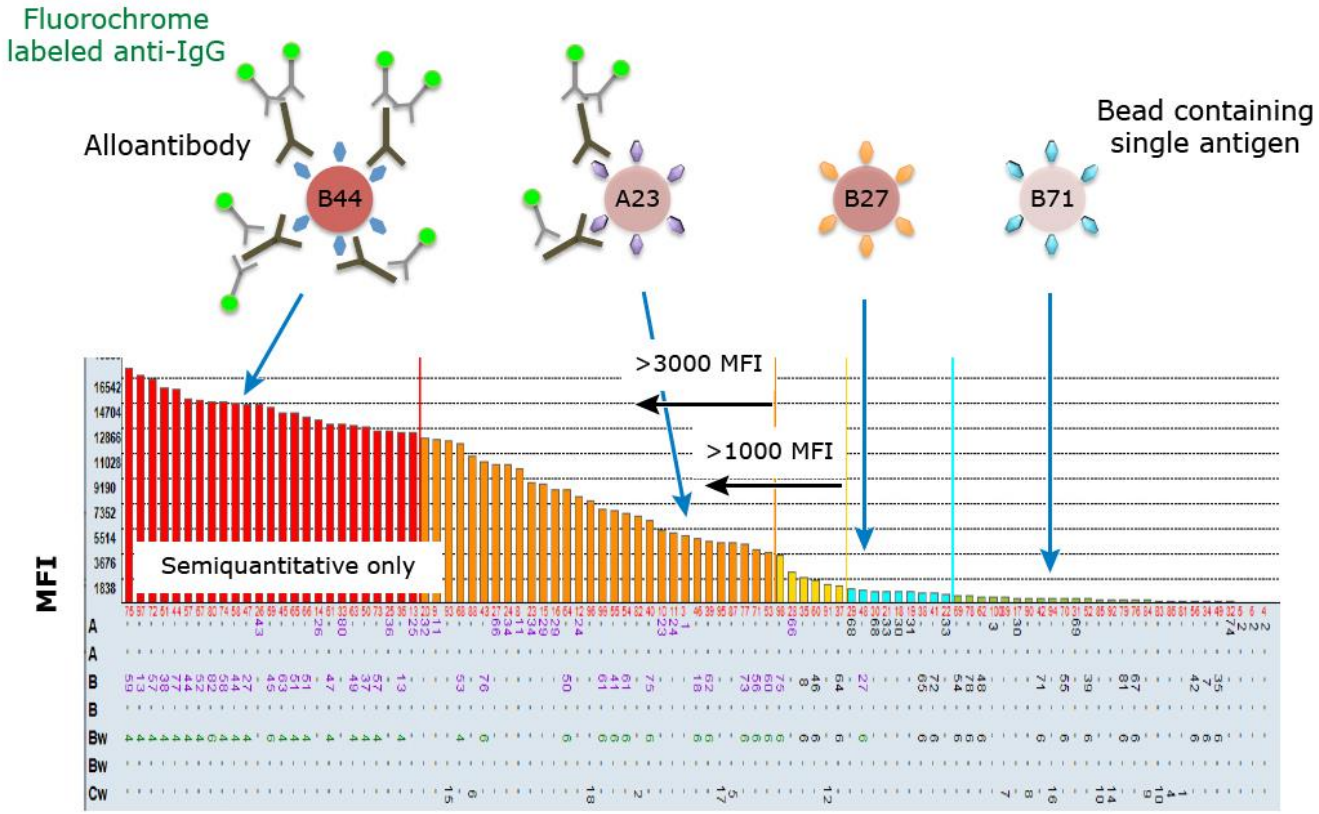
Luminex





Montgomery, Nature Rer Neph, 2018

Identifying HLA antibodies using single-antigen bead (SAB) testing



HLA antigen expressed on a particular bead

Identifying anti-HLA antibodies using SAB testing. Shown is a representative histogram of a patient's serum reacting to multiple class I HLA antigens that are coupled to individual beads. Each histogram bar represents reactivity against a single bead, with results reported in median fluorescence intensity (MFI).

HLA: human leukocyte antigen; IgG: immunoglobulin G.

Courtesy of Melissa Y Yeung, MD, FRCPC.

UpToDate®

False-positive results

- ✓Improper protein conformation and/or denaturation of HLA Ags during the process of generation and coupling to beads that may unveil not naturally found epitopes.

