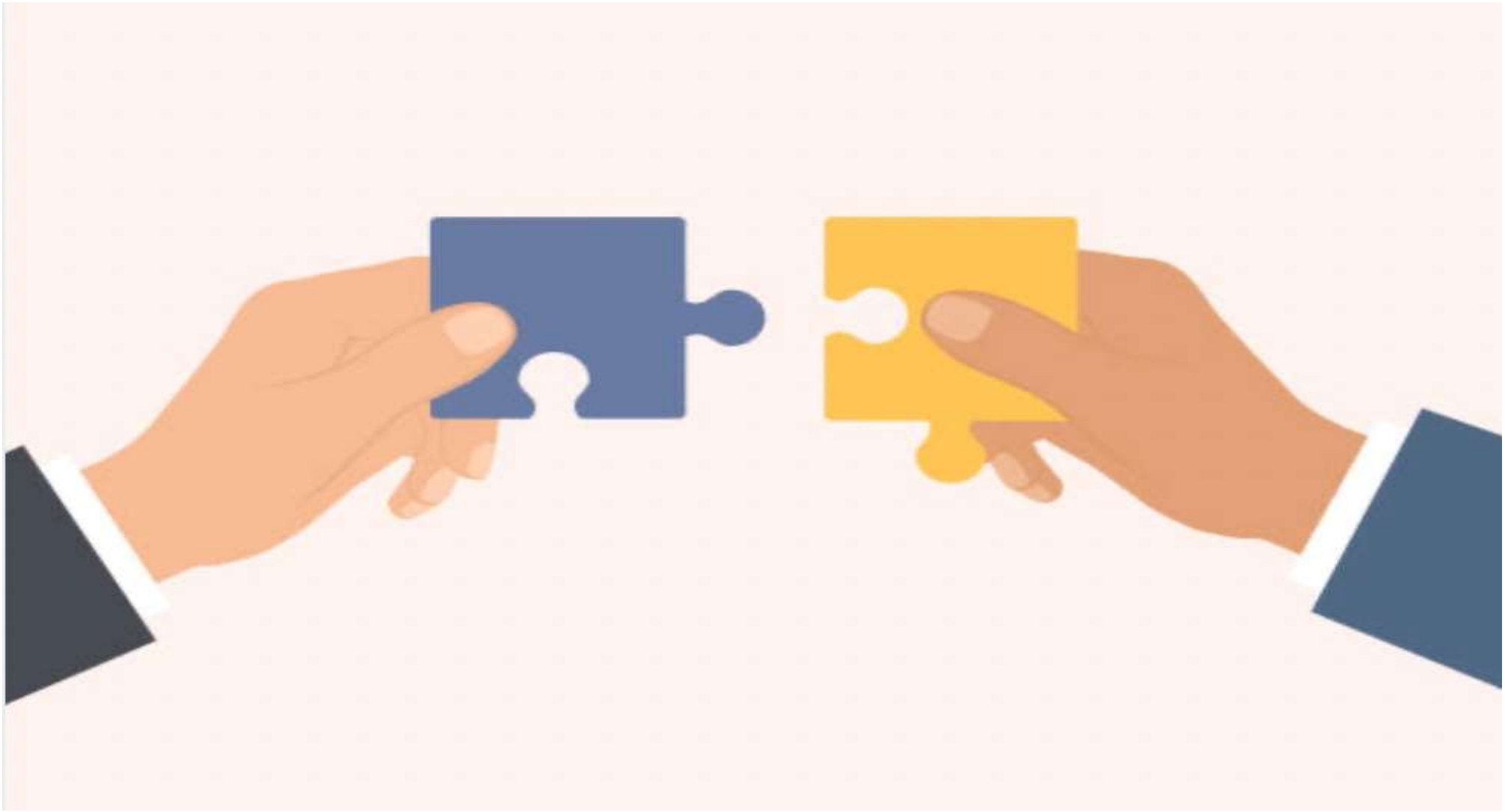
დონორ-რეციპიენტის თავსებადობა: პრე-ტრანსპლანტაციური შეფასება და არსებული გამოწვევების დაძლევის სამომავლო გზები

გვანცა მეცხვარიშვილი MD

1954წ

პირველი წარმატებული თირკმლის ტრანსპლანტაცია

რიჩარდ და რონალდ ჰერიკები „City Life „*ერიკ რენდალის*ER6/4/2015



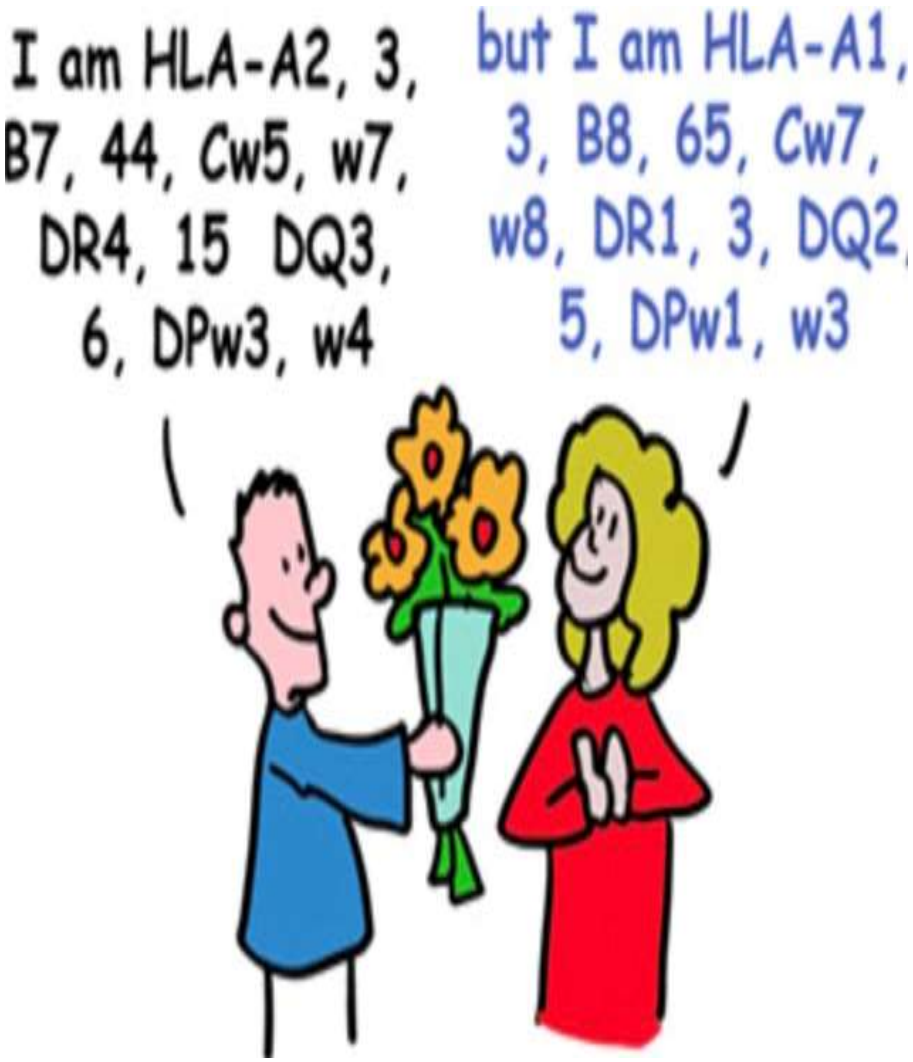
სისხლის ჯგუფობრივი თავსებადობა

რეციპიენტი / დონორი	A	B	AB	0
A				
B				
AB	✗	✗	✓	✗
0	✓	✓	✓	✓

იზოაგლუტინინების თავიდან აცილება

როგორია პაციენტის იმუნოლოგიური რისკი?

ადამიანის ლეიკოციტის ანტიგენის თავსებადობა



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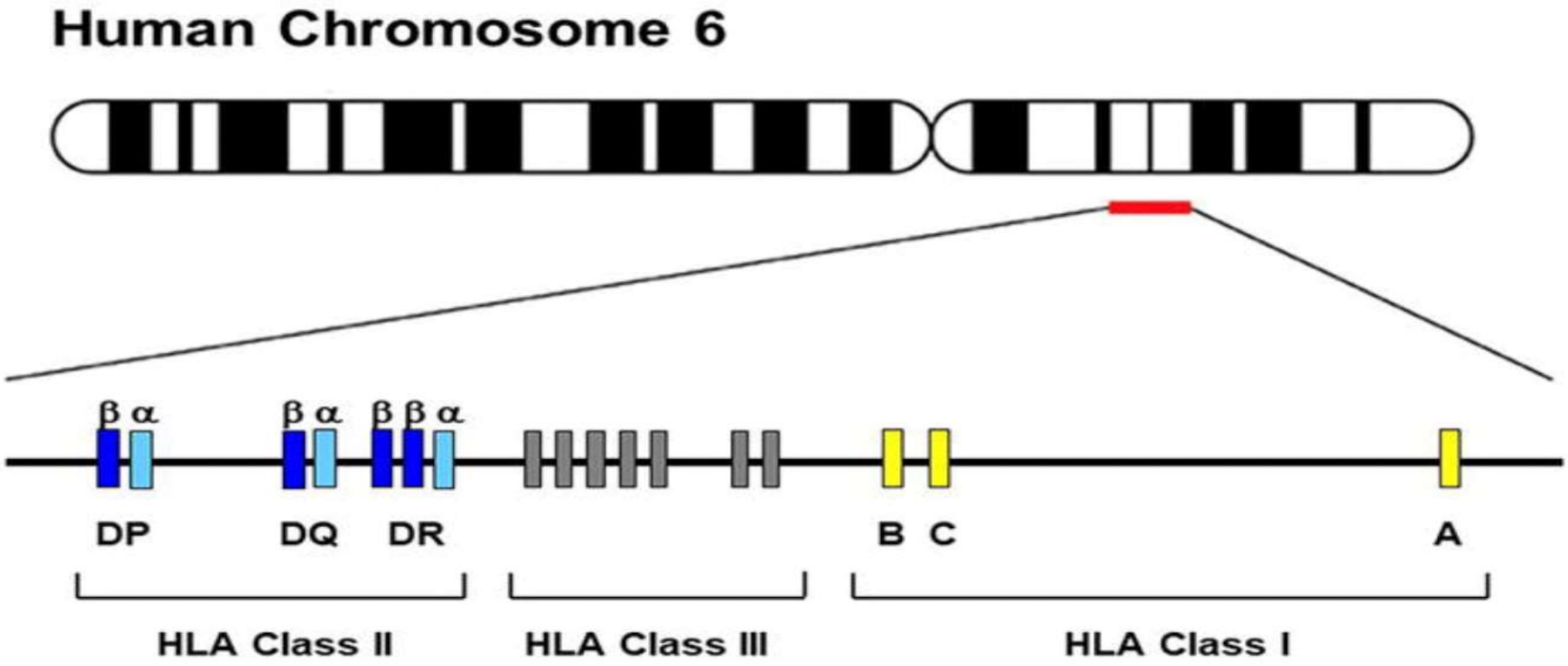
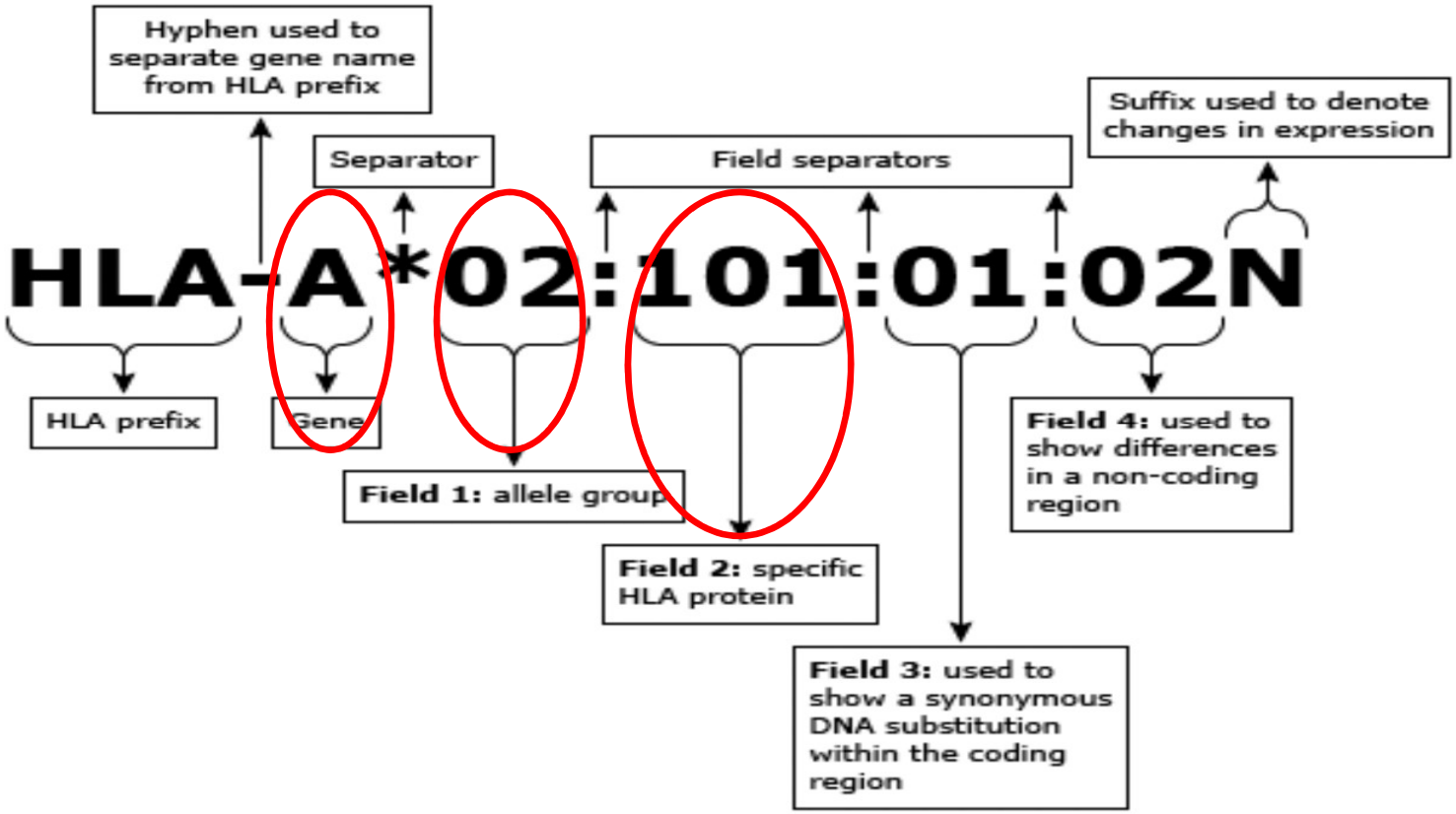
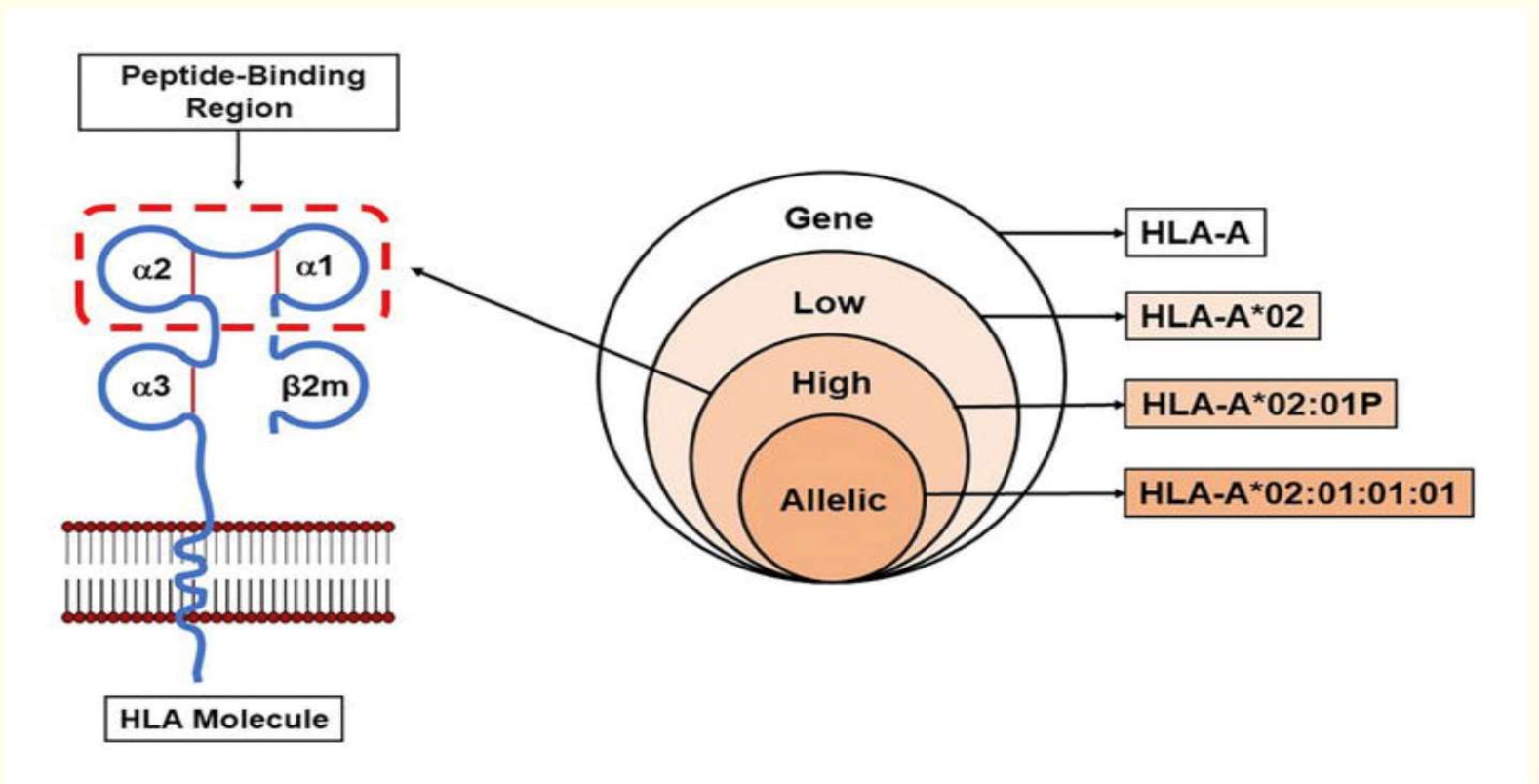


