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The universal organ donor fact or fiction?

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Introduction

- Inequity of organ transplant with ABO – blood groups
- Allocation programmes – implication for use of O donors
  - HLA – antibody status (cPRA) - Transplant Score
- A2 into to B/O programmes and status of ABO incompatible programmes
  - Accommodation
- Organ perfusion revolution (marginal organs – surgeon salvage!)
- Enzyme technology to remove AB- blood groups – all organs to O

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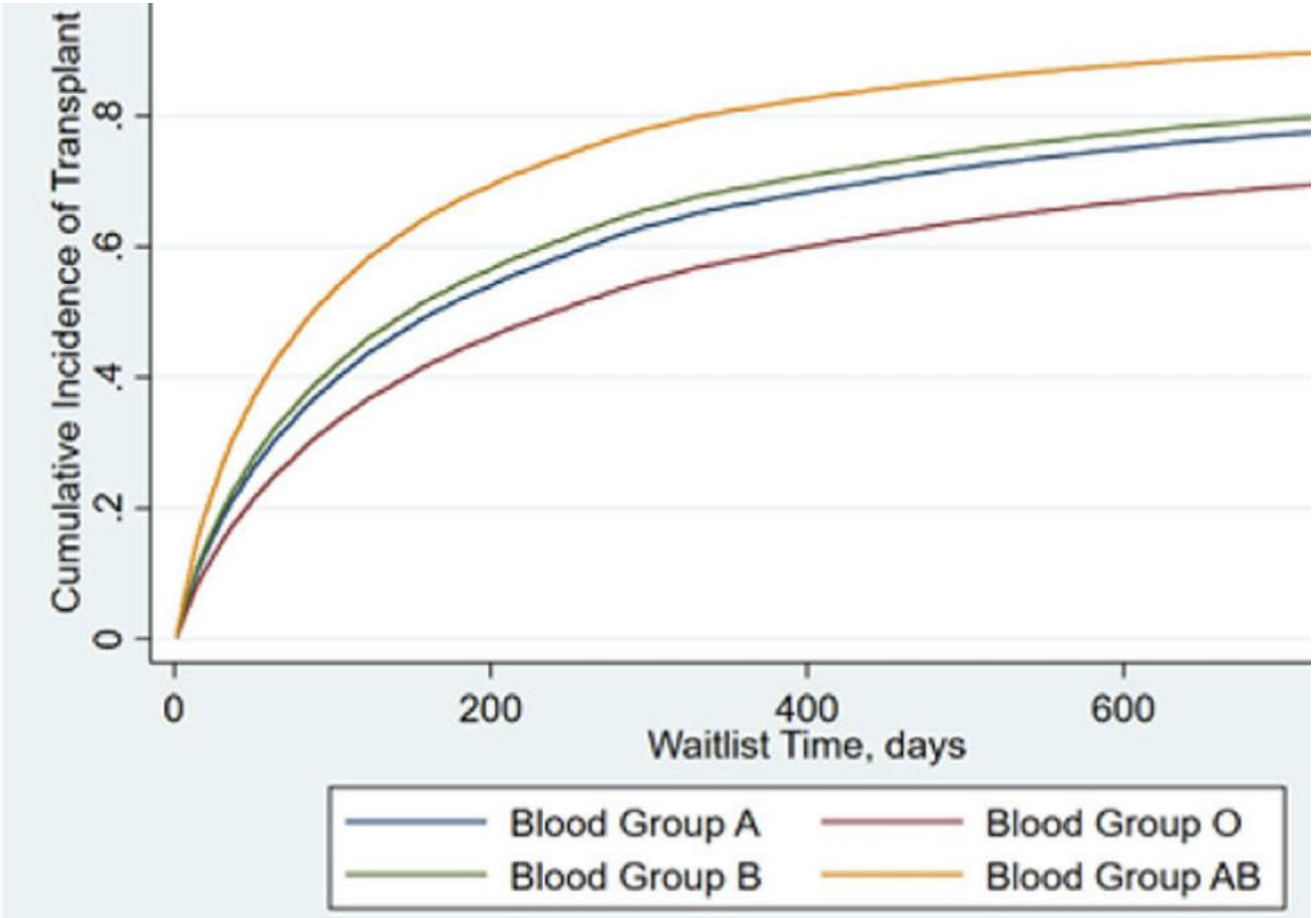
Published in final edited form as:
J Heart Lung Transplant. 2023 April ; 42(4): 480–487. doi:10.1016/j.healun.2022.10.024.