- ✓Binding of the patient's IgG antibody to the latex beads themselves, or to a non-HLA protein used in bead manufacture, can lead to a high **background signal** and obscure the true results of the assay.

- ✓This is often detected by the high MFI values of the negative control bead, which does not contain any bound antigen.

1-Cai J, Transplantation. 2009;88(2):226.
2- One Lambda product insert. http://www.onelambda.com/content/dam/onelambda/en/TDX/Documents/securedocs/docs/PS-ENGLISH_LANGUAGE/LS-LSCN-PI-EN-00.pdf (Accessed on October 19, 2020).

False-negative results: Interfering factors in the patient's serum

- ✓**Inhibitors** such as various complement components (C1q and C3/C4 activation products) can bind to the anti-HLA Ab and stereotypically hinder the ability of the detection antibody to bind (the prozone effect).

- ✓The presence of **IVIG** in a patient's serum and/or **IgM antibody of the same HLA specificity** can also mask the recognition of IgG alloantibody

- ✓**Low-level** antibody directed against a public/shared epitope

Cai J, Transplantation. 2009;88(2):226.

Virtual crossmatch *(in silico)*

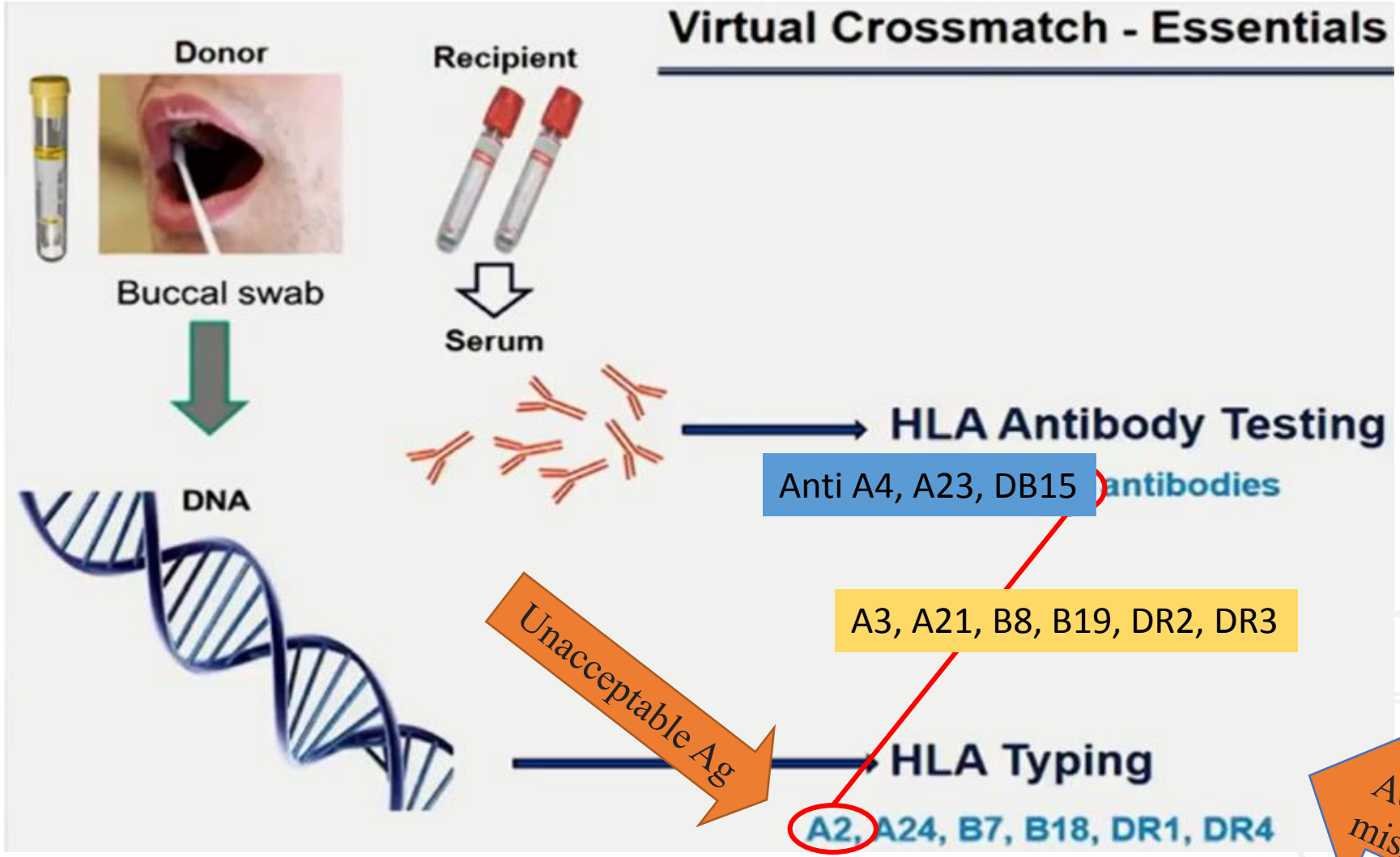
- ✓Choosing donors with ***acceptable mismatches*** mainly used for highly sensitized patients