Andrés Jaramillo and Katrin HackeHuman Leukocyte Antigens - Updates and Advances, 27 February 2023

ნომენკლატურა



HLA ტიპირების რეზოლუცია



Andrés Jaramillo and Katrin HackeHuman Leukocyte Antigens - Updates and Advances, 27 February 2023

TEST RESULT FOR HLA-DRB345

Genotype — **DRB3*01 DRB5*01** | Phenotype — **DR52 DR51**

This is a clean test result.

GROUP	ALLELES	ANTIGEN
DRB3 1 common 114 rare	(95 rare alleles)	-
	DRB3* 01:01:02:01 (+19 rare alleles)	**DR52**
DRB5 3 common 138 rare	**DRB5* 01:01:01:01**, **01:02:01** (+18 rare alleles)	**DR51**
	DRB5* 01:03 (+120 rare alleles)	-

Cannot exclude the following RARE alleles from another locus:
*DRB1*01:57e, DRB1*03:42e, DRB1*03:86e, DRB1*03:87e, DRB1*04:220e, DRB1*09:07e, DRB1*09:23e, DRB1*11:121e, DRB1*12:22e, DRB1*12:88e, DRB1*14:46e*

ALLELES BY GROUP

GROUP	ALLELES
DRB3 1 common	**DRB3* 01:01:02:01** (+114 rare alleles)

ლოკუსების რაოდენობა	• რეკომენდებულია 11 ლოკუსის ტიპირება (HLA-A, -B, -C, -DRB1, -DRB3/4/5, - DQB1, -DQA1, -DPB1, -DPA1)
ალოკაციისათვის ქულების მინიჭება	• HLA Mismatch (მაგ. ABDR)

ალოკაციის სქემები

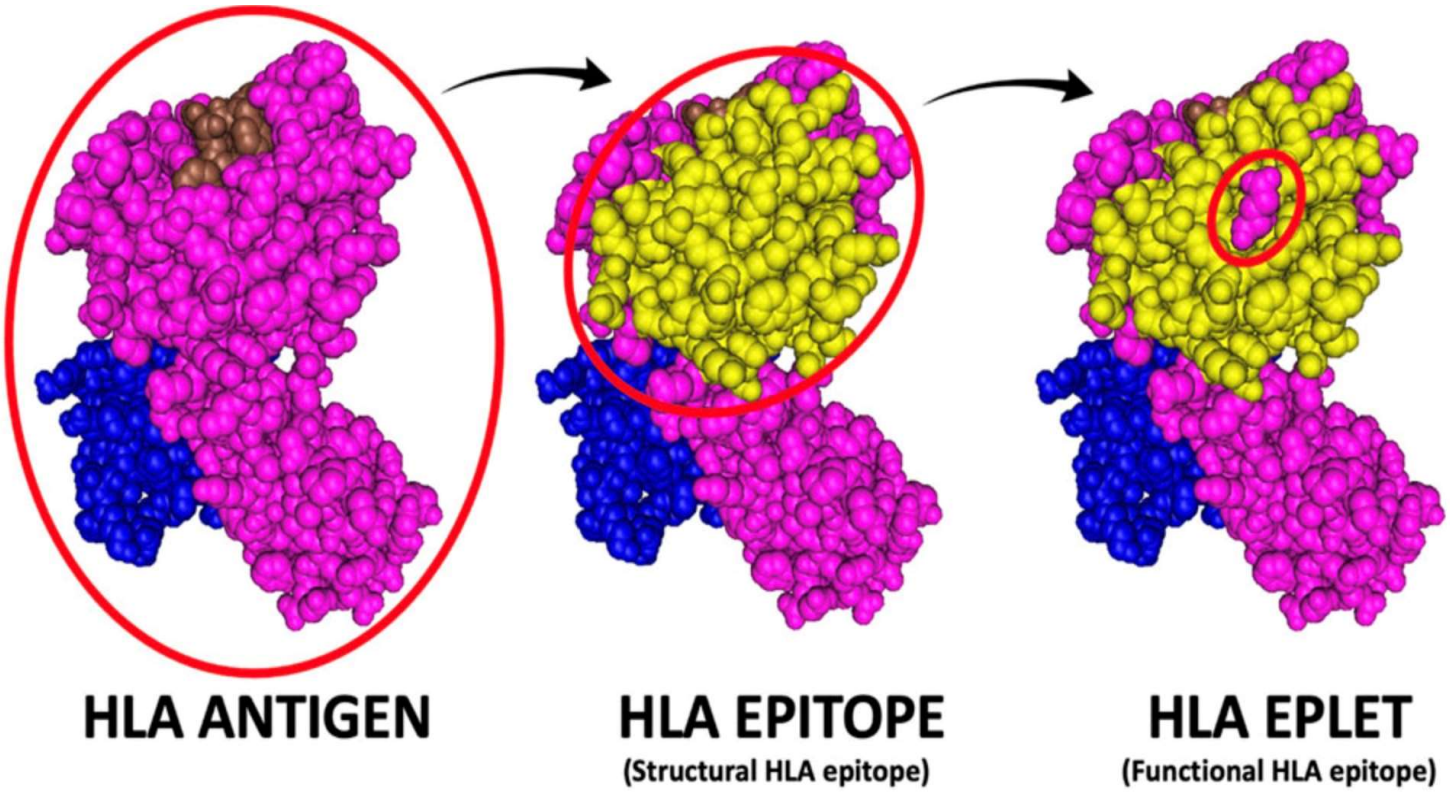
Table 1 | Examples of HLA allocation schemes

Allocation organization	Allocation system	HLA priority points	Points' equivalency for 1-year wait time
Eurotransplant	ETKAS	Consider A-B-DR. The 0 mismatch = 400 points. Points are doubled for pediatric patients.	33.3 Points
UNOS	KAS	Consider only DR. The 0 mismatch = 2 points. Up to 4 points for pediatric patients aged 0–10 y.	1.0 Point
French		Consider A-B-DR-DQ. The 0 mismatch is the equivalent of 600 points.	10 Points for the first year with algorithm to incorporate where patient is on dialysis
NHSBT		Consider A-B-C-DR-DQ. Point deduction system, with 0 mismatch being equivalent of 500 points.	365 Points (1 point per day)
New Zealand		Point elimination system. The 0 mismatch is the equivalent of 6000 points.	12 Points
Canada[19]		Up to 3 points for HLA-DR$\beta_{1/3/4/5}$ and HLA-DQβ_{1}. Pediatric patients treated as high priority over adults, except for highly sensitized patients.	1.0 Point

ETKAS, Eurotransplant Kidney Allocation System; HLA, human leukocyte antigen; KAS, kidney allocation system; NHSBT, British National Health System Blood and Transplant; UNOS, United Network of Organ Sharing.

Anat R. Tambur et al, Significance of HLA-DQ in kidney transplantation: time to reevaluate human leukocyte antigen–matching priorities to improve transplant outcomes? An expert review and recommendations, KI, 11.2021

ეპიტოპები, ეპლეტები



Mattoo A et al (2024) Improving long-term kidney allograft survival by rethinking HLA compatibility: from molecular matching to nonHLA genes. Front. Genet. 1

ეპლეტებით შესაბამისობა- HLA Match Maker

	HLA Antigen Mismatch	Eplet Mismatch
Advantages	1. Ease of measurement 2. Widespread use	1. HLA typing information already available for analysis 2. High-resolution view at molecular level 3. Can guide clinicians to tailor immunosuppression-lowering trials 4. Can help predict patients at risk of long-term graft loss
Disadvantages	1. Lack of granularity 2. Restricts a donor locus without taking into account recipient's whole repertoire of epitopes	1. Needs continued, experimental verification of Ab binding 2. Unclear thresholds and cutoffs

Abbreviations—Ab: antibody.

André Renal et al, Transplantology 2021 2, 336–347

Human Immunology 83 (2022) 264–269

Contents lists available at ScienceDirect

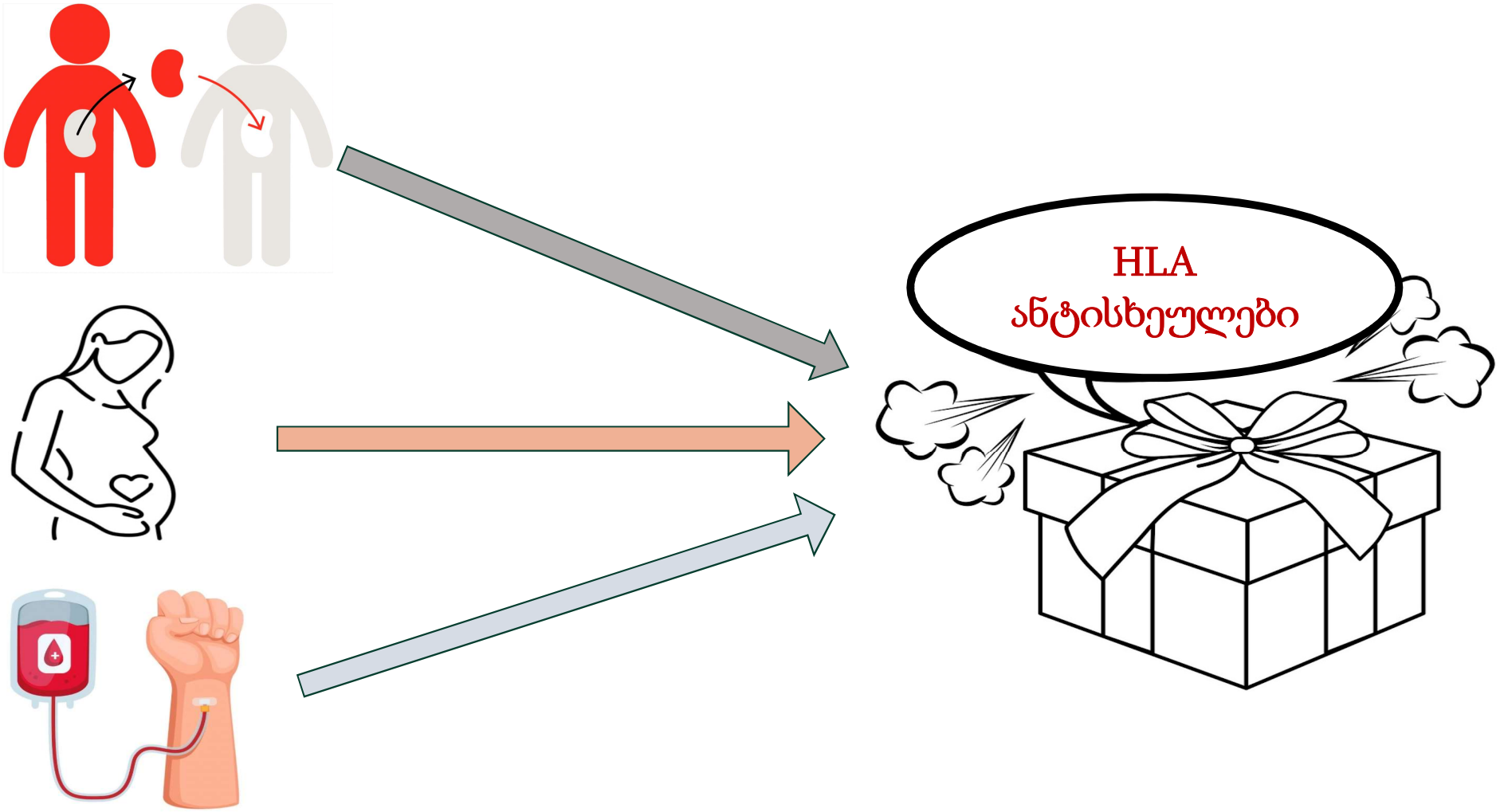
journal homepage: www.elsevier.com/locate/humimm

Research article

Genome Canada precision medicine strategy for structured national implementation of epitope matching in renal transplantation

K.R. Sherwood [a,b], J. Tran [a], O.P. Günther [c], J. Lan [a,b], O. Aiyegbusi [b], R. Liwski [d], R. Sapir-Pichhadze [e], S. Bryan [f], T. Caulfield [g], P. Keown [a,b,*], Genome Canada Transplant Consortium [1]