Lung transplant waitlist outcomes among ABO blood groups vary based on disease severity

- Group O compared to Group A
- 20% reduced transplantation (0.8, 95%CI: 0.7–0.8)
- higher waitlist death/removal (1.3, 95%CI: 1.2–1.6)



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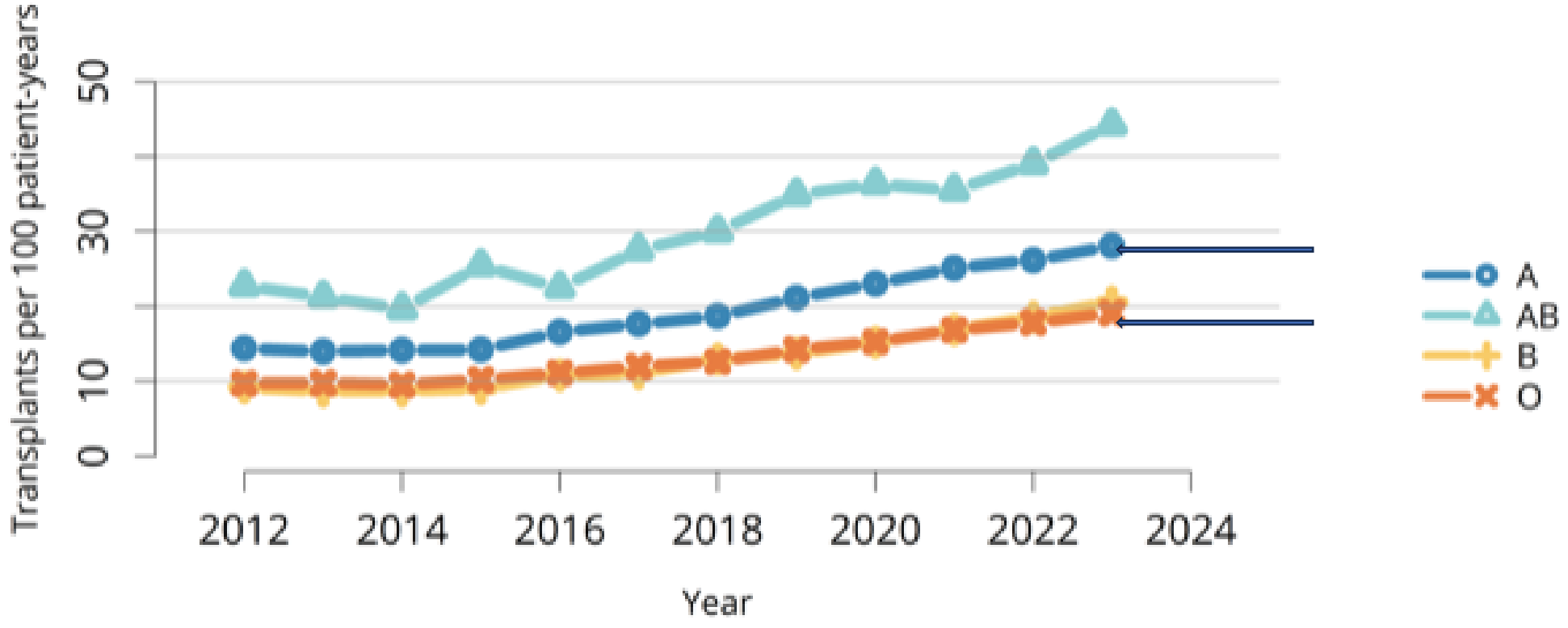
Blood groups O/B kidney transplanted the slowest

Figure KI 19: Deceased donor kidney transplant rates among adult waitlist candidates by blood type



OPTN/SRTR 2023 Annual Data Report

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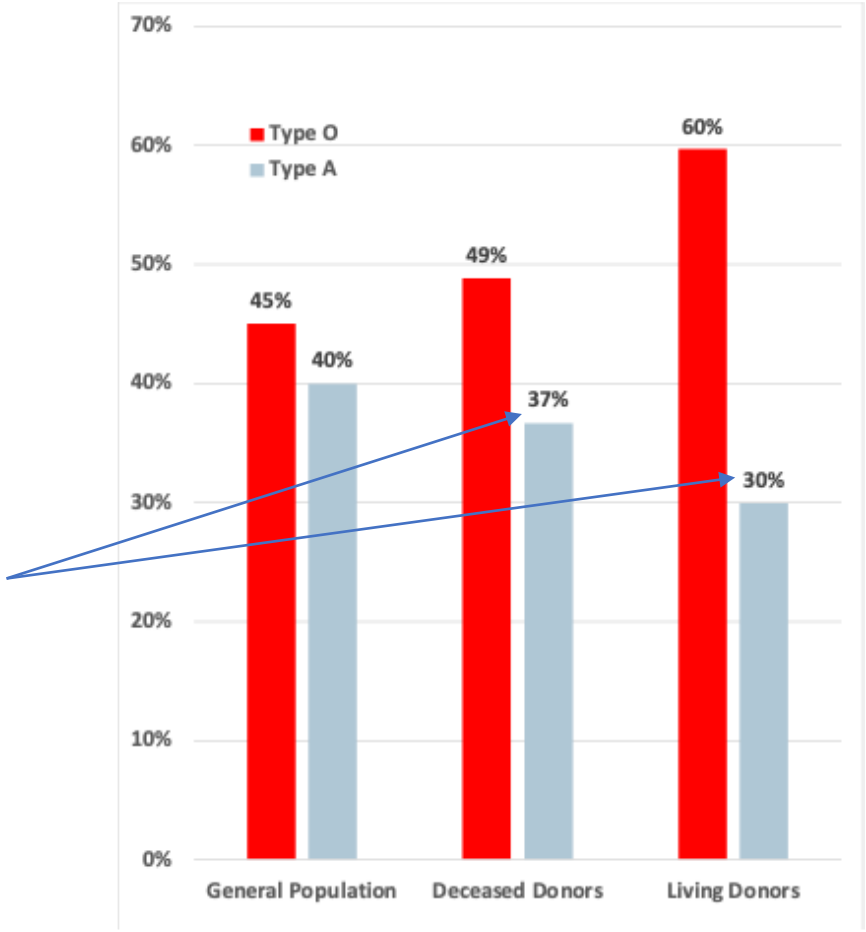
Group A donors are not used to the same extent as O donors