- ✓Uses the results of two actual laboratory tests

1. The anti-HLA screening

2. The HLA typing of the donor

Virtual cross matching



R. Rajalingam, PhD, UCSF (lecture)

Single bead assay and cPRA

A*01:01	0	Low Risk Antigen
A*02:01	20800	High Risk Antigen
A*03:01	32000	High Risk Antigen
B*49:01	17600	High Risk Antigen
A*25:01	275200	High Risk Antigen
A*29:02	20800	High Risk Antigen
A*30:01	36800	High Risk Antigen
A*26:01	73600	High Risk Antigen
A*68:01	102400	High Risk Antigen
A*11:01	64000	High Risk Antigen
A*34:01	89600	High Risk Antigen
A*24:02	200	Low Risk Antigen
A*32:01	38400	High Risk Antigen
A*33:01	30400	High Risk Antigen
A*31:01	44800	High Risk Antigen
A*23:01	3200	High Risk Antigen
B*51:01	600	Moderate Risk Antigen
B*13:01	400	Low Risk Antigen
B*18:01	19200	High Risk Antigen
B*35:01	38400	High Risk Antigen
B*15:01	128000	High Risk Antigen
B*45:01	6400	High Risk Antigen
B:40:01	100	Low Risk Antigen
B*44:02	0	Low Risk Antigen
B*38:01	400	High Risk Antigen
B*57:01	300	High Risk Antigen
B*07:02	9600	High Risk Antigen
B*52:01	14400	High Risk Antigen
B*27:05	9600	High Risk Antigen
B*08:01	90	High Risk Antigen
B*14:02	0	Low Risk Antigen
B*55:01	0	Low Risk Antigen

DRB1*01:01	100	Low Risk Antigen
DRB1*01:03	100	Low Risk Antigen
DRB1*04:01	100	Low Risk Antigen
DRB1*07:01	0	Low Risk Antigen
DRB1*08:01	100	Low Risk Antigen
DRB1*04:05	50	Low Risk Antigen
DRB1*10:01	100	Low Risk Antigen
DRB1*11:01	0	Low Risk Antigen
DRB1*12:01	0	Low Risk Antigen
DRB1*13:01	0	Low Risk Antigen
DRB1*13:03	200	Low Risk Antigen
DRB1*14:01	50	Low Risk Antigen
DRB1*15:01	40000	High Risk Antigen
DRB1*16:01	52000	High Risk Antigen
DRB1*03:01	200	Low Risk Antigen
DRB1*03:02	0	Low Risk Antigen
DRB5*01:01	9000	High Risk Antigen
DRB3*02:02	0	Low Risk Antigen
DRB4*01:03	100	Low Risk Antigen
DRB1*01:02	0	Low Risk Antigen
DRB1*04:04	100	Low Risk Antigen
DRB1*09:01	0	Low Risk Antigen
DRB1*12:02	100	Low Risk Antigen
NA	-	
DRB1*15:02	0	Low Risk Antigen
DQB1*02:01	12000	High Risk Antigen
DQB1*04:02	0	Low Risk Antigen
DQB1*05:01	100	Low Risk Antigen
DQB1*06:02	150	Low Risk Antigen
DQB1*03:01	200	Low Risk Antigen
DQB1*03:02	10000	High Risk Antigen
DQB1*03:03	250	Low Risk Antigen

cPRA 99%

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.