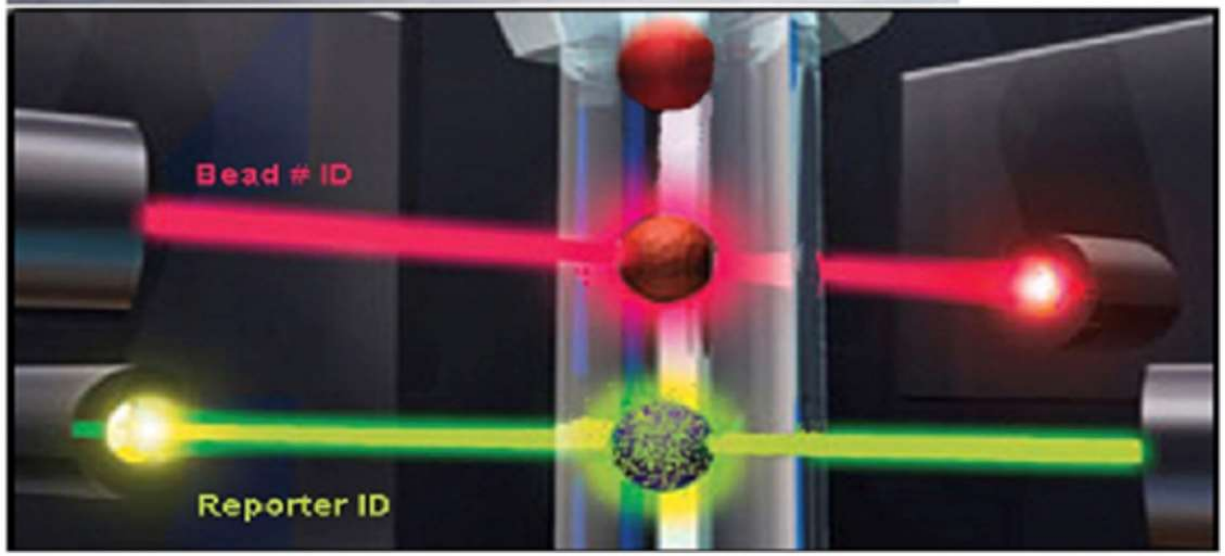
[a] Departments of Pathology and Laboratory Medicine, Vancouver, Canada
[b] Medicine, University of British Columbia, Vancouver, Canada
[c] Günther Analytics, Vancouver, Canada
[d] Department of Pathology, Dalhousie University, Halifax, Canada
[e] Department of Medicine, McGill University and MU-HRI, Montreal, Canada
[f] School of Population and Public Health, University of British Columbia, Vancouver, Canada
[g] Faculty of Law and School of Public Health, University of Alberta, Edmonton, Canada

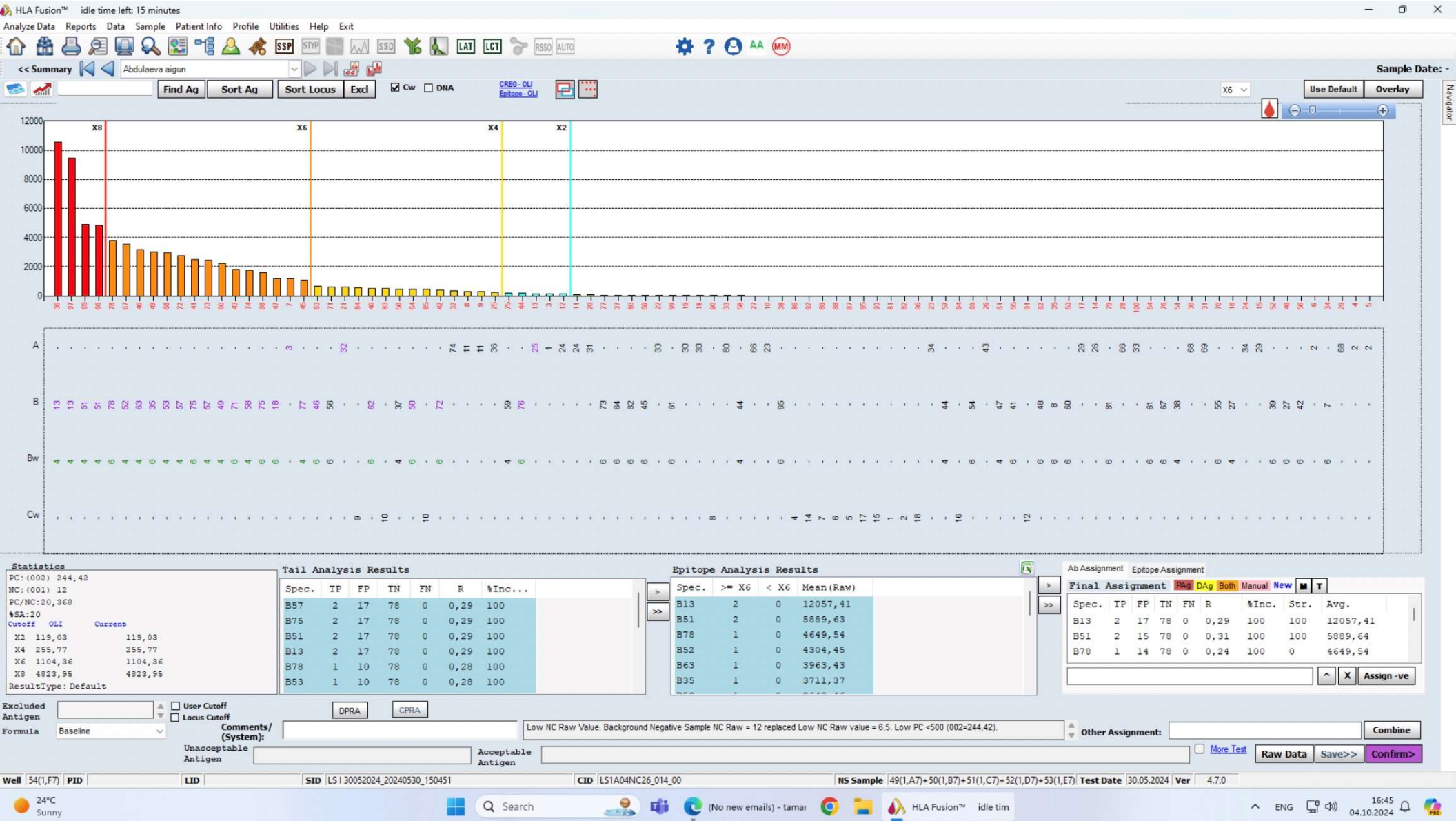

HLA
ანტისხეულები

სენსიბილიზებული პაციენტი - პაციენტი მაღალი HlA ანტისხეულებით

- **რამდენად სენსიბილიზებულია პაციენტი?**
- **რამდენია vPRA, cPRA ან cRF?**

HLA, SAB

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Analyze Data Reports Data Sample Patient Info Profile Utilities Help Exit
<< Summary
Abdulaeva aigun
Sample Date: -
Find Ag
Sort Ag
Sort Locus
Excl
Cw
DNA
CREG - OLI
Epitope - OLI
X6
Use Default
Overlay
X8
X6
X4
X2
12000
10000
8000
6000
4000
2000
0
A
B
Bw
Cw
Statistics
PC:(002) 244,42
NC:(001) 12
PC/NC:20,368
%SA:20
Cutoff OLI Current
X2 119,03 119,03
X4 255,77 255,77
X6 1104,36 1104,36
X8 4823,95 4823,95
ResultType: Default
Tail Analysis Results
Spec. TP FP TN FN R %Inc...
B57 2 17 78 0 0,29 100
B75 2 17 78 0 0,29 100
B51 2 17 78 0 0,29 100
B13 2 17 78 0 0,29 100
B78 1 10 78 0 0,28 100
B53 1 10 78 0 0,28 100
Epitope Analysis Results
Spec. >= X6 < X6 Mean(Raw)
B13 2 0 12057,41
B51 2 0 5889,63
B78 1 0 4649,54
B52 1 0 4304,45
B63 1 0 3963,43
B35 1 0 3711,37
Ab Assignment
Epitope Assignment
Final Assignment
PAg DAg Both Manual New
Spec. TP FP TN FN R %Inc. Str. Avg.
B13 2 17 78 0 0,29 100 100 12057,41
B51 2 15 78 0 0,31 100 100 5889,64
B78 1 14 78 0 0,24 100 0 4649,54
Assign -ve
Excluded Antigen
User Cutoff
Locus Cutoff
Formula
Baseline
DPRA
CPRA
Comments/ (System):
Low NC Raw Value. Background Negative Sample NC Raw = 12 replaced Low NC Raw value = 6,5. Low PC <500 (002=244,42).
Other Assignment:
Combine
Unacceptable Antigen
Acceptable Antigen
More Test
Raw Data
Save>>
Confirm>
Well 54(1,F7) PID LID SID LS I 30052024_20240530_150451 CID LS1A04NC26_014_00 NS Sample 49(1,A7)+50(1,B7)+51(1,C7)+52(1,D7)+53(1,E7) Test Date 30.05.2024 Ver 4.7.0
24°C Sunny
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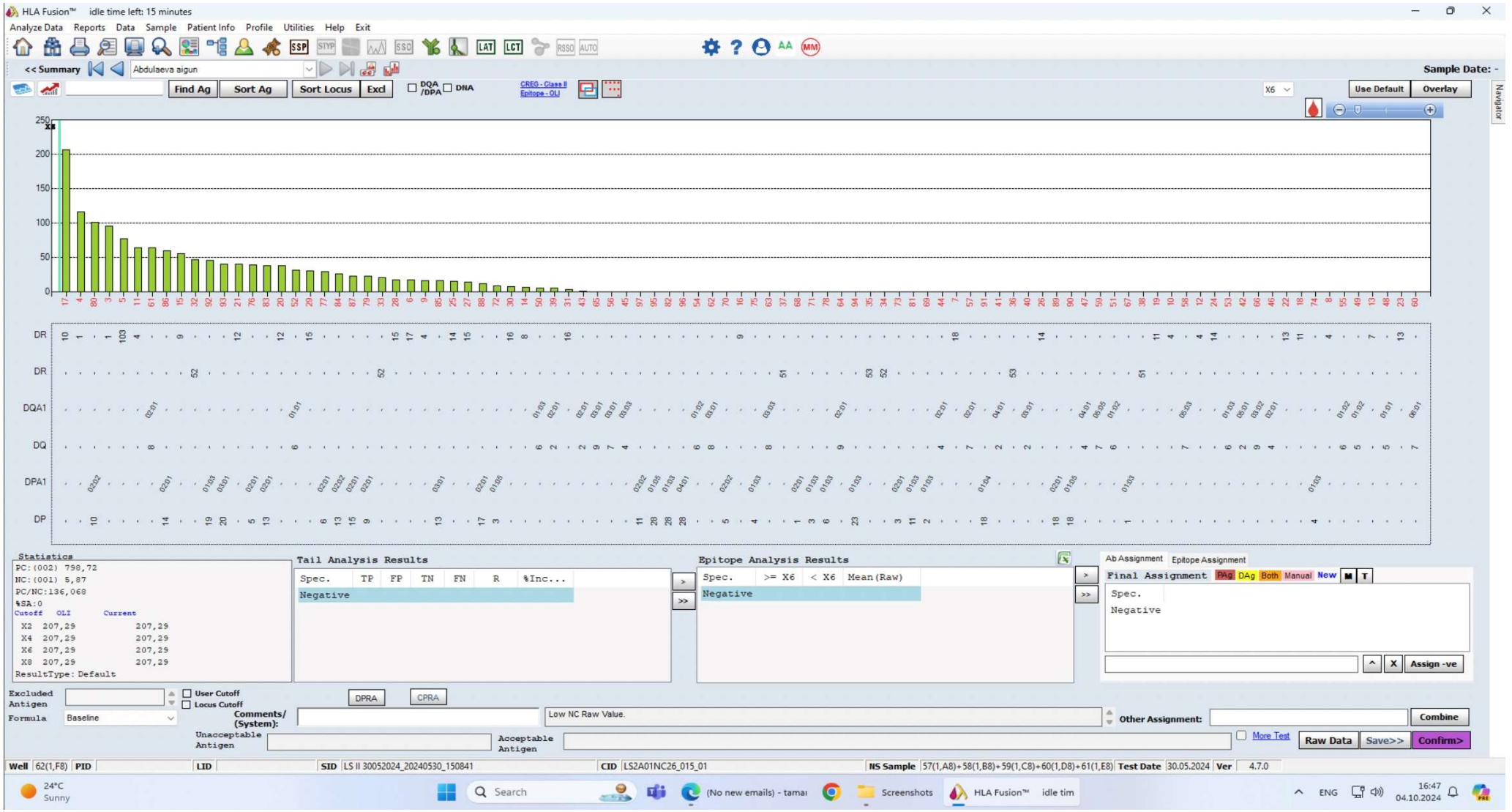
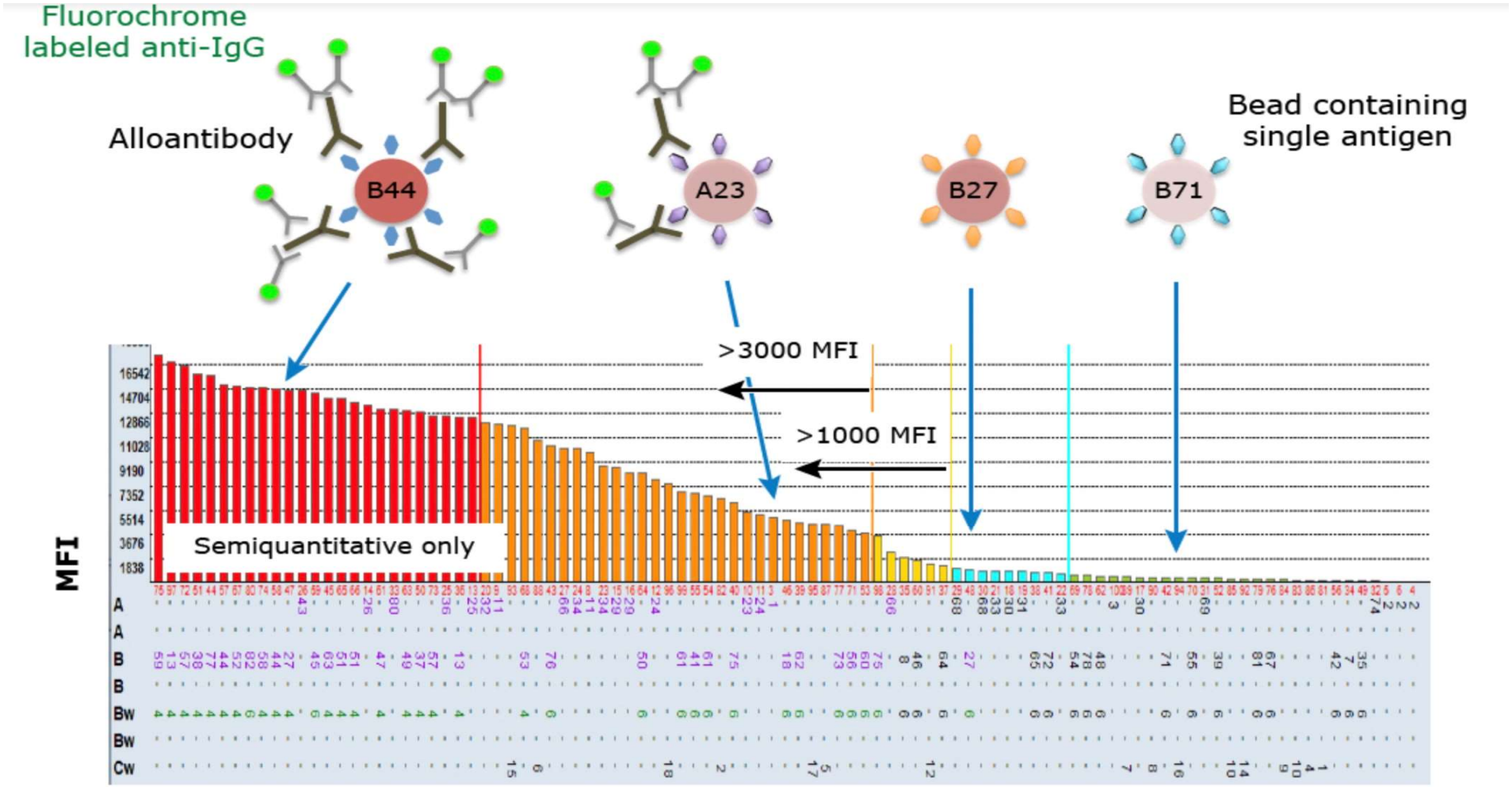
ENG
16:45
04.10.2024


HLA Fusion™ idle time left: 15 minutes
Analyze Data Reports Data Sample Patient Info Profile Utilities Help Exit
<< Summary
Abdulaeva aigun
Sample Date: -
Find Ag
Sort Ag
Sort Locus
Excl
DQA /DPA
DNA
CREG - Class II
Epitope - OLI
X6
Use Default
Overlay
Navigator
DR
DR
DQA1
DQ
DPA1
DP
Statistics
PC:(002) 798,72
NC:(001) 5,87
PC/NC:136,068
%SA:0
Cutoff OLI Current
X2 207,29 207,29
X4 207,29 207,29
X6 207,29 207,29
X8 207,29 207,29
ResultType: Default
Tail Analysis Results
Spec. TP FP TN FN R %Inc...
Negative
Epitope Analysis Results
Spec. >= X6 < X6 Mean(Raw)
Negative
Ab Assignment
Epitope Assignment
Final Assignment
PAg DAg Both Manual New
Spec.
Negative
Assign -ve
Excluded Antigen
User Cutoff
Locus Cutoff
Formula
Baseline
Comments/ (System):
DPRA
CPRA
Low NC Raw Value.
Other Assignment:
Combine
Unacceptable Antigen
Acceptable Antigen
More Test
Raw Data
Save>>
Confirm>
Well 62(1,F8) PID LID SID LS II 30052024_20240530_150841 CID LS2A01NC26_015_01 NS Sample 57(1,A8)+58(1,B8)+59(1,C8)+60(1,D8)+61(1,E8) Test Date 30.05.2024 Ver 4.7.0
24°C Sunny
Search
(No new emails) - tamai
Screenshots
HLA Fusion™ idle tim
ENG
16:47
04.10.2024

HLA ერთი ანტიგენის ბიდზე (SAB)



Melissa Y Yeung, MD, FRCPC.