"A" donors consistent lower



- 30% of live group A donors cannot donate due to blood group incompatibility
- 25% of live related donors will be HLA matched !
- Extended criteria A kidneys not retrieved no blood group suitable recipient ?

Ref: 2026 Organ Procurement & Transplant Network (OPTN) Data

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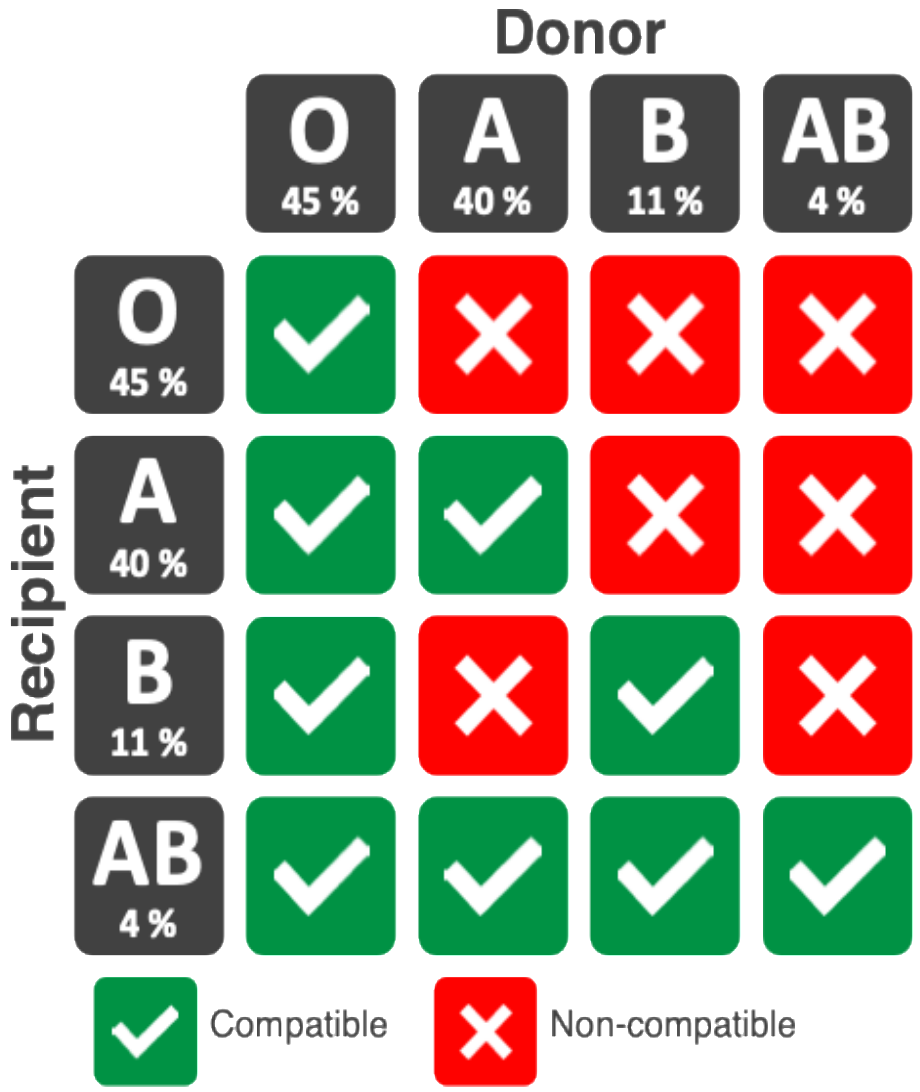
Blood group O can only accept O group kidneys



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Organ allocation systems try to get HLA antibody sensitized recipients a match

- Australia – KOALA – reversion away from ABO compatible
- ScandiaTransplant – TS – ABO identical – ABO compatible
- Fundamental is that majority of HLA antibody patients are female