Courtesy of Dr. Y. Shakiba

Searching for familial donor

A*01:01	0	Low Risk Antigen
A*02:01	20800	High Risk Antigen
A*03:01	32000	High Risk Antigen
B*49:01	17600	High Risk Antigen
A*25:01	275200	High Risk Antigen
A*29:02	20800	High Risk Antigen
A*30:01	36800	High Risk Antigen
A*26:01	73600	High Risk Antigen
A*68:01	102400	High Risk Antigen
A*11:01	64000	High Risk Antigen
A*34:01	89600	High Risk Antigen
A*24:02	200	Low Risk Antigen
A*32:01	38400	High Risk Antigen
A*33:01	30400	High Risk Antigen
A*31:01	44800	High Risk Antigen
A*23:01	3200	High Risk Antigen
B*51:01	100	Low Risk Antigen
B*13:01	400	Low Risk Antigen
B*18:01	19200	High Risk Antigen
B*35:01	38400	High Risk Antigen
B*15:01	128000	High Risk Antigen
B*45:01	6400	High Risk Antigen
B:40:01	100	Low Risk Antigen
B*44:02	0	Low Risk Antigen
B*38:01	400	High Risk Antigen
B*57:01	300	High Risk Antigen
B*07:02	9600	High Risk Antigen
B*52:01	14400	High Risk Antigen
B*27:05	9600	High Risk Antigen
B*08:01	90	High Risk Antigen
B*14:02	0	Low Risk Antigen
B*55:01	0	Low Risk Antigen

DRB1*01:01	100	Low Risk Antigen
DRB1*01:03	100	Low Risk Antigen
DRB1*04:01	100	Low Risk Antigen
DRB1*07:01	0	Low Risk Antigen
DRB1*08:01	100	Low Risk Antigen
DRB1*04:05	50	Low Risk Antigen
DRB1*10:01	100	Low Risk Antigen
DRB1*11:01	0	Low Risk Antigen
DRB1*12:01	0	Low Risk Antigen
DRB1*13:01	0	Low Risk Antigen
DRB1*13:03	200	Low Risk Antigen
DRB1*14:01	50	Low Risk Antigen
DRB1*15:01	40000	High Risk Antigen
DRB1*16:01	52000	High Risk Antigen
DRB1*03:01	200	Low Risk Antigen
DRB1*03:02	0	Low Risk Antigen
DRB5*01:01	9000	High Risk Antigen
DRB3*02:02	0	Low Risk Antigen
DRB4*01:03	100	Low Risk Antigen
DRB1*01:02	0	Low Risk Antigen
DRB1*04:04	100	Low Risk Antigen
DRB1*09:01	0	Low Risk Antigen
DRB1*12:02	100	Low Risk Antigen
NA	-	
DRB1*15:02	0	Low Risk Antigen
DQB1*02:01	12000	High Risk Antigen
DQB1*04:02	0	Low Risk Antigen
DQB1*05:01	100	Low Risk Antigen
DQB1*06:02	150	Low Risk Antigen
DQB1*03:01	200	Low Risk Antigen
DQB1*03:02	10000	High Risk Antigen
DQB1*03:03	250	Low Risk Antigen

Rel.	Class I PCR	Class II PCR
Mother	A*11-A*24 B*35-B*51 C*04-C*14	DQB1*03- DQB1*05 DRB1*01-DRB1*11 DRB3
Sibling 1	A*01-A*11 B*14-B*35 C*04-C*08	DQB1*05 DRB1*01
Sibling 2	A*24 B*35-B*51 C*12-C*14	DQB1*03- DQB1*05 DRB1*11-DRB1*14 DRB3
Sibling 3	A*01-A*24 B*14-B*51 C*08-C*14	DQB1*03- DQB1*05 DRB1*01-DRB1*11 DRB3
Patient	A*01-A*24 B*14-B*51 C*08-C*14	DQB1*03- DQB1*05 DRB1*01-DRB1*11 DRB3

Courtesy of Dr. Y. Shakiba

cPRA Calculation

- ✓The cPRA calculates the **likelihood of transplantation** by using the results of the SAB assay, in combination with the known frequencies of HLA antigens within the donor population.
- ✓e.g.:
  - cPRA of a patient with anti- HLA-A2, present in 48% of the donors:

    48%
  - cPRA of a patient with anti-HLA- B44, present in 27% of the donors:

    27%
  - cPRA of a patient with both: **59% (possibility of the donor to have either or both Ags)**

UpToDate, 2023, Kidney transplantation in adults: Overview of HLA sensitization and crossmatch testing
https://www-uptodate-com.proxybibl.vgregion.se/contents/kidney-transplantation-in-adults-overview-of-hla-sensitization-and-crossmatch-testing?search=virtual%20cross%20match&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H1256329285