Eurotransplant Reference Laboratory
Virtual PRA Calculator

Information

Unacceptable antigens:

A24,
B35, CW4, DR11
DQ1

Unacceptable antigens can only be entered divided by a space or a comma.

Calculate VPRA

Clear

Frequency of donors within the Eurotransplant area harbouring unacceptable antigens: **85,990% (8599 out of 10000, ETRL HLA database version 4.0)**

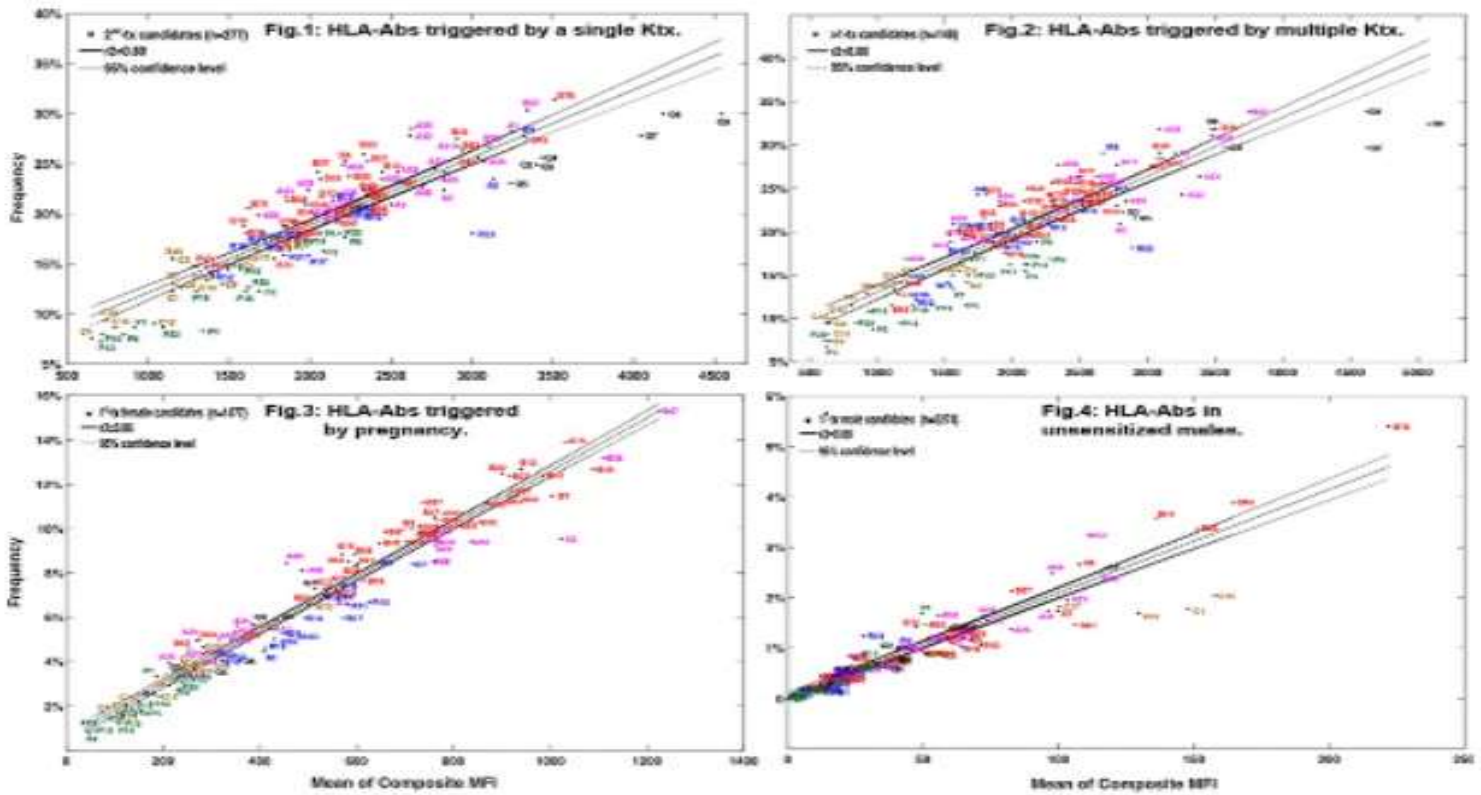
გასათვალისწინებელია

- ყველა DSA არ არის კლინიკურად აქტიური
- არ არის კონსესუსი მიღწეული MFI ზღურბლზე- cut- off

STAR სამუშაო ჯგუფმა შემოგვთავაზა MFI cut- off 1400

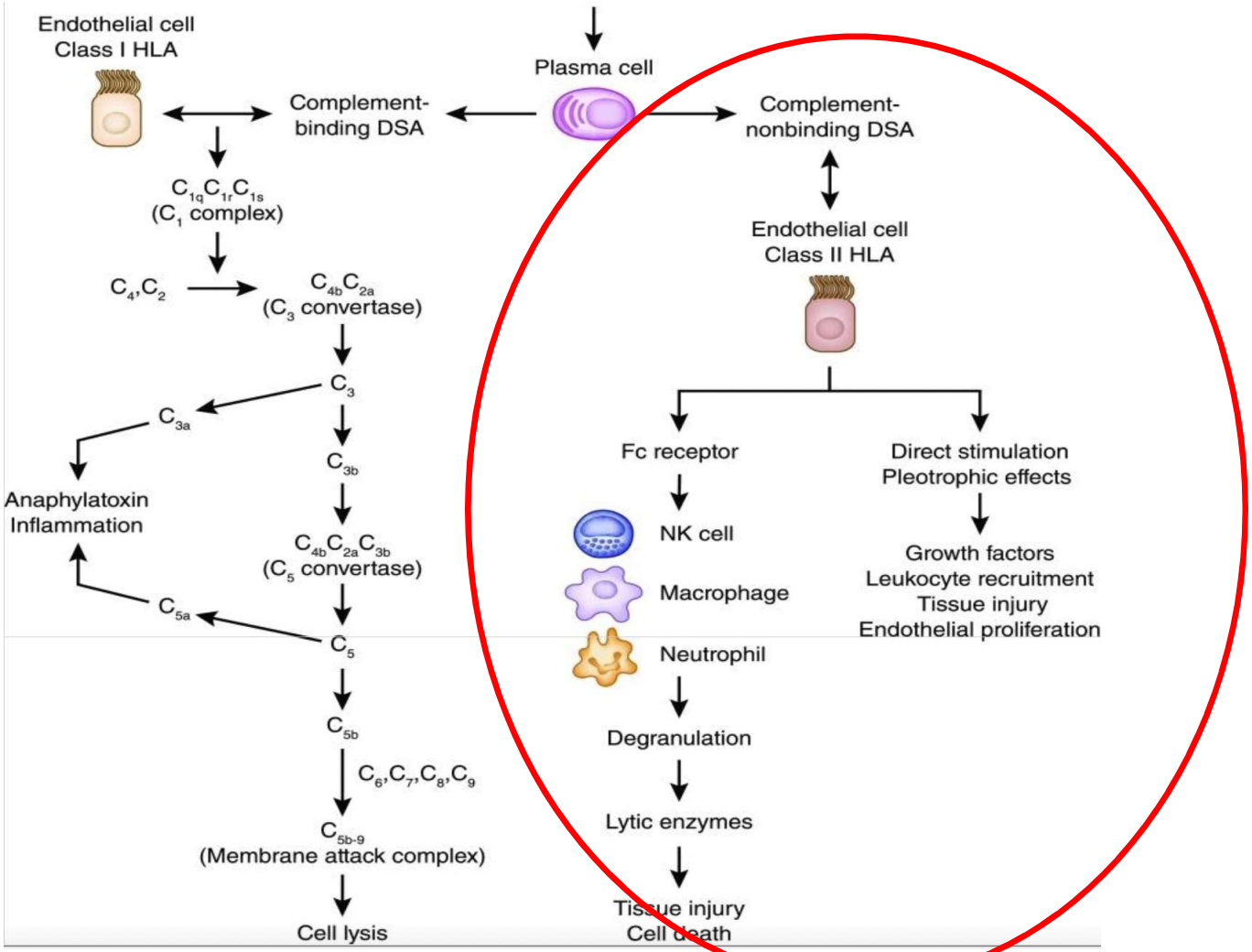
- ორი სხვადასხვა კიტი იძლევა განსხვავებულ და ზოგჯერ ურთიერთგამომრიცხავ შედეგებს (OL/LC)
- DSA - ს კომპლემენტთან დაკავშირების უნარი მოცილების სარწმუნო პრედიქტორია
- თუ DSA არ უკავშირდება კომპელემენტს DSA უვნებლად არ ითვლება
- IgG1/G3 აქვს კომპლემენტთან მეტად დაკავშირების უნარი
- განზავება/პროზონის ეფექტი

HLA-DQ, DR53-CREG და A2-CREG ანტიგენების იმუნოგენურობა



•Rajalingam, Raja et al Antibody Analysis of 4176 Candidates waiting for Kidney Transplantation Discover the Hierarchy of Antibody-Provoking HLA Types that Warrant Matching in Kidney Transplantation. Transplantation 102():p S216, July 2018. | DOI: 10.1097/01.tp.0000542876.15139.80

The three proposed pathogeneses of donor-specific antibodies (DSAs) in antibody-mediated rejection

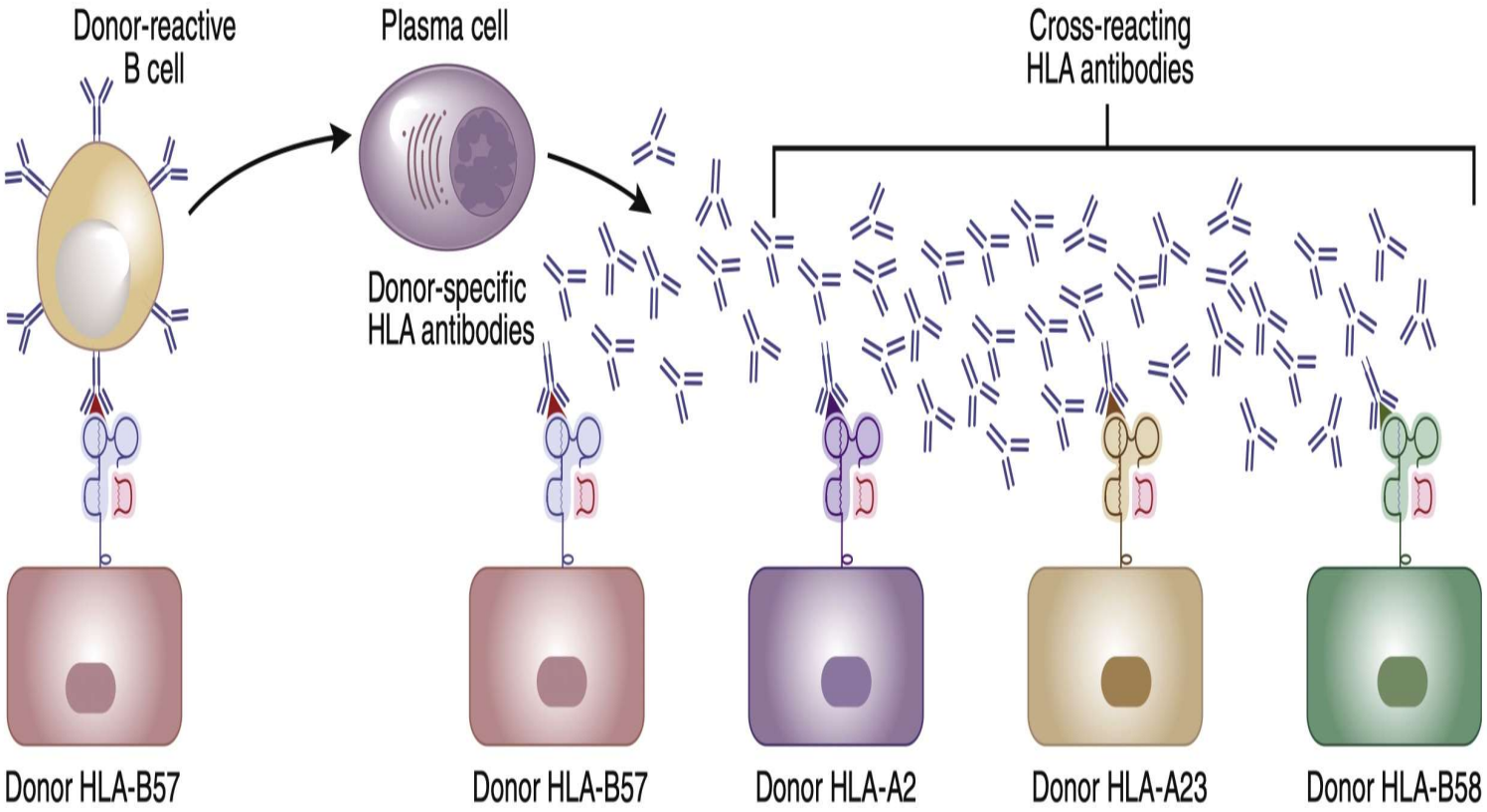


Clin J Am Soc Nephrol, 2017 Apr

		MFI observed		Cut-off				Bead-specific reactivity assignment			
Patient #	**Bead**	**LC**	**OL**	**LC**	**int OL (tx)**	**int OL (exp)**	**int OL (val)**	**LC**	**OL (tx)**	**OL (exp)**	**OL (val)**
Cutoff: Lifecodes (1000 MFI) and interpolated OL MFI											
7	*A*01:01*	1121	223	1000	3479	4942	5994	pos	neg	neg	neg
4	*C*01:02*	1260	6122	1000	6403	6646	7574	pos	neg	neg	neg
3	*DRB1*07:01*	1028	2328	1000	3073	2141	2895	pos	neg	pos	neg
9	*DRB3*01:01*	3529	32	1000	3073	2141	2895	pos	neg	neg	neg
7	*DQB1*02:01-DQA1*05:01*	293	13,775	1000	4083	5078	6392	neg	pos	pos	pos
Cutoff: One Lambda (3000 MFI) and interpolated LC MFI											
7	*A*01:01*	1121	223	3000	621	556	439	neg	pos	pos	pos
11	*C*03:04*	892	2952	3000	331	366	291	neg	pos	pos	pos
3	*DRB1*07:01*	1028	2328	3000	738	1435	1041	neg	pos	neg	neg
9	*DRB3*01:01*	3529	32	3000	738	1435	1041	neg	pos	pos	pos
7	*DQB1*02:01-DQA1*05:01*	293	13,775	3000	662	531	372	pos	neg	neg	neg
7	*DQB1*05:02-DQA1*01:02*	807	32	3000	662	531	372	neg	pos	pos	pos