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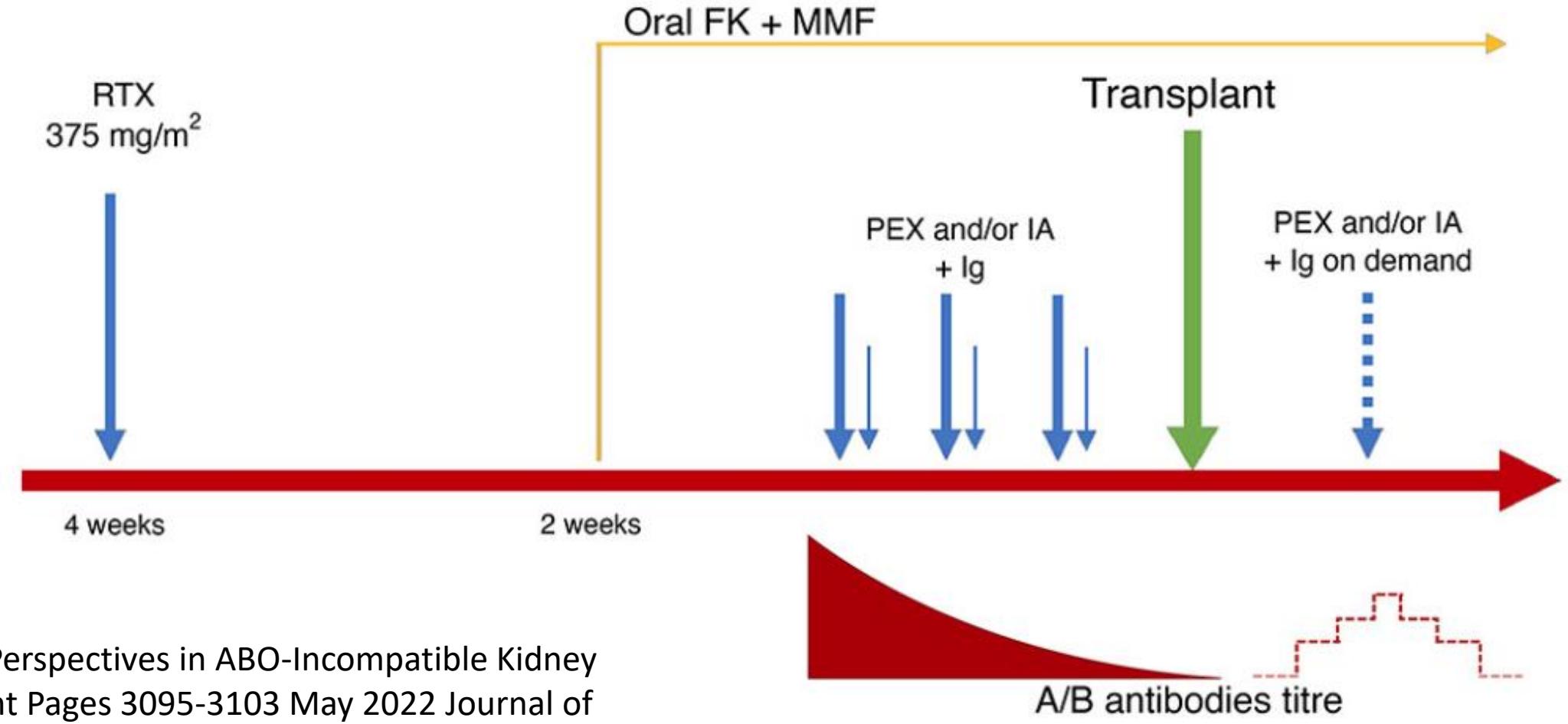
Blood group incompatible transplant: removing anti blood group antibodies before and after surgery



Current Perspectives in ABO-Incompatible Kidney Transplant Pages 3095-3103 May 2022 Journal of inflammatory research