The Kidney Allocation System

John J. Friedewald, MD[a,*], Ciara J. Samana, MSPH[b], Bertram L. Kasiske, MD[c,d], Ajay K. Israni, MD, MS[c,d,e], Darren Stewart, MS[b], Wida Cherikh, PhD[b], Richard N. Formica, MD[f,g]

KEYWORDS

• Kidney transplant • Organ allocation • Transplant waiting list

KEY POINTS

- The current kidney allocation system is outdated and has not evolved to reflect the changing demographics of patients on the waiting list.
- Without additional donor kidneys, any change in the allocation system shifts kidneys between different patient groups.
- Any changes in the allocation system will be trade-offs between equity and utility.
- The new proposed system will significantly reduce mismatches between possible donor kidney longevity and life expectancy of recipients.

Continued

✓KDRI

✓KDPI

✓EPTS

✓cPRA

Surg Clin N Am 93 (2013) 1395–1406

Accordingly, allocation is based on a sliding scale point system—additional points for sensitization begin at 20% cPRA and increase exponentially as it approaches 100%.

MC Bhaskaran, KI reports, 2022

✓Several transplant centers have reported their success with proceeding to transplant based on VXM results and eliminating pretransplant PXM.

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The Impact of Virtual Crossmatch on Cold Ischemic Times and Outcomes Following Kidney Transplantation

Sadaf Aslam, MD, MS[1], Jacentha Buggs, MD[2], Kasey Wyatt, BS[1], Ambuj Kumar, MD[1], Ebonie Rogers, BS[3], and Robert Watson, MD[2]

Abstract

Background: Prolonged cold ischemic time (CIT) in deceased donor kidney transplantation (DDKT) has been associated with adverse graft outcomes. Virtual crossmatch (VXM) facilitates reliable prediction of crossmatch results based on the profile of human leukocyte antigen antibodies of the recipient and the donor in reduced time compared with a physical crossmatch (PXM). We hypothesized a shorter CIT since the implementation of the VXM in recipients of DDKT.

Methods: We conducted a retrospective cohort study of consecutive adult recipients of DDKT. The data were analyzed for differences in CIT before and after the implementation of VXM.

Results: After the exclusion of 59 recipients (age less than 18 years and/or CIT ≥ 20 hours), our study compared outcomes of 81 PXMs from February to June 2018 against 68 VXMs from February to June 2019. There were no statistical differences between groups based on donor age (P = .09), donor type (P = .38), kidney donor profile index (P = .43), or delayed graft function (P = .20). Recipients with VXM were older (58 vs 51 years, P = .002) and had a higher estimated post-transplant survival score (59% vs 46%, P = .01). The CIT was significantly lower for the VXM group (P = .04).

Conclusion: Our study demonstrated a significantly shorter CIT with VXM in DDKT recipients. Our study was limited with small sample size, but the trend of increased graft survival with higher estimated post-transplant scores and older recipients is encouraging as the donor pool expands with marginal kidneys and national sharing.

S. Aslam. The American Surgeon, 2021

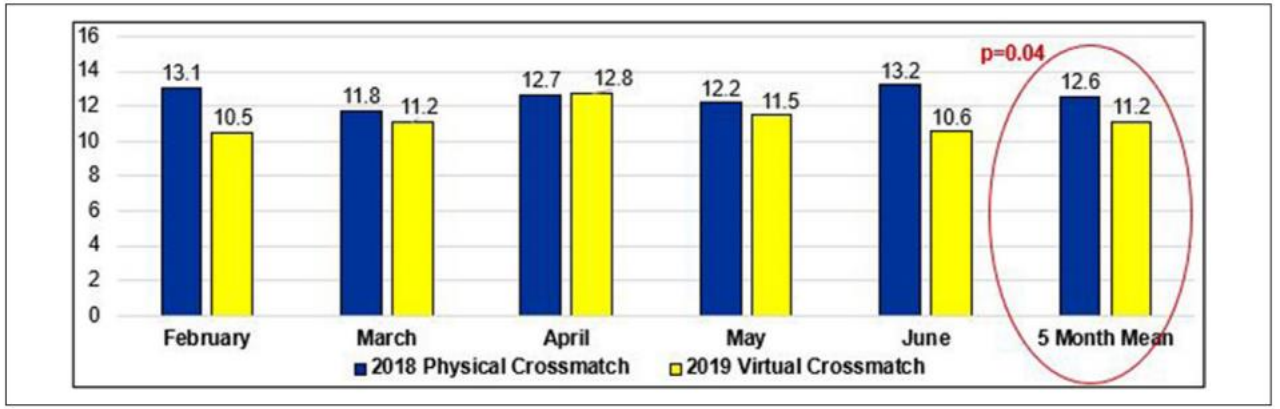


Figure 1. CIT by month and crossmatch type.