Gonca E. Karahan et al, HLA, 2023

ჯვარედინი რეაქტილობა



Anat R. Tambur et al, Significance of HLA-DQ in kidney transplantation: time to reevaluate human leukocyte antigen–matching priorities to improve transplant outcomes? An expert review and recommendations, KI, 11.2021

ჯვარედინი რეაქტიულობის ჯგუფები

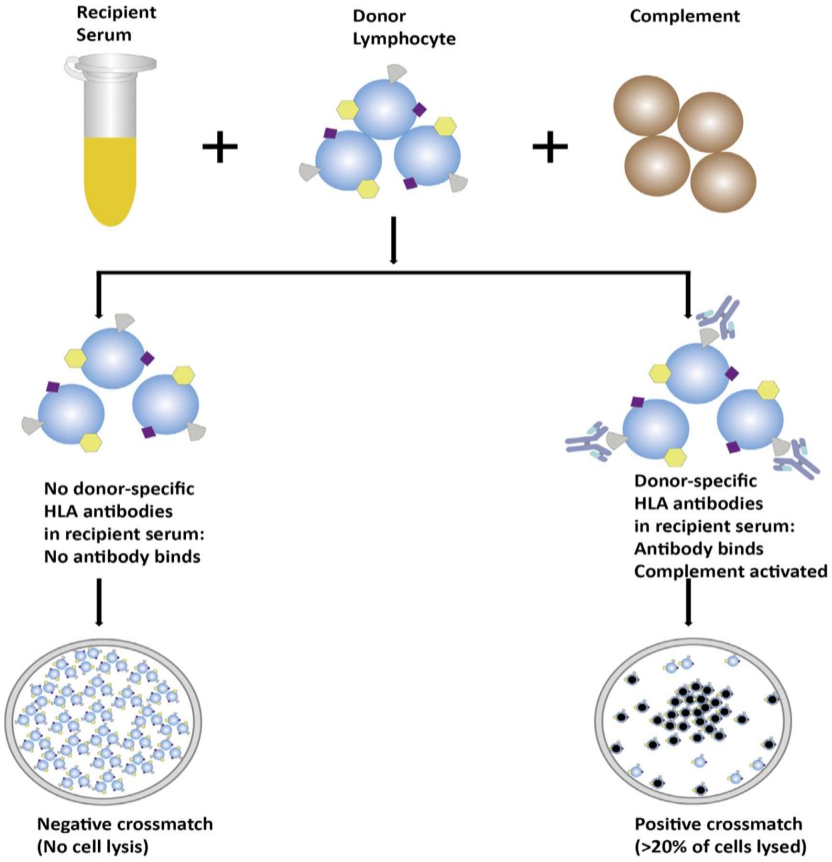
CREG groups	HLA antigens		
A1 CREG	A1, A3, A11, A23, A24, A29, A30, A31, A36, A80		
A2 CREG	A2, A23, A24, A68, A69, B57, B58		
A10 CREG	A11, A25, A26, A32, A33, A34, A43, A66, A68, A69, A74		
Bw4 CREG	A23, A24, A25, A32, B13, B27, B37, B44, B47, B38, B49, B51, N52, B53, B57, B58, B59, B63, B77		
Bw6 CREG	B7, B8, B18, B27: 08, B35, B39, B40, B4005, B41, B42, B45, B48, B50, B54, B55, B56, B60, B61, B62, B64, B65, B67, B70, B71, B72, B75, B76, B78, B81, B82		
B5 CREG	B18, B35, B46, B49, B50, B51, B52, B53, B57, B58, B62, B63, B71, B72, B73, B75, B76, B77, B78, B7		
B7 CREG	B7, B8, B13, B27, B41, B42, B47, B48, B54, B55, B56, B59, B60, B61, B67, B81, B82		
B8 CREG	B8, B18, B38, B39, B59, B64, B65, B67		
B12 CREG	B13, B37, B41, B44, B45, B47, B49, B50, B60, B61		
C1 CREG	Cw1, Cw7, Cw8, Cw9, Cw10, Cw12, Cw14, Cw16, Bw46, B73		
C2 CREG	Cw2, Cw4, Cw5, Cw6, Cw15, Cw17, Cw18		
DR1 CREG	DR1, DR10, DR103	DR51 CREG	DR51, DR15, DR16
DR52 CREG	DR52, DR11, DR12, DR13, DR14, DR17, DR18	DR53 CREG	DR53, DR4, DR7, DR9
DQ1 CREG	DQ5, DQ6	DQ2 CREG	DQ2
DQ3 CREG	DQ7, DQ8, DQ9	DQ4 CREG	DQ4
DP1c CREG	DP2, DP3, DP4, DP6, DP9, DP10, DP11, DP14, DP17, DP18, DP20, DP28	DP2c CREG	DP1, DP5, DP13, DP15, DP19, DP23

CREG: Cross-reactive group

Indian Journal of Transplantation ¦ Volume 15 ¦ Issue 1 ¦ January-March 2021

CDC Crossmatch 1969 წ

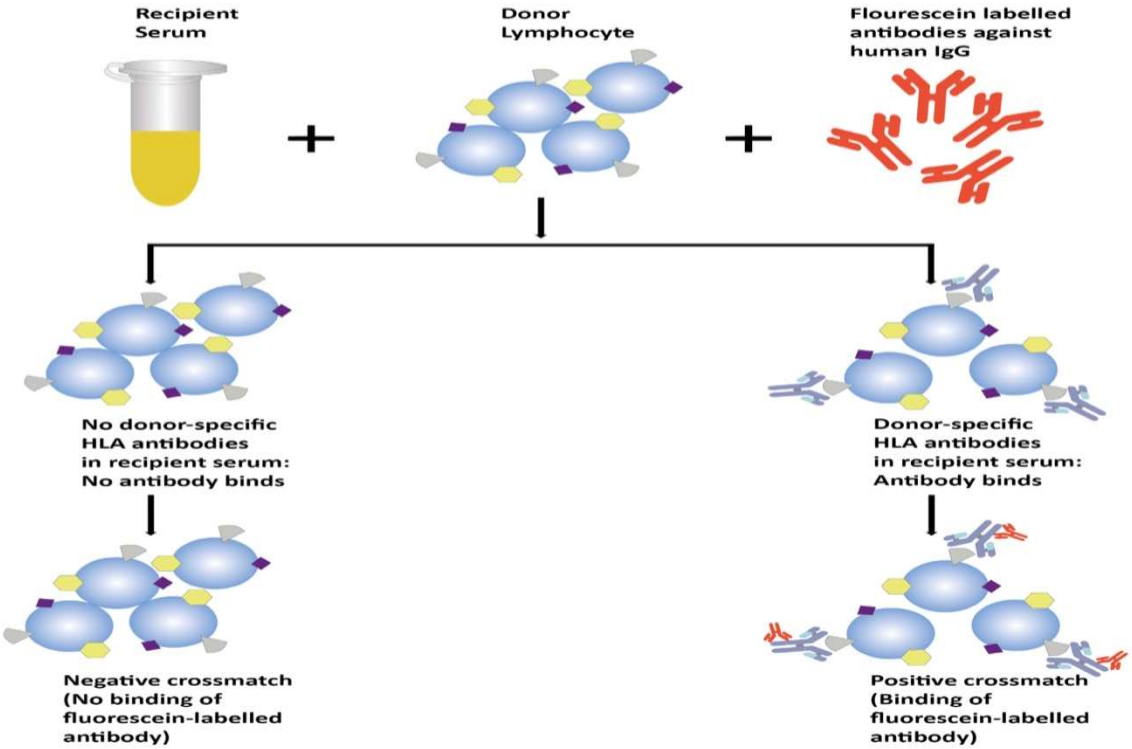
შეთავსება დაფუძნებული კომპლემენტზე დამოკიდებულ ციტოტოქსიურობაზე



Transplantology 2024, 5, 85–97, Vikash Chandra Mishra et al

პოლ ტერასაკი

Flow Crossmatch 1980’ → ჰოლოფასტერის პროტოკოლი 2014 წ



Transplantology 2024, 5, 85–97, Vikash Chandra Mishra et al

ვირტუალური შეთავსება

აქვს პაციენტს HLA ანტისხეულები?

თუ კი, რამდენია MFI ?

არის რომელი ანტისხეული მიმართული დონორის HLA-ს წინააღმდეგ? DSA

ადაპტირებული Transplantology 2024, 5, 85–97, Vikash Chandra Mishra et al

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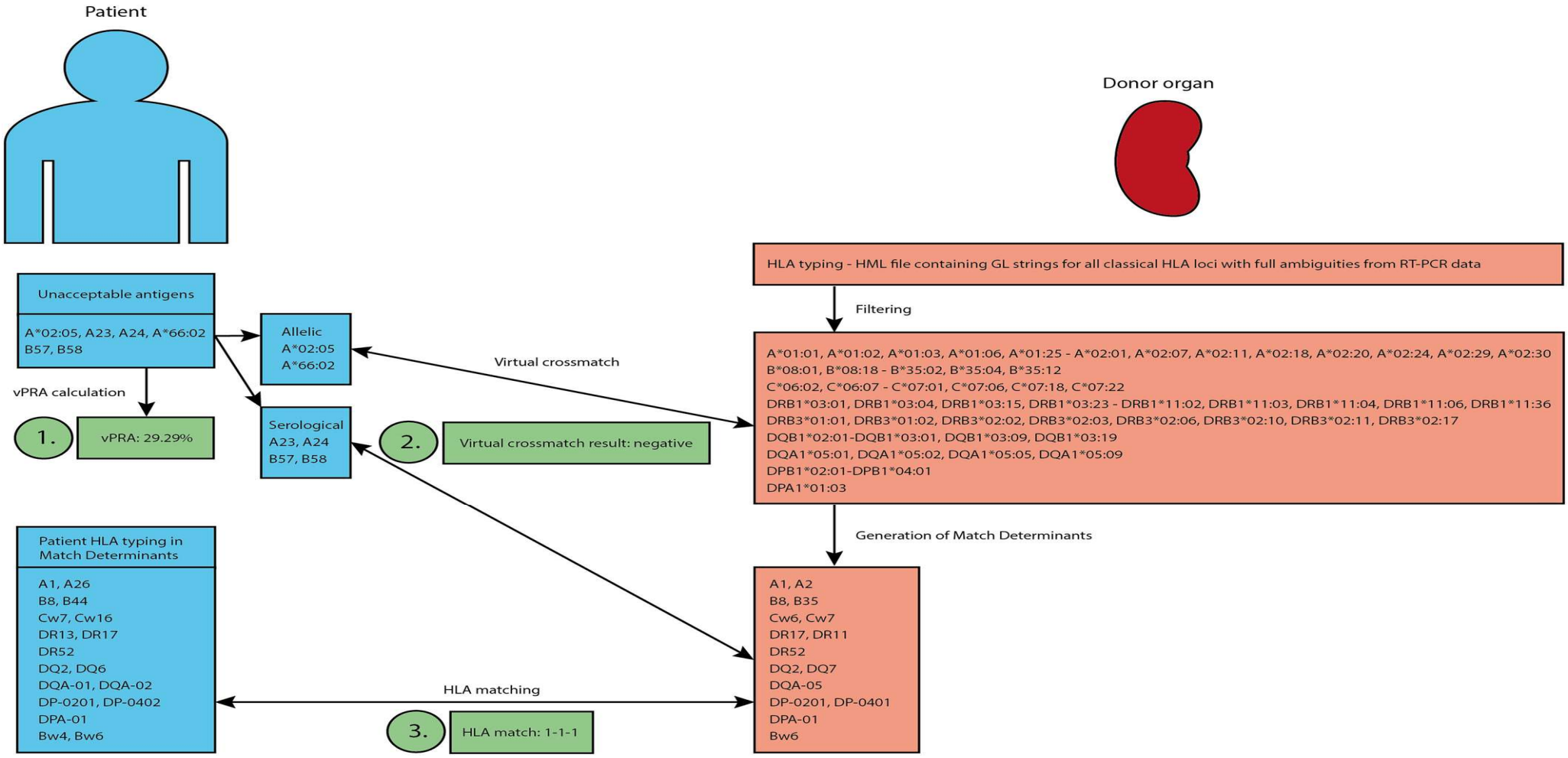
ვირტუალური შეთავსება ევროტრანსპლანტში



HLA, Volume: 104, Issue: 2, First published: 22 August 2024, DOI: (10.1111/tan.15653)

CDC Crossmatch	Flow Crossmatch	Single-Antigen Bead (SAB) (Virtual Cross Match)	Perspective
Positive	Positive	Positive	▪ Substantial burden of DSA. ▪ Elevated potential for hyperacute rejection.
Negative	Positive	Positive	▪ Moderate level of DSA impact ▪ Non-complement-fixing DSA
Negative	Negative	Positive	▪ Minimizing the impact of DSA ▪ False-positive SAB test and the Possible causes include • High background due to serum factors binding to latex beads • Binding to denatured antigen • Setting a low threshold for designating an antibody as positive (overcalling)
Positive	Positive	Negative	▪ Binding of non-HLA IgG to antigens present on the surface of lymphocytes. ▪ Drug interference (e.g., Rituximab, ATG, alemtuzumab, IVIG). ▪ False-negative SAB test and the reason could be: • The bead panel lacks representation of the donor antigen/allele. • The presence of inhibitors in serum, causing a “prozone” effect. • IgM/IVIG binding to the beads, masking the detection of IgG alloantibody. • Low-level anti-HLA antibody against a shared epitope, which is “diluted out” across multiple beads, leading to an under-representation of the true antibody burden.
Positive	Negative	Negative	▪ IgM antibody (can be either anti-HLA or non-HLA)
Negative	Positive	Negative	▪ Low-level IgG non-HLA antibody ▪ False-negative SAB test (see above for details)

Transplantology **2024**, *5*(2), 85-97;

Flow შეთავსების ნაკლოვანებები

- არ განირჩევა Class I Class II-სგან
  - მხოლოდ დადებითი T უჯრედები - HLA კლასი უცნობია, ორივე T და B უჯრედები შეიძლება იყოს Class I
  - მხოლოდ დადებითი B უჯრედები - HLA კლასი უცნობია, ორივე კლასი I და II წარმოდგენილია B უჯრედებზე
- ცრუ დადებითი შედეგი:
  - აუტოანტისხეულები, Non HLAანტისხეულები...
  - მკურნალობის გავლენა (მაგ, რიტუქსიმაბი, ATG, IVIG)