ACCOMMODATION

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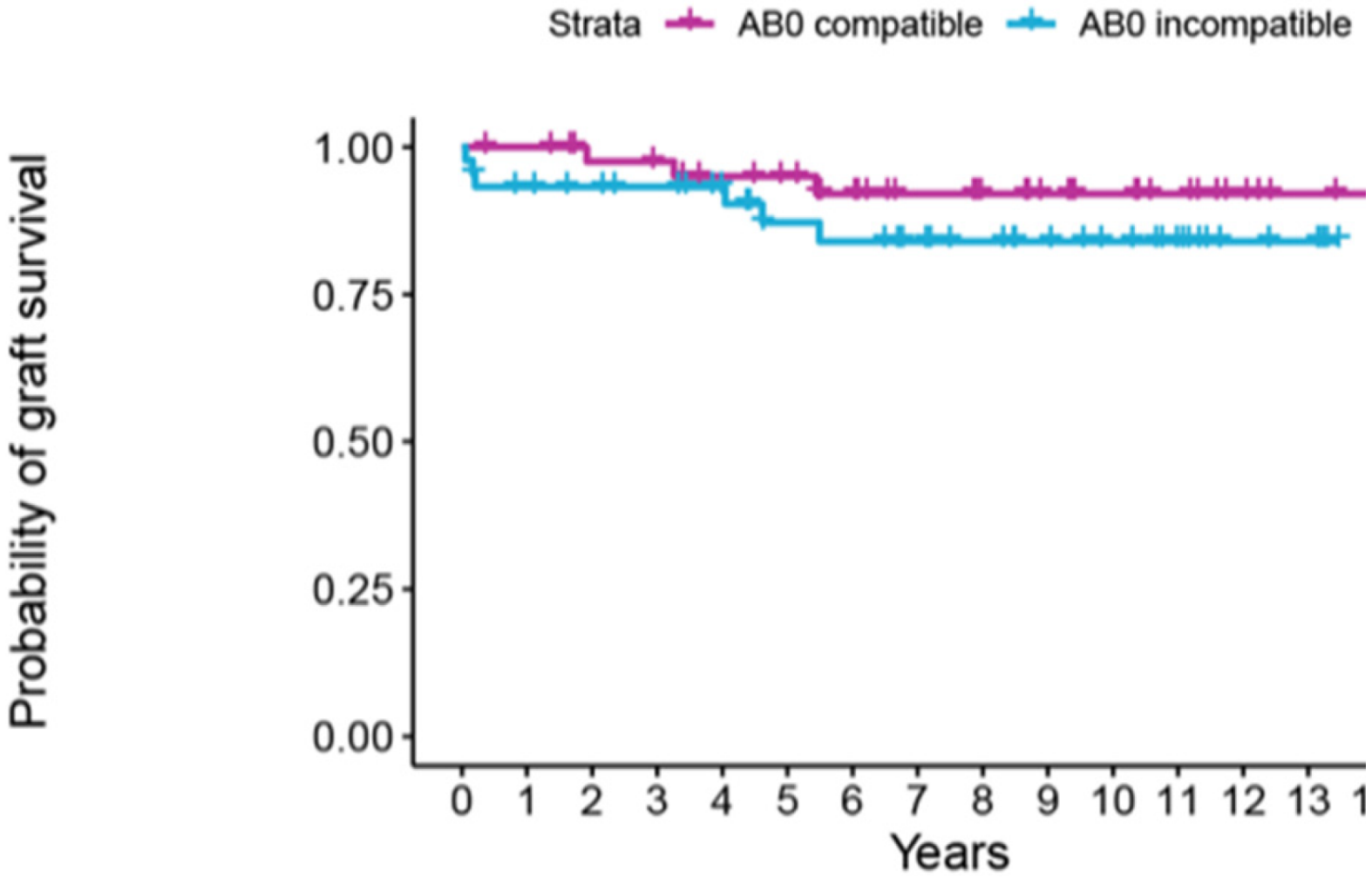
ABOi kidney transplants have similar outcomes – even though the antigen is still present on the kidney



J. Clin. Med. **2024**, *13*(23), 7477; https://doi.org/10.3390/jcm13237477

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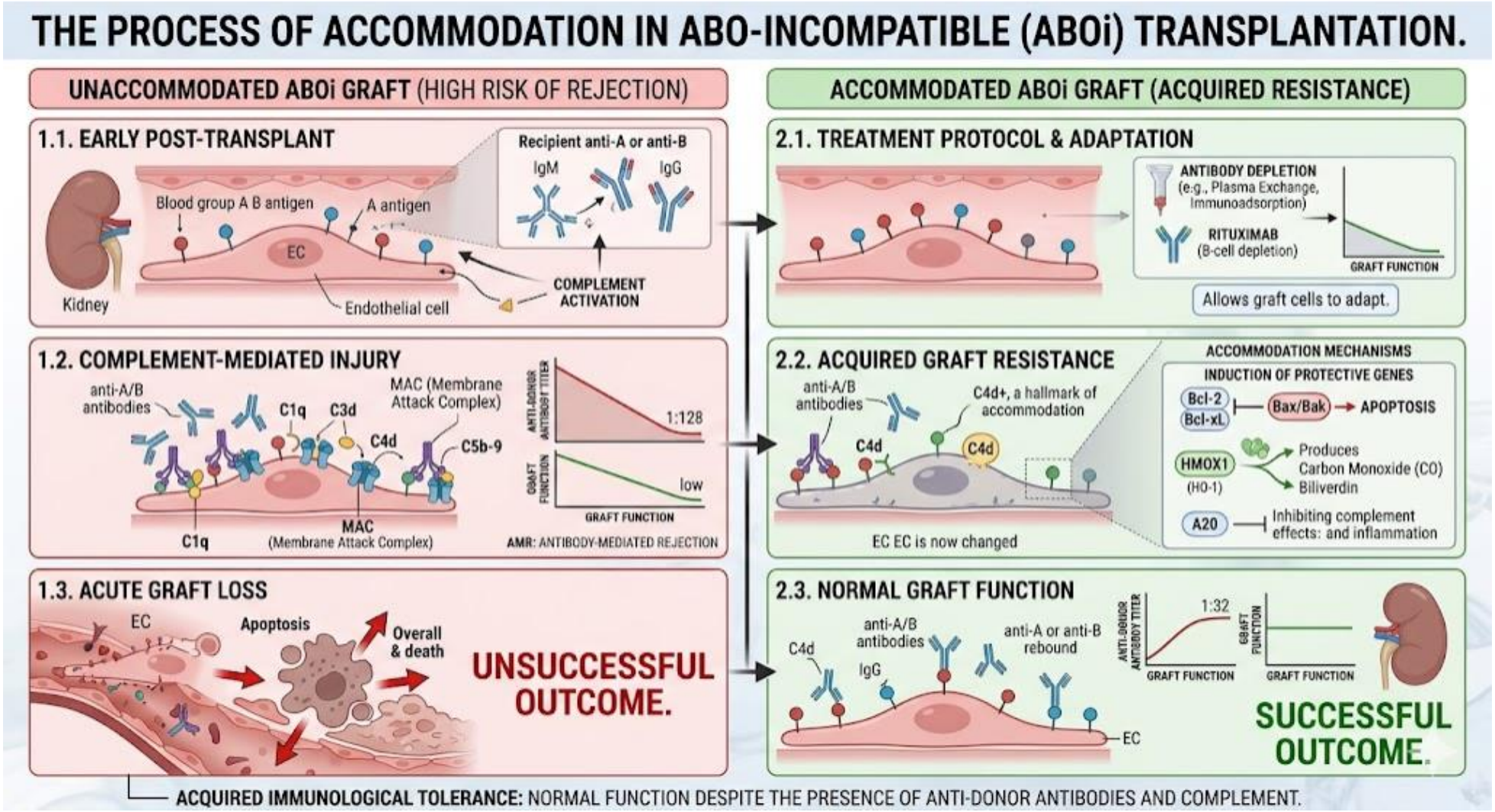
Accommodation – Group A antigen present but slow addition of antibody to the antigen