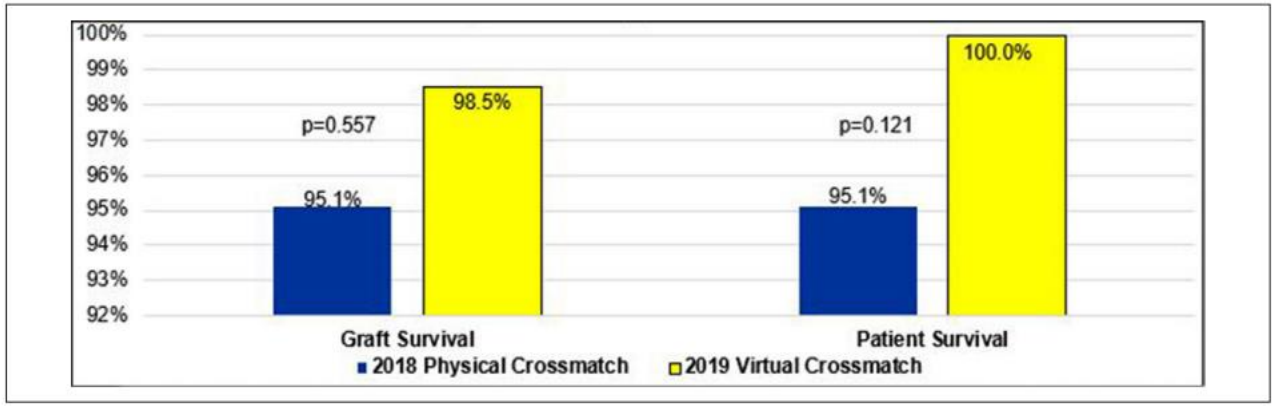


Figure 2. Overall graft and patient survival by crossmatch type.

S. Aslam. The American Surgeon, 2021

clinical investigation

www.kidney-international.org

Trends and impact on cold ischemia time and clinical outcomes using virtual crossmatch for deceased donor kidney transplantation in the United States

Chethan M. Puttarajappa[1], Dana Jorgensen[2], Jonathan G. Yabes[3], Kwonho Jeong[3], Adriana Zeevi[4], John Lunz[5], Amit D. Tevar[2], Michele Molinari[2], Sumit Mohan[6,7,8] and Sundaram Hariharan[1,8]

[1]Department of Medicine, Renal-Electrolyte Division, University of Pittsburgh, Pittsburgh, Pennsylvania, USA; [2]Department of Surgery, Thomas E. Starzl Transplantation Institute, University of Pittsburgh, Pittsburgh, Pennsylvania, USA; [3]Center for Research on Healthcare Data, Division of General Internal Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania, USA; [4]Department of Pathology, University of Pittsburgh, Pittsburgh, USA; [5]Transplant Immunology Laboratory, LifeLink Foundation, Tampa, Florida, USA; [6]Department of Medicine, Division of Nephrology, Vagelos College of Physicians and Surgeons, Columbia University, New York, New York, USA; and [7]Department of Medicine, Mailman School of Public Health, Columbia University, New York, New York, USA

Puttarajappa CM. KI 2021

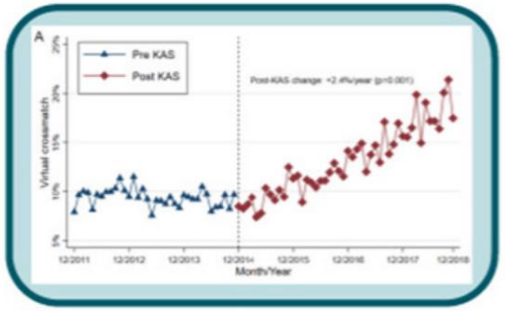
Trends and impact on cold ischemia time and clinical outcomes using virtual crossmatch for deceased donor kidney transplantation in the United States.

kidney INTERNATIONAL

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Deceased donor kidney transplant recipients in the US before and after 2014 kidney allocation system (KAS) (2011-2018)