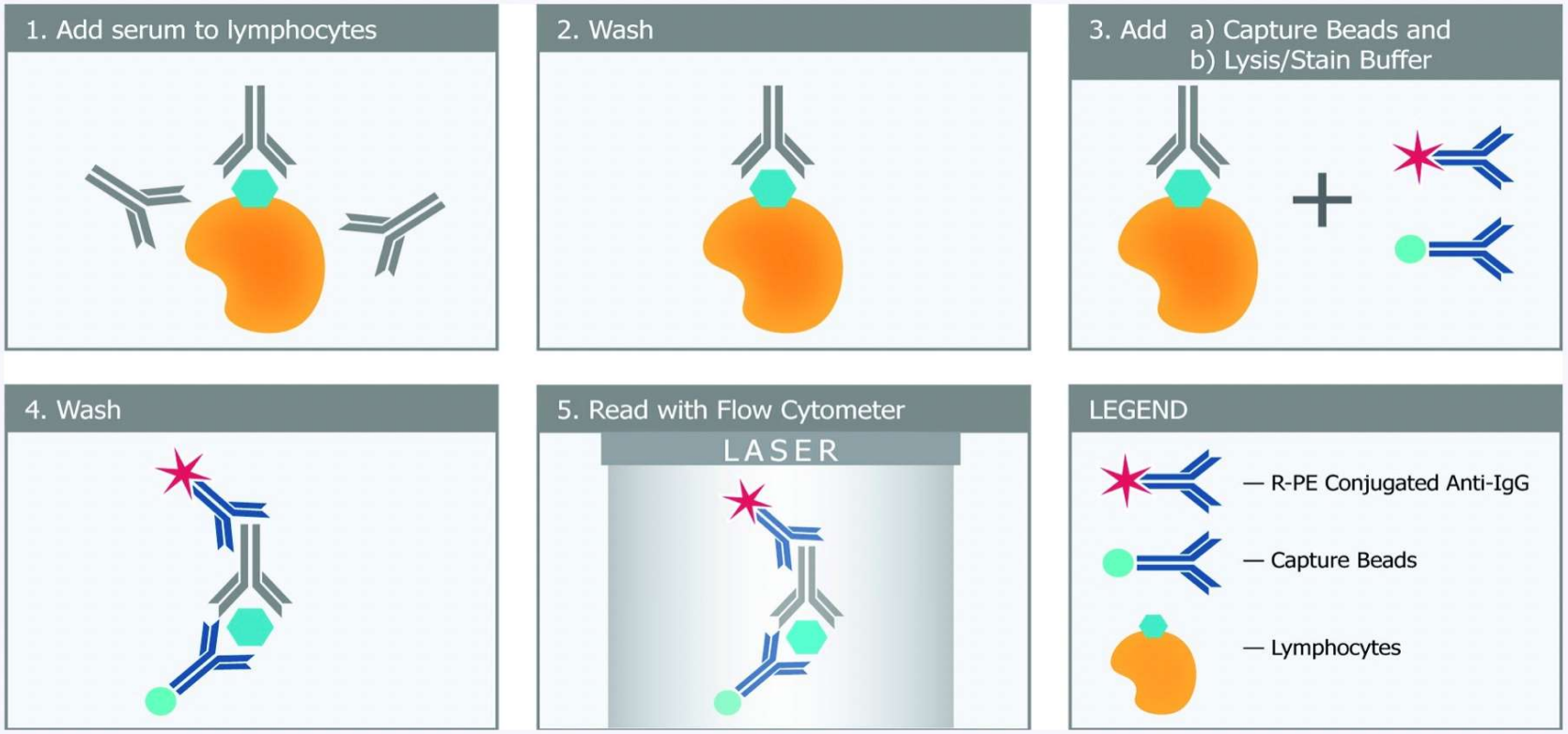
Original Clinical Science—General

DSA-FXM: Accelerated Donor-specific Flow Crossmatch Discriminating Class I and II Antibody Specifically and Only to Donor HLA for Determining True Incompatibility

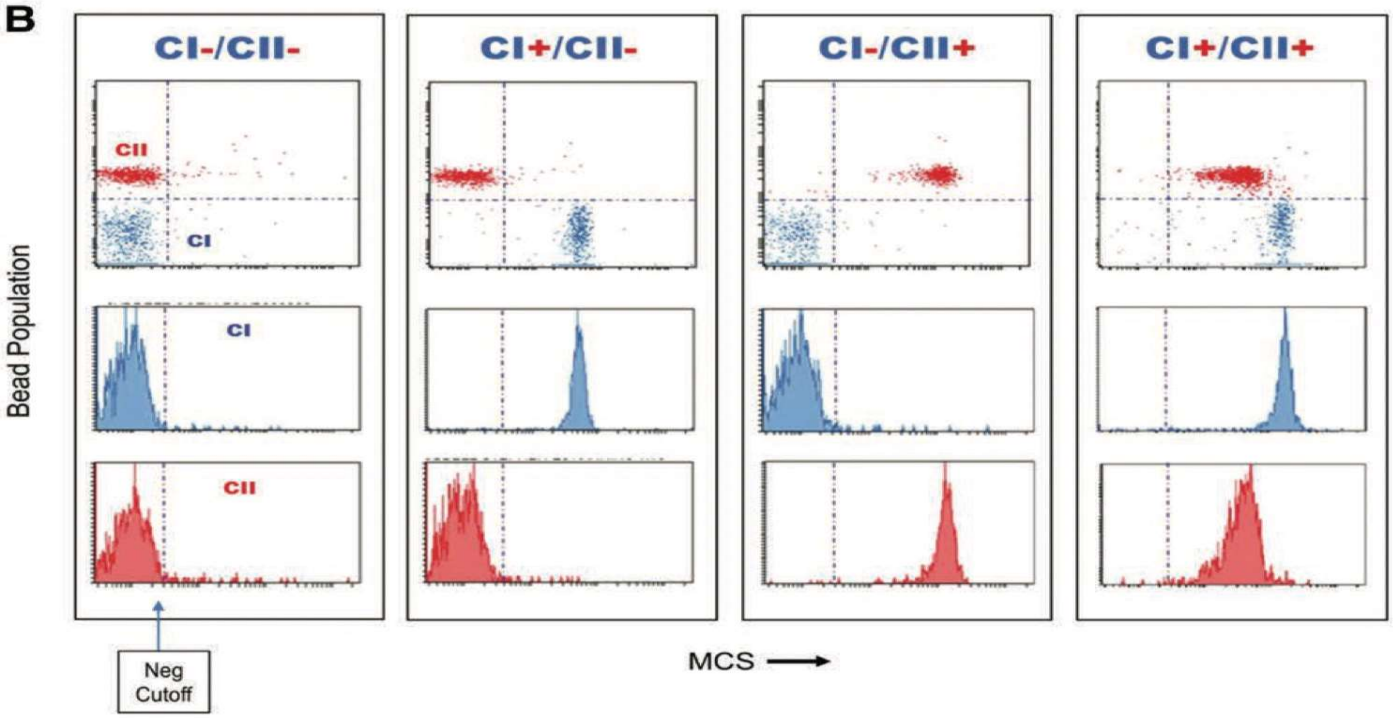
Ge Chen, MD,[1] Lingling Lin, MD,[1] and Dolly B. Tyan, PhD[1,2]

Background. Worldwide, a final crossmatch is the gold standard for determining compatibility between patient and donor before solid organ transplantation and preventing hyperacute rejection. In the absence of autoantibodies, an incompatible crossmatch in a sensitized patient is attributed to mismatched donor HLA. However, current physical crossmatch methods cannot distinguish reactivity to HLA from other clinically irrelevant cell surface targets nor the class of HLA if it is the target. Result interpretation is difficult or impossible when autoantibodies, alloantibodies, or therapeutic antibodies coexist. **Methods.** Herein, we describe a unique donor-specific flow crossmatch (DSA-FXM) that distinguishes HLA class I or II donor-specific antibody bound to HLA antigens on the donor cell surface in their native conformation that is not impacted by rituximab, anti-thymocyte globulin (after absorption), or autoantibodies. It is HLA specific. **Results.** We compared the results of single-antigen antibody testing, autoreactive and alloreactive flow cytometry crossmatches (FXM) using traditional FXM and our DSA-FXM method from 94 patients (enriched for auto+/allo+ pairs; n = 64) against 110 donors (338 tests) and show that, in our cohort, positive traditional FXM results are not directed to donor HLA 60.25% of the time and negative traditional FXM results are missing HLA donor-specific antibody 36.2% of the time based on the DSA-FXM. **Conclusions.**

DSA უკავშირდება სამიზნეHLA-s წინასწარი ექსტრაქციის, კონიუგაციის და დონორის HLA -ს პურიფიკაციის გარეშე



Flow DSA Crossmatch Readout



Chen, Ge; Lin, Lingling; Tyan, Dolly B. Transplantation104(4):813-822, April 2020.
DSA-FXM: Accelerated Donor-specific Flow Crossmatch Discriminating Class I and II Antibody Specifically and Only to Donor HLA for Determining True Incompatibility

ბიდების მონიშვნა

The MCS cutoff 3 ბიდითვის:
CI ≥93%, CIIa ≥66%, and CIIb ≥46%

Class II a	• ყველა DQ და სუსტად ზოგი DR
Class IIb	• ყველა CII მაგრამ ნაკლებად ეფექტური DQ2 და DQ6 -ზე

სენსიტიურობა და სპეციფიურობა Class I

Sensitivity comparison of CI HLA antibody detection using FXM, DSA-FXM, and SAB methods

	FXM (MCS)		DSA-FXM (MCS)		LMX-IgG (MFI)
Serum dilution	**T**	**B**	**CI**	**CII**	**HLA-B7**
Neat	404[a]	423[a]	681[a]	17	10 455[a]
1:10	194[a]	229[a]	397[a]	33	3288[a]
1:25	112[a]	128[a]	288[a]	9	1338[a]
1:50	64	55	214[a]	15	688
1:100	33	9	162[a]	–10	359
1:500	0	–1	37	–6	82
1:1000	–3	1	12	5	23

[a]Positive cutoff thresholds: LMX-IgG (SAB) ≥1000 MFI; FXM: T ≥88 MCS, B ≥100 MCS; DSA-FXM: CI ≥93 MCS, CII ≥66 MCS.
CI, class I; CII, class II; DSA-FXM, donor-specific flow crossmatch; FXM, flow cytometry crossmatch; LMX, Luminex; MCS, median channel shift; MFI, mean fluorescence intensity; SAB, single-antigen bead.

Sensitivity and Specifisity

Sensitivity comparison of CII HLA antibody detection using FXM, DSA-FXM, and SAB methods

	FXM (MCS)		DSA-FXM (MCS)		LMX-IgG (MFI)
Serum dilution	T	B	CI	CII	HLA-DR4
NEAT	9	346[a]	166[a]	741[a]	13 369,[a] 12 473,[a] 12 188,[a] 9559,[a] 8646[a]
1:100	6	199[a]	–10	356[a]	1447,[a] 1440,[a] 1413,[a] 1049,[a] 847
1:500	4	42	–44	158[a]	253, 232, 227, 188, 114
1:1000	3	–3	–43	94[a]	15, 12, 12, 11, 10

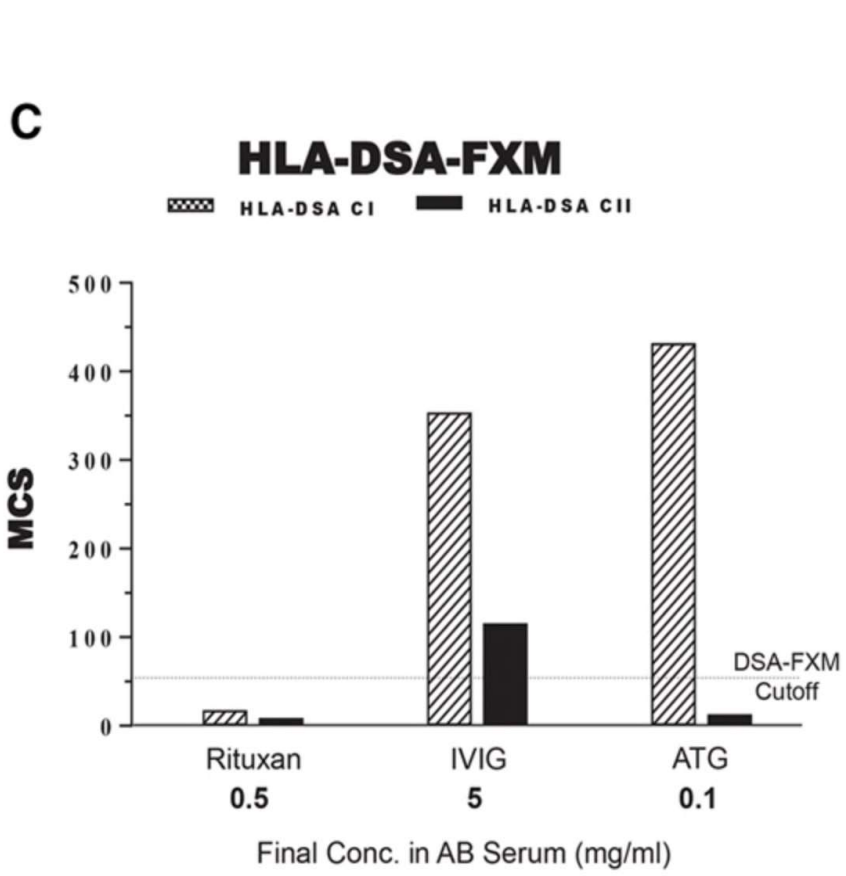
Sensitivity comparison of CI and II HLA antibody detection using FXM, DSA-FXM, and SAB methods simultaneously

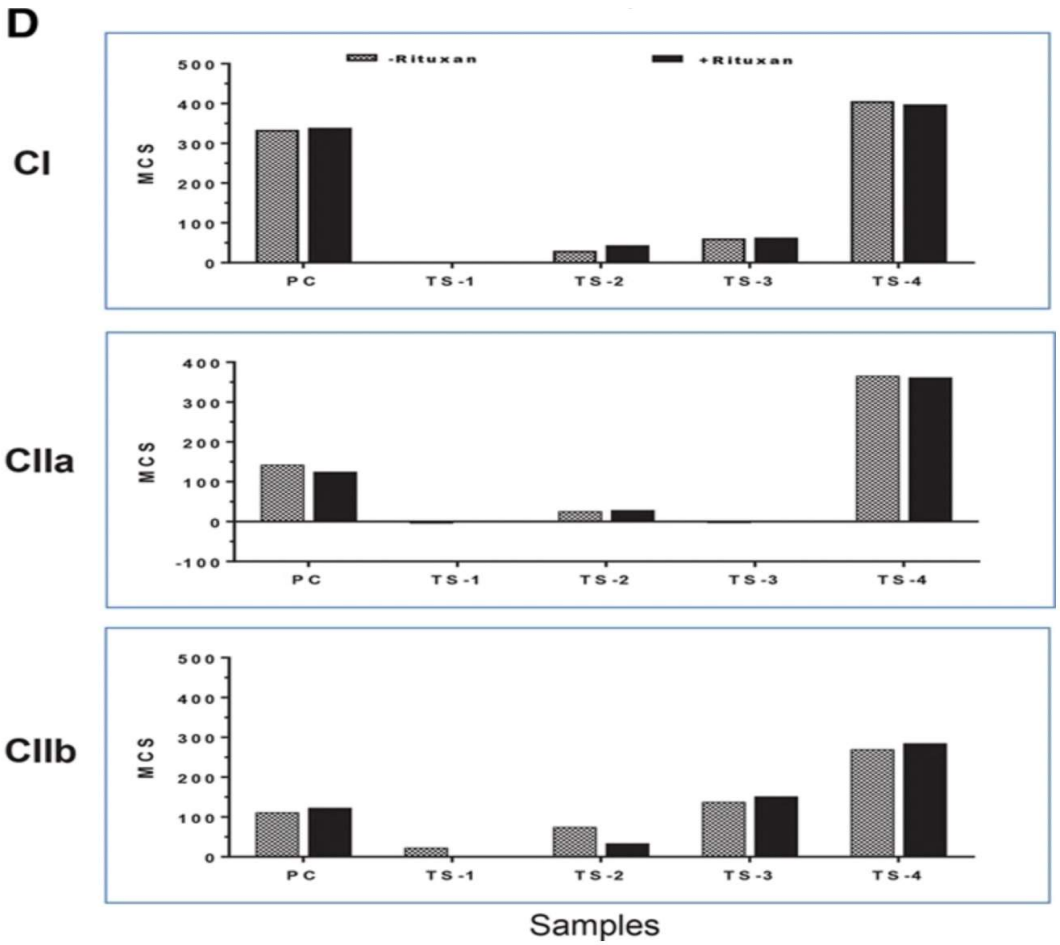
	FXM (MCS)		DSA-FXM (MCS)		LMX-IgG-DSA (MFI)					
Pos control dilution	T	B	CI	CII	CI			CII		
1:500	271[a]	251[a]	368[a]	390[a]	3846,[a] 3106,[a] 2656[a]	1716[a]	1872[a]	921, 594	1064[a]	2381,[a] 974
1:1000	205[a]	183[a]	284[a]	327[a]	2808,[a] 2240,[a] 2005[a]	1164[a]	1389[a]	413, 269	540	658, 265
1:2000	146[a]	119[a]	201[a]	225[a]	1577,[a] 1218,[a] 1086[a]	560	680	219, 144	282	658, 238
1:4000	94[a]	41	133[a]	167[a]	715, 512, 486	242	292	122, 88	148	132, 53
1:8000	58	1	90	110[a]	409, 296, 280	116	149	69, 49	81	77, 32

[a]Positive cutoff thresholds: LMX-IgG (SAB) ≥1000 MFI; FXM: T ≥88 MCS, B ≥100 MCS; DSA-FXM: CI ≥93 MCS, CII ≥66 MCS.