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ESOT | Transplant International

TYPE Original Research
PUBLISHED 26 May 2026
DOI 10.3389/ti.2026.16059

Check for updates

OPEN ACCESS

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‡These authors share last authorship

RECEIVED 13 December 2025

ABO-incompatible kidney transplantation: impact of apheresis on graft and patient survival in recipients with low isoagglutinin titer

If people have “low” (<1:8) isoagglutinin titre – can we avoid plex

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A1 into O/B with low agglutination scores and no PLEX have poorer outcomes

Variables	Apheresis n=41	No apheresis n=37	p
DGF or primary non function	2 (5%)	7 (19%)	0.077
At least one rejection	**6 (14.6%)**	**15 (40.5%)**	**0.01**
ABMR	4 (9.8%)	10 (27%)	0.075

- IgM 1:32 (hyperacute rejection)
- Even low agglutination scores associated with damage and rejection.
- Why is agglutination score not an accurate measure of risk of organ rejection …..?

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Why is agglutination or low score not a readout of risk and what are the implications the clinic?

- Glycan expression on red cells versus the blood vessel of organs
- If cannot risk assess the antibody -reduce the level of antigen/glycan
- A2- into B or O – programmes are these well used and if not why not?

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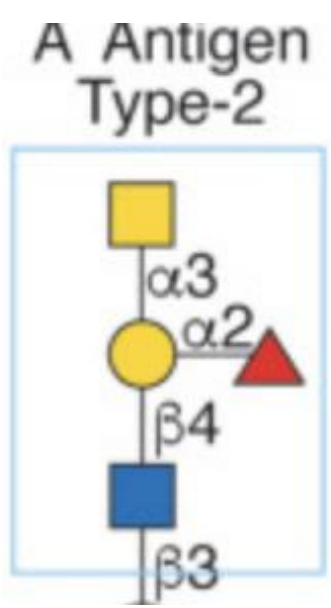
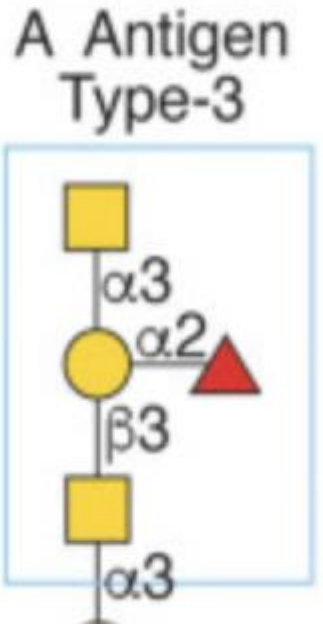
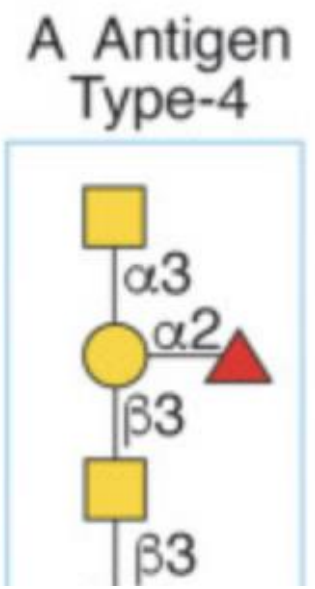
Agglutination is a reaction against all Red Cell glycans: possible to measure antibodies to individual Gylcan?