VXM use before and after KAS implementation



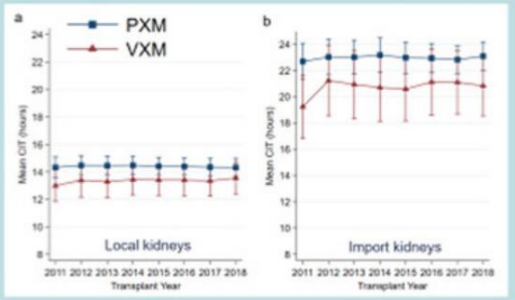
Impact of VXM on CIT and survival

Physical crossmatch (PXM) (N = 71,839)

Vs

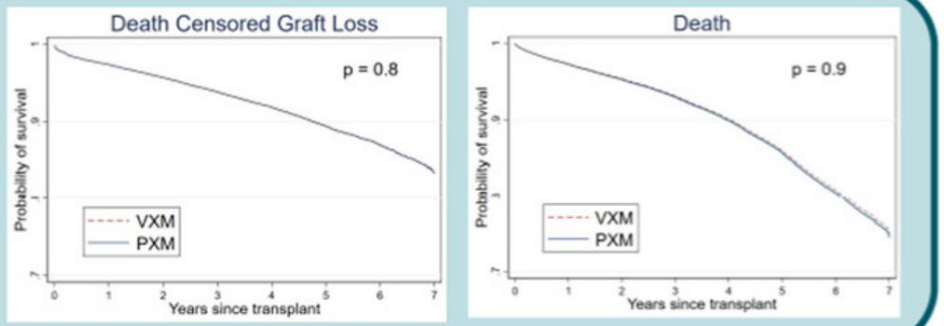
Virtual crossmatch (VXM) (N = 9,632)

Shorter cold Ischemia Time



Mean CIT
15 hours (VXM) Vs
16.5 hours (PXM)
p = 0.02

Similar Patient and Graft Survival
(median follow-up = 2.9 years)



Puttarajappa et al, 2021

CONCLUSION: For deceased donor kidney transplantation, virtual crossmatch is associated with shorter cold ischemia time and similar graft and patient survival compared to physical crossmatch

Puttarajappa CM. KI 2021

A Virtual Crossmatch Protocol Significantly Increases Access of Highly Sensitized Patients to Deceased Donor Kidney Transplantation

Adam W. Bingaman,[1,3] Cathi L. Murphey,[2] Juan Palma-Vargas,[1] and Francis Wright[1]

Background. Patients with preexisting antihuman leukocyte antigen (HLA) antibodies (sensitized patients) are more likely to have a positive crossmatch with possible donors and have a lower likelihood of receiving a renal transplant with longer wait times. A virtual crossmatch protocol using solid-phase technology to determine the specificity of anti-HLA antibodies may improve the probability of identifying a crossmatch-negative compatible donor and increase access of sensitized patients to kidney transplantation.

Methods. A virtual crossmatch protocol was implemented on October 1, 2006 with solid-phase HLA antibody characterization for all sensitized patients on the waiting list. Transplant rates for the period from October 2006 to June 2008 were compared with Scientific Registry of Transplant Recipients (SRTR) data from 2006 to determine national transplant rates for sensitized patients.

Results. SRTR data for 2006 showed that nationally 590 of 10,659 transplants (5.5%) were in-patients with panel reactive antibody (PRA) more than or equal to 80%. During 2006 to 2008, after initiation of the virtual crossmatch protocol, we performed 122 deceased donor kidney transplants, of which 15 (12.3%) sensitized patients (PRA≥80%) received transplants (P=0.004 compared with SRTR national data), with 9 (7.4%) patients having a PRA more than 90%. The virtual crossmatch protocol was predictive of a negative-final crossmatch and eliminated the use of preliminary cross-matching with attendant cost savings of more than $100,000.

Conclusion. Initiation of a virtual crossmatch protocol using solid-phase histocompatibility techniques significantly increased access of sensitized patients to kidney transplantation and was more cost effective. Usage of a virtual crossmatch may facilitate greater sharing of kidneys to improve access to transplantation for sensitized recipients.

Keywords: Kidney, Allocation, Crossmatch.