CI, class I; CII, class II; DSA-FXM, donor-specific flow crossmatch; FXM, flow cytometry crossmatch; LMX, Luminex; MCS, median channel shift; MFI, mean fluorescence intensity; SAB, single-antigen bead.

Therapeutic Drug Interference





ჩვენი ცენტრის იმუნოლოგიური თავსებადობადობის ტესტების დინამიკა
Work in progress

2019	• Flow DSA Cross match (N-220)
2021	• HLA Typing -11 ლოკუსი LikSeq SSO(N-223)
2024	• HLA antibody screening- Luminex (N-62)

DSA FXM /SABკორელაცია

FLOW DSA crossmatch Class I neg / DSA Class I neg	36 (97%)	
FLOW DSA crossmatch Class I pos / DSA Class I pos	0	
FLOW DSA crossmatch Class II neg /DSA Class II neg	34(92%)	
FLOW DSA crossmatch Class II pos /DSA Class II pos	0	
FLOW DSA crossmatch Class I **neg** /DSA Class I **pos**	1(0.02%)	DSA - A24:03- **1864?**
FLOW DSA crossmatch Class II **neg** /DSA Class II **pos**	3 (0.08	1. DSA: DQA1:01:02- **3007**, DQA101:01-**2240** ,DQA101:03- **1289** DQ5-**2972,** 2. Class II- DR53- **2842** 3. RDB11:01- **1890,** DQB1:03:01**-1579**
FLOW DSA crossmatch Class I **pos** /DSA Class I **neg**	0	
FLOW DSA crossmatch Class II **pos** /DSA Class II **neg**	0	

Total N- 37

კლინიკური შემთხვევა 1

- პაციენტი 50 წლის ქალი, დონორი- და 54 წ
- პირველი ტრანსპლანტაცია, ორი ორსულობა
- Flow DSA Crossmatch – Class I, II a,II b negative
- SAB- **Class I** -B7-7074,B81- 6518, B60- 4546, B27- 4429, B48-4268,B61- 4136, B47-3230, B13- 2781, B51- 2607, B73- 2262,A66-2028, B52- 1651, B49- 1649, B42- 1563, B67- 1482, B64- 1218,B63-1212, B18- 1194, B78- 1112
- SAB **Class II**- neg

HLA mismatch

დღე 0- DSA neg

დონ	A*24, A*26	B*38 B*55	C* 01 C*12	DRB1*11	DRB3*01 DRB3*02	DQA1*01 DQA1*01	DPA1*01 DPA1*03	DQB1*03 DQB1*06
პაც	A*26 A*29	B*35 B*38	C*04 C*05	DRB1*01 DRB1*11	DRB3*02	DQA1*01 DQA1*05	DPA1*01 DPA1*01	DQB1*03 DQB1*05

კლინიკური შემთხვევა 2

- **პაციენტი 31 წლის ქალი, დონორი- მეგობარი 35 წ**
- **მეორე ტრანსპლანტაცია,** პირველი ტრასნპლანტაცია (დონორი დედა) 2 წლის წინ დასრულდა მოცილებით იმუნოსუპრსანტების არარეგულარული მიღების გამო. **3 ორსულობა**
- Flow DSA Crossmatch – Class I, II a,II b negative
- DSA- neg

HLA Mismatch

დონ	A*02 A*24	B*35B*51	C*04 C*15	DRB1*04 DRB1*11	DRB3*02 DRB4*02	DQA1*03 DQA1*05	DPA1*01 DPA1*01	DQB1*03 DQB1*03
რეც	A*02 A*26	B*38 B*44	C*07 C*12	DRB 1*11 DRB1*16	DRB3*02 DRB5*02	DQA1*01 DQA1*05	DPA1*01 DPA1*01	DQB1*03 DQB1*05

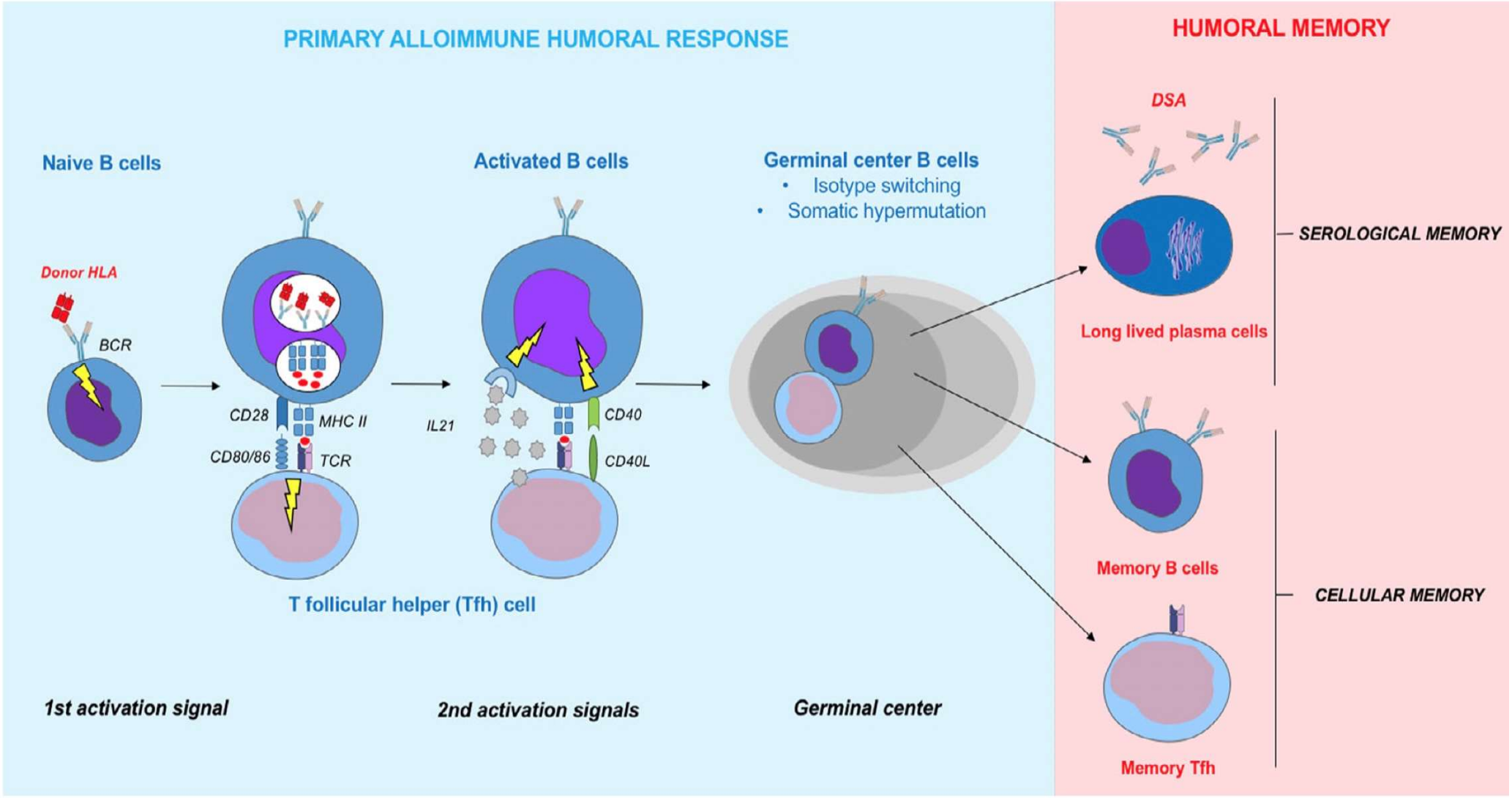
კლინიკური შემთხვევა 3

- პაციენტი 27 წლის ქალი , პირველი ტრანსპლანტაცია, 2 ორსულობა
- დონორობის სურვილს გამოთქვამს მეუღლე 30 წ (შვილების მამა) და საუკეთესო მეგობარი 28 წ

- Flow DSA Crossmatch ორივე დონორთან – Class I, II a,II b negative
- HLA neg, DSA neg ორივე დონორთან

რომელი დონორს აირჩევთ?

მეგობარი	A*02A*26	B*44 B*39	DRB1*01 DRB1*16	DQA1*01 DQA1*05	DPA1*01 DPA 1*04	C*07 C*12	DRB3*01 DRB5*02	DQB1*05 DQB1*05
ქმარი	A*02A*03	B*38 B*39	DRB1*11 DRB1*16	DQA1*01 DQA1*05	DPA1*01 DPA 1*04	C*12 C*06	DRB3*02 DRB5*02	DQB1*03 DQB1*05
პაც	A*02,	B*35 B*39	DRB1*10 DRB1*16	DQA1*01 DQA1*01	DPA1*01 DPA 1*01	C*04 C*	DRB5*02	DQB1*05 DQB11*05



Oriol Bestard **Stratifying the humoral risk of candidates to a solid organ transplantation: a proposal of the ENGAGE working group Transp. Int 2021** | June

მაღალი DSA
წარსულში

ESOT | Transplant International

GUIDELINES
published: 10 August 2022
doi: 10.3389/ti.2022.10511

ახალი კონცეფცია: DSA ნეგატიური სენსიბილიზებული პაციენტი

Transplantation Working Group

Nizam Mamode[1], Oriol Bestard[2], Frans Claas[3,4], Lucrezia Furian[5], Siân Griffin[6], Christophe Legendre[7], Liset Pengel[8] and Maarten Naesens[9]*

[1]Department of Transplantation, Guys Hospital, London, United Kingdom, [2]Department of Nephrology and Kidney Transplantation, Vall d'Hebrón University Hospital, Barcelona, Spain, [3]Department of Immunology, Leiden University Medical Center, Leiden, Netherlands, [4]Department of Immunology, University of Antwerp, Antwerp, Belgium, [5]Kidney and Pancreas Transplantation Unit, Department of Surgical Gastroenterological and Oncological Sciences, University Hospital of Padua, Padua, Italy, [6]Department of Nephrology, University Hospital of Wales, Cardiff, United Kingdom, [7]Department of Nephrology and Adult