Type II glycan alone is expressed on vessels

Essentials of Glycobiology [Internet]. 4th edition. Varki A, Cummings RD, Esko JD, et al., editors.

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American Journal of Transplantation 25 (2025) 1884–1894

Contents lists available at ScienceDirect

American Journal of Transplantation

journal homepage: www.amjtransplant.org

Original Article

Multiplex bead immunoassay in ABO-A2-incompatible kidney transplantation

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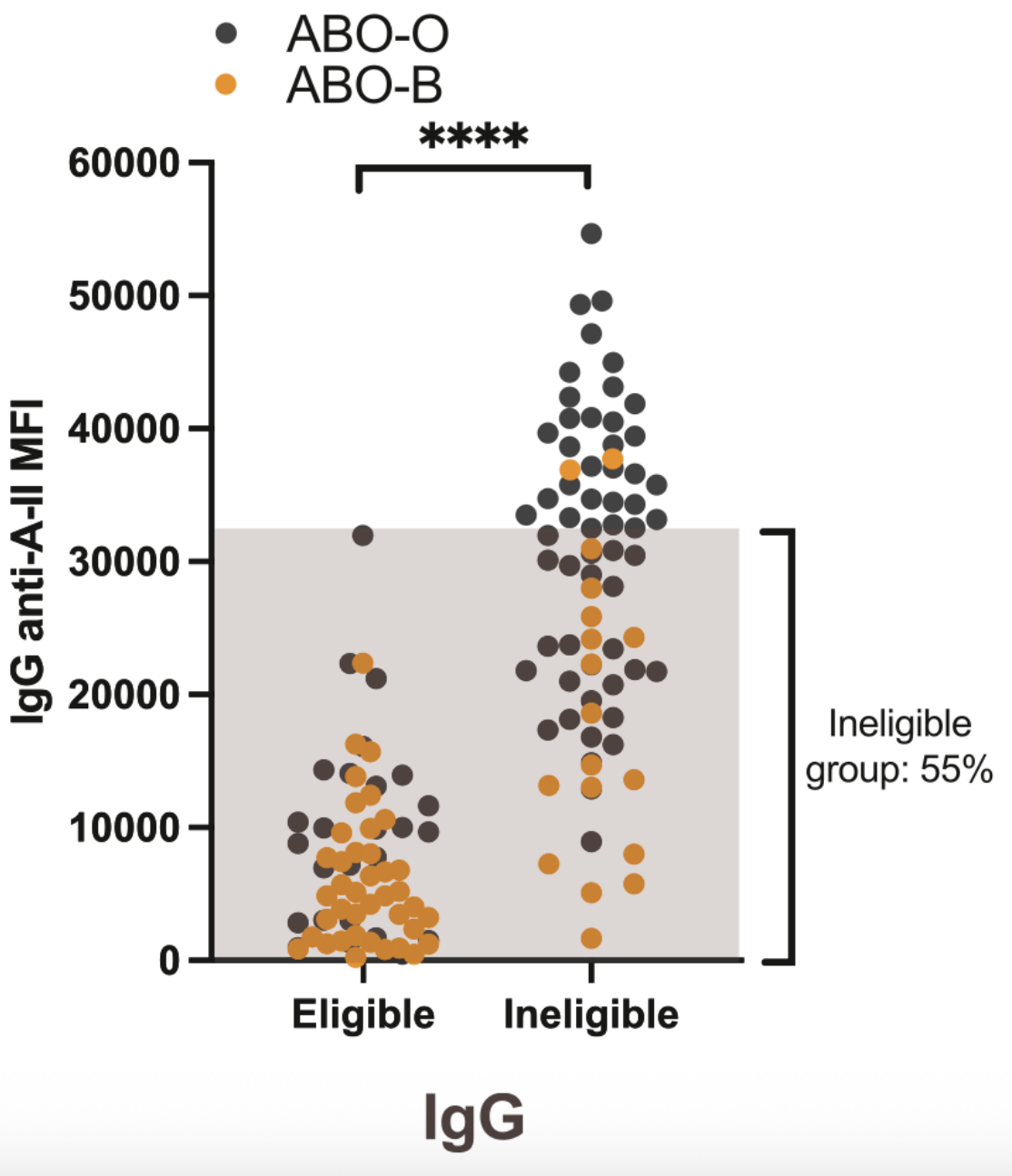
Anti A Glycan II antibody can be the same with differing haemagglutinin titre

A2 kidney only express 20% of the A-II glycan and no type III or IV on the interstitial areas

A1 Kidney do express type III and IV on the interstitium



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If we can fix the demand (eligibility-anti-glycan antibody) can we fix supply ?

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Current supply depends on serology….

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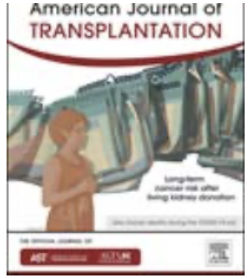

Original Article

ABO Genotyping finds more A_2 to B kidney transplant opportunities than lectin-based subtyping

Abigail Joseph [1,†], Cody J. Murray [2,†], Natasha D. Novikov [1,3], Randall W. Velliquette [4], Sunitha Vege [4], Justin B.L. Halls [1,3], Helen H. Mah [1], Jamie L. Dellagatta [1], Edward Comeau [1], Maria Aguad [1], Richard M. Kaufman [1,3], Martin L. Olsson [5,6], Indira Guleria [3,7], Sean R. Stowell [1,3], Edgar L. Milford [3,7], Annika K. Hult [5,6], Melissa Y. Yeung [3,7], Connie M. Westhoff [4], Cathi L. Murphey [2,†], William J. Lane [1,3,*,†]

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Every 500 donors PCR finds – 50 more A2 donors

Table 1
Summary of anti-A_1 lectin and *ABO* PCR genotyping results of deceased donors at SWID and BWH.

Donor Ethnicity	Anti-A_1 Lectin phenotype			PCR genotype prediction	
	A_1	A_2	Ind	A_1	A_2
	% (number of samples)				
SWID & BWH deceased donors					
All donors (n = 554)	86% (476)	13% (72)	1.1% (6)	79% (435)	21% (119)

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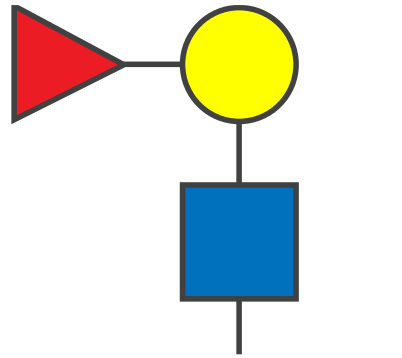
Carbohydrate structure A,B and O Blood Groups

Group O is the **Universal donor**



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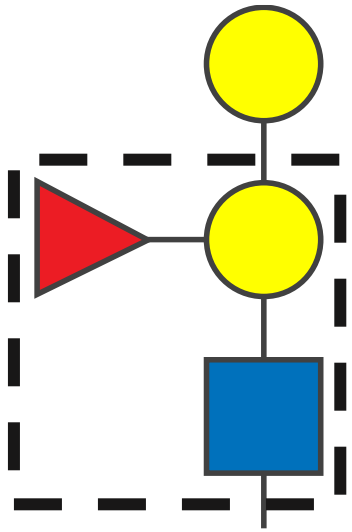
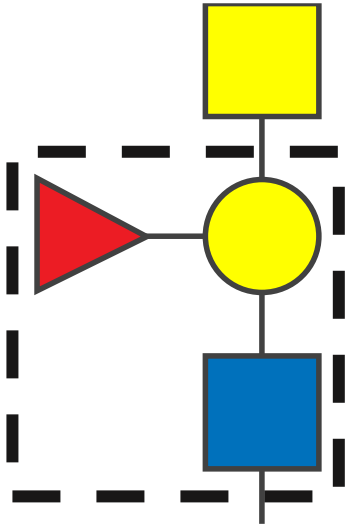
A and B antigens have one additional sugar

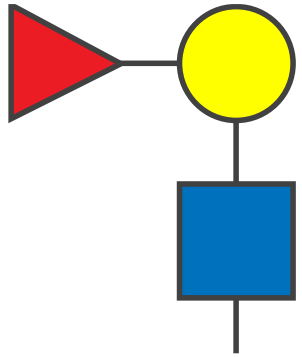


B antigen



A antigen

Universal donor



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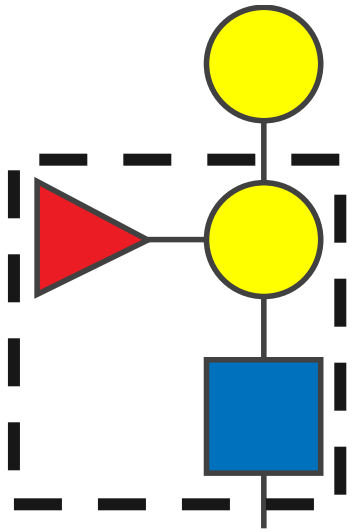
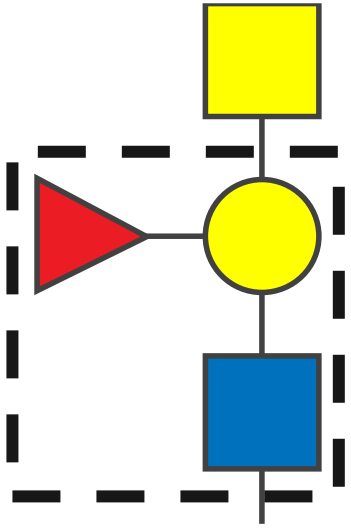
The A and B sugars seen as foreign to O people : anti A and anti B blood group antibodies