(*Transplantation* 2008;86: 1864–1868)

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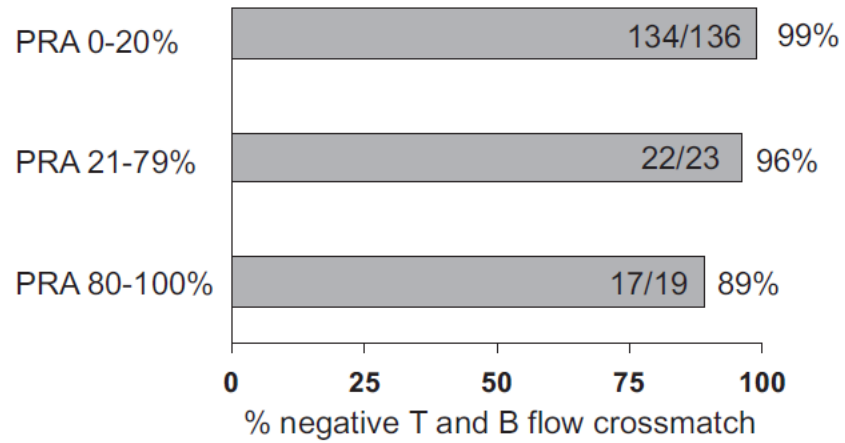

FIGURE 3. Predictive value of negative virtual crossmatch. All final T- and B-flow crossmatches that were predicted to be negative by virtual crossmatch during the study period were reviewed. The percentage of negative flow crossmatch results (predictive value of virtual crossmatch) is shown in relationship to the patient's PRA.

TABLE 1. Outcome of transplants in sensitized patients

Patient	Peak PRA	Rejection (yes/no)	1 mo creatinine
1	93	No	1.0
2	84	No	2.1
3	85	No	0.8
4	84	No	1.0
5	95	Yes, day 227: Banff 2A	0.9
6	93	No	1.3
7	89	No	0.7
8	91	Yes, day 10: antibody mediated	0.7
9	93	No	0.9
10	84	No	1.2
11	93	No	1.5
12	91	No	0.9
13	93	No	1.2
14	85	No	1.6
15	100	No	1.4

PRA, panel reactive antibody.

The virtual crossmatch protocol was predictive of a negative-final crossmatch and eliminated the use of preliminary cross-matching with attendant cost savings of more than $100,000.

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Why virtual crossmatch is not being used routinely?

- ✓The concept is not new (Delmonico Transplantation.36:629–633.1983)
- ✓However the CDC assay that was used to determine the antibodies was largely based on HLA class I antigens and could not define all antibody specificities, especially in patients who were broadly sensitized.
- ✓With the advent of DNA-based methods for typing HLA specificities at a higher resolution and the solid-phase assays for detecting antibodies against individual HLA, VXM has come to the limelight
- ✓After the implementation of kidney allocation system in the United States, there has been a steady increase in the use of VXM—in 2018, 18% of kidney transplants were done relying on a VXM.

The obstacles in Iran

- ✓The cost of solid phase assays (not covered by insurance companies)
- ✓The scarcity of labs doing accurate solid-phase tests with fast response
- ✓Rapid and accurate report of HLA typing for the cadaver

	Primary disease	Tx Date	Last F/U Date	Desensitization	Complications	Last Cr:
HN	Crescentic IgAN	1400/06/07 (2ed)	1402/07/01	-	-	1.32
M R	Unknown CKD (2^{nd} Tx)	1400/10/05	1402/06/05	3 sessions of PLEX and IVIG and MMF were administered before Tx.	Allograft Malrotatio: Corrected	0.9
AS	FSGS (3^{rd})	1401/04/21	1402/06/12	3 sessions of PLEX and IVIG and MMF	-	1.07
MS	Unknown	1401/05/30	1402/07/02	-	ATN + ACR	1.27
EY	Unknown	1401/08/01	1402/06/02	-	-	1.5
FZ	Unknown	1401/08/27	1402/06/05	11 Vial IVIG	DGF+ severe incisional hernia+ ACR/AMR+ FSGS	1.76
SK B	MPGN (3^{rd} Tx)	1401/09/15	Once came	PLEX	-	1.7
SK	Unknown	1402/2/09		PLEX	-	0.98
ZS	Unknown	1402/04/13	1402/7/03	PLEX	UTI	1.1
NH	Unknown	1402/05/03	1402/7/03	PLEX	-	1.19

Conclusion

1. Virtual X match is an in silico method of X match which may be more feasible in the lab.
2. It reduces the cold ischemia time.
3. It is highly recommended in highly sensitized recipients and increases the chance of Tx in a well-managed program.
4. It reduces or abolishes the need for desensitization.
5. With progressing the methods and positive and negative predictive values and universality of HLA typing, especially at allele level, it may substitute PXM methods.

Thanks for listening!

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