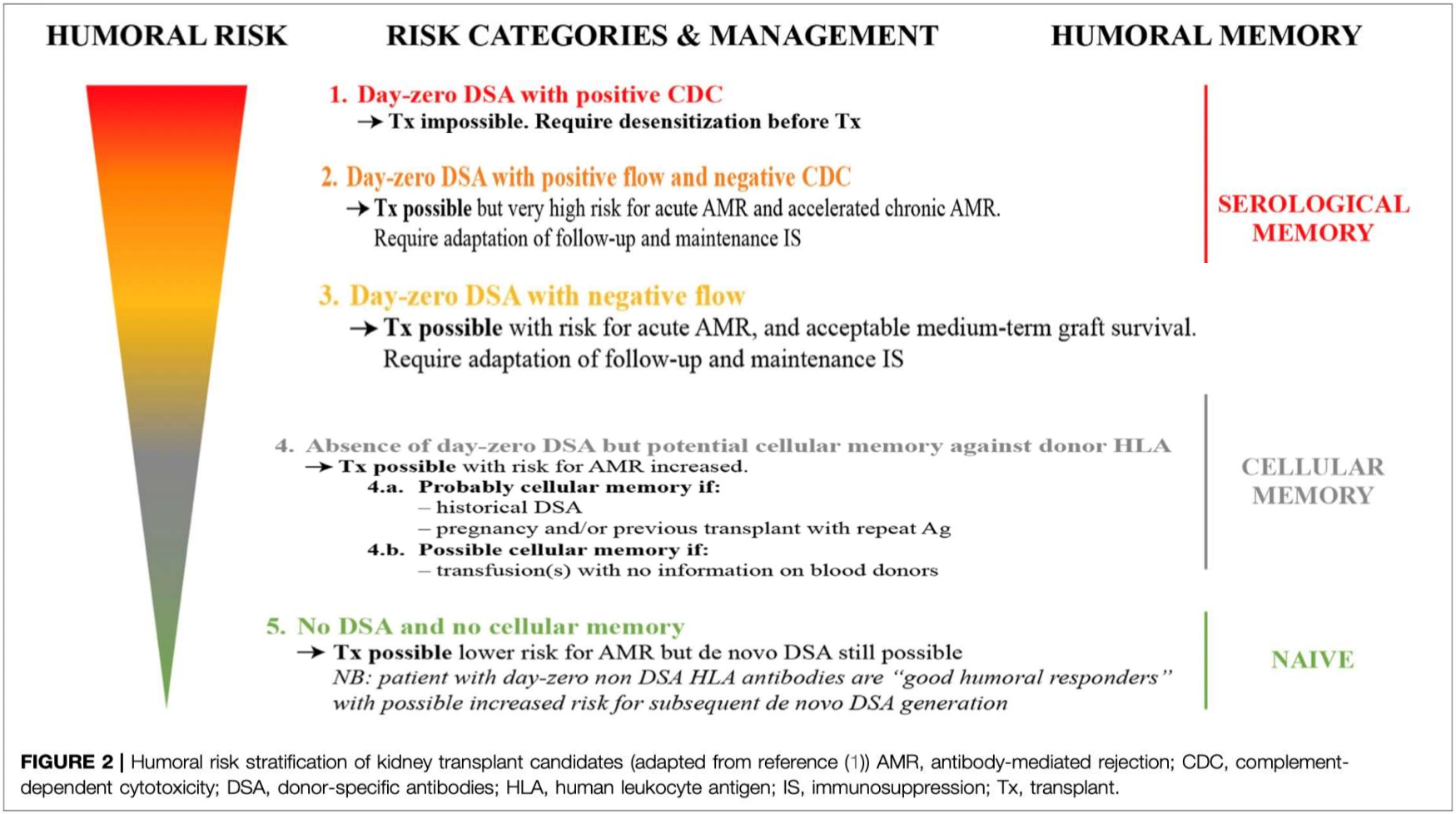
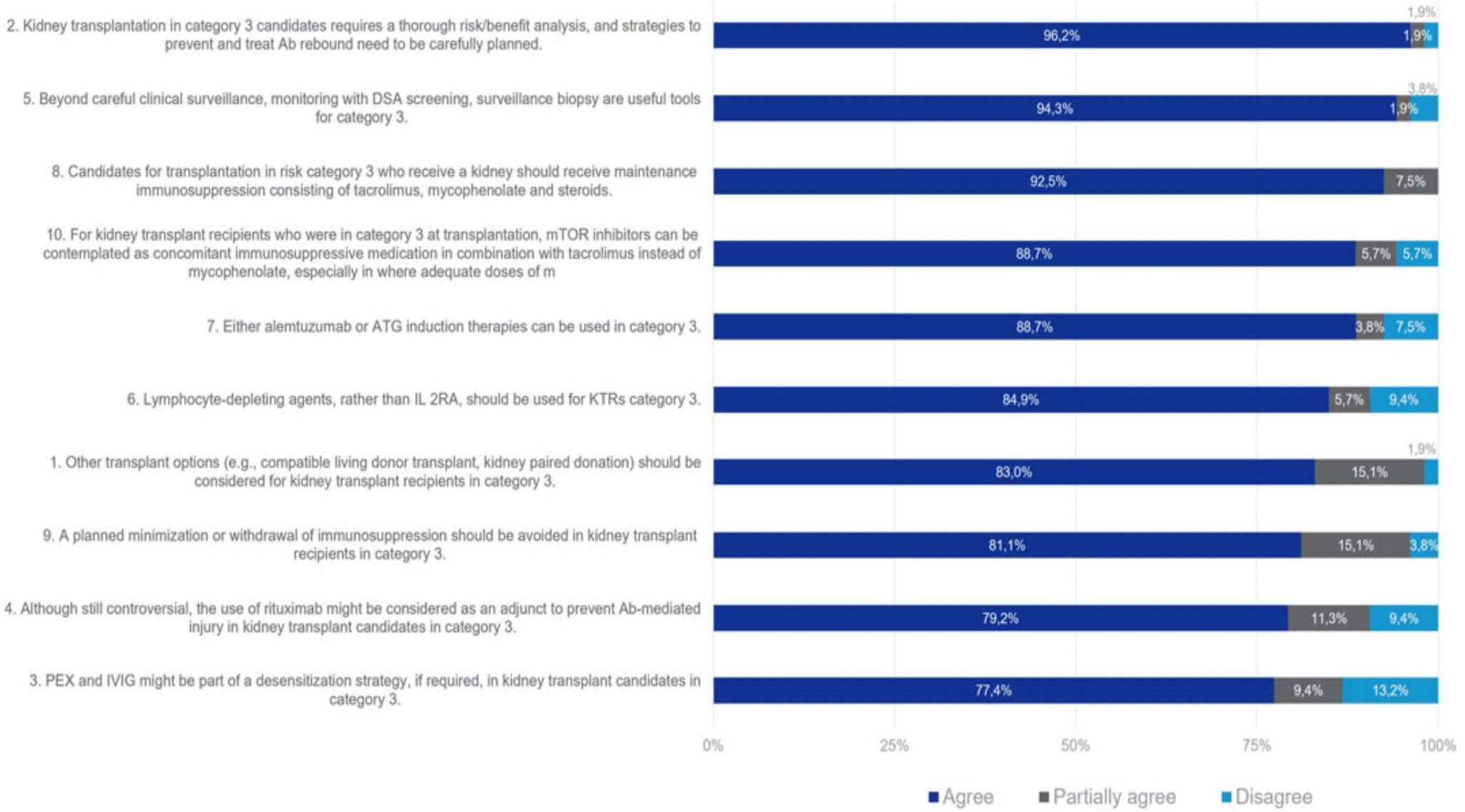
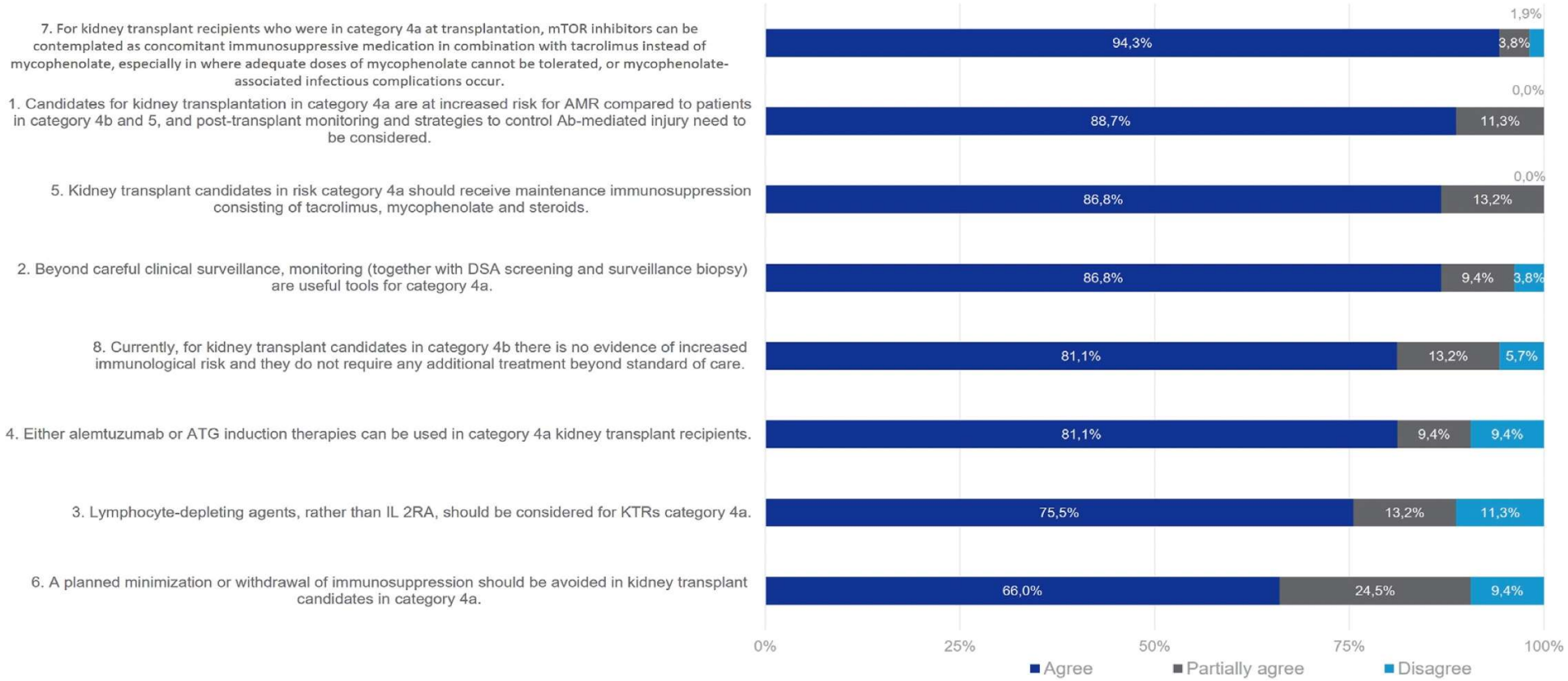


FIGURE 2 | Humoral risk stratification of kidney transplant candidates (adapted from reference (1)) AMR, antibody-mediated rejection; CDC, complement-dependent cytotoxicity; DSA, donor-specific antibodies; HLA, human leukocyte antigen; IS, immunosuppression; Tx, transplant.


2. Kidney transplantation in category 3 candidates requires a thorough risk/benefit analysis, and strategies to prevent and treat Ab rebound need to be carefully planned.
96,2%
1,9%
1,9%
5. Beyond careful clinical surveillance, monitoring with DSA screening, surveillance biopsy are useful tools for category 3.
94,3%
1,9%
3,8%
8. Candidates for transplantation in risk category 3 who receive a kidney should receive maintenance immunosuppression consisting of tacrolimus, mycophenolate and steroids.
92,5%
7,5%
10. For kidney transplant recipients who were in category 3 at transplantation, mTOR inhibitors can be contemplated as concomitant immunosuppressive medication in combination with tacrolimus instead of mycophenolate, especially in where adequate doses of m
88,7%
5,7%
5,7%
7. Either alemtuzumab or ATG induction therapies can be used in category 3.
88,7%
3,8%
7,5%
6. Lymphocyte-depleting agents, rather than IL 2RA, should be used for KTRs category 3.
84,9%
5,7%
9,4%
1. Other transplant options (e.g., compatible living donor transplant, kidney paired donation) should be considered for kidney transplant recipients in category 3.
83,0%
15,1%
1,9%
9. A planned minimization or withdrawal of immunosuppression should be avoided in kidney transplant recipients in category 3.
81,1%
15,1%
3,8%
4. Although still controversial, the use of rituximab might be considered as an adjunct to prevent Ab-mediated injury in kidney transplant candidates in category 3.
79,2%
11,3%
9,4%
3. PEX and IVIG might be part of a desensitization strategy, if required, in kidney transplant candidates in category 3.
77,4%
9,4%
13,2%
0%
25%
50%
75%
100%
Agree
Partially agree
Disagree

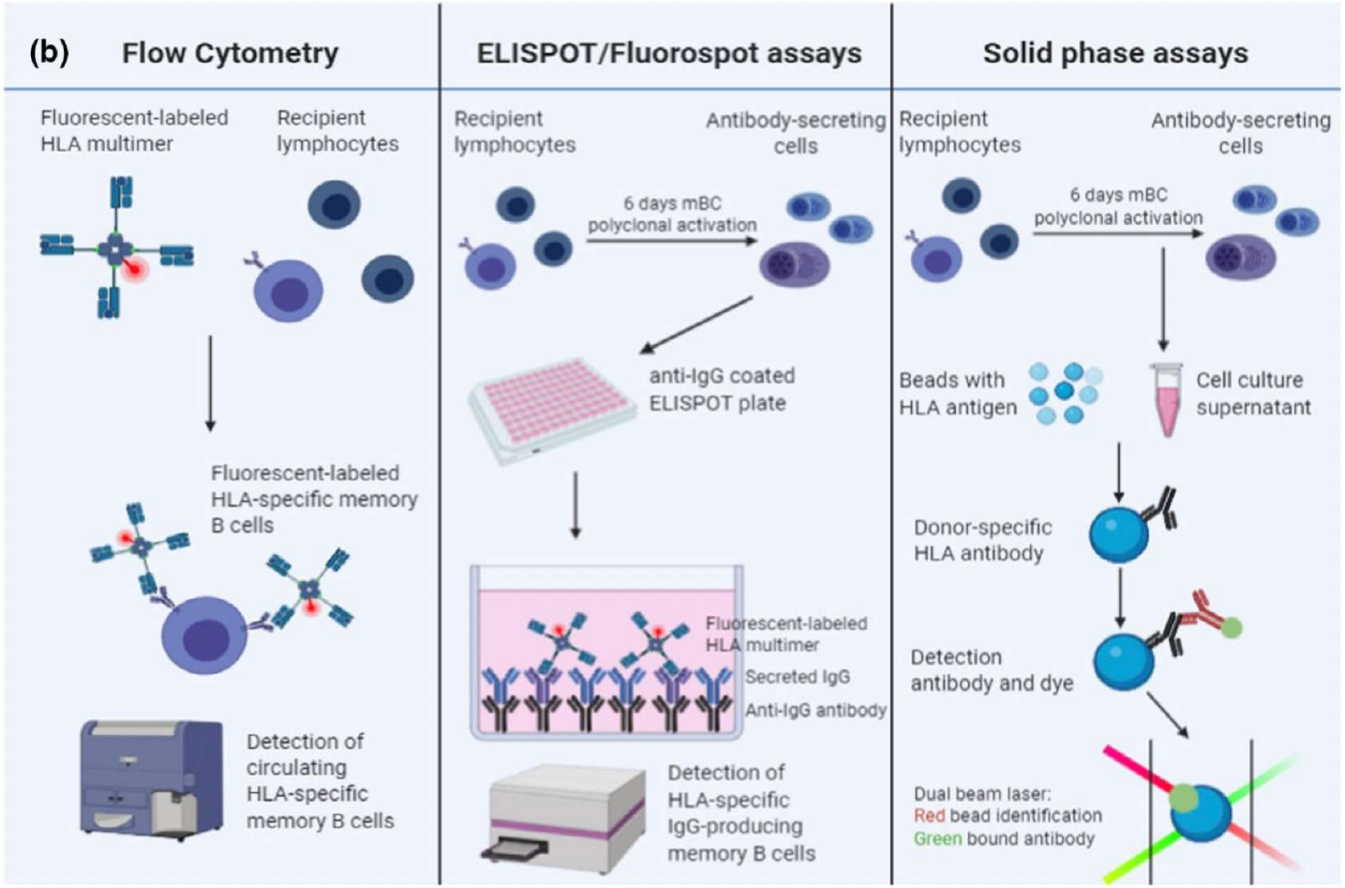
A


7. For kidney transplant recipients who were in category 4a at transplantation, mTOR inhibitors can be contemplated as concomitant immunosuppressive medication in combination with tacrolimus instead of mycophenolate, especially in where adequate doses of mycophenolate cannot be tolerated, or mycophenolate-associated infectious complications occur.
94,3%
3,8%
1,9%
1. Candidates for kidney transplantation in category 4a are at increased risk for AMR compared to patients in category 4b and 5, and post-transplant monitoring and strategies to control Ab-mediated injury need to be considered.
88,7%
11,3%
0,0%
5. Kidney transplant candidates in risk category 4a should receive maintenance immunosuppression consisting of tacrolimus, mycophenolate and steroids.
86,8%
13,2%
0,0%
2. Beyond careful clinical surveillance, monitoring (together with DSA screening and surveillance biopsy) are useful tools for category 4a.
86,8%
9,4%
3,8%
8. Currently, for kidney transplant candidates in category 4b there is no evidence of increased immunological risk and they do not require any additional treatment beyond standard of care.
81,1%
13,2%
5,7%
4. Either alemtuzumab or ATG induction therapies can be used in category 4a kidney transplant recipients.
81,1%
9,4%
9,4%
3. Lymphocyte-depleting agents, rather than IL 2RA, should be considered for KTRs category 4a.
75,5%
13,2%
11,3%
6. A planned minimization or withdrawal of immunosuppression should be avoided in kidney transplant candidates in category 4a.
66,0%
24,5%
9,4%
0%
25%
50%
75%
100%
Agree
Partially agree
Disagree

B


6. A planned strategy of minimization* of maintenance immunosuppression should be avoided in kidney transplant candidates in category 4a. (*Please see the definition of desensitization in the introduction section).
81,1%
15,1%
3,8%

Available assays to evaluate humoral alloimmune (b) cellular memory.



შეჯამება

- პაციენტის სწორი იმუნოლოგიური შეფასება წარმატებული ტრანსპლანტაციის ერთ-ერთი გარანტია

- გასათვალისიწინებელია არამხოლოდ პაციენტის ამჟამინდელი იმუნოლოგიური სტატუსი, არამედ წარსულში არსებული მაღალი DSA ან DSA-ს შესაძლო არსებობა

მადლობა ყურადღებისათვის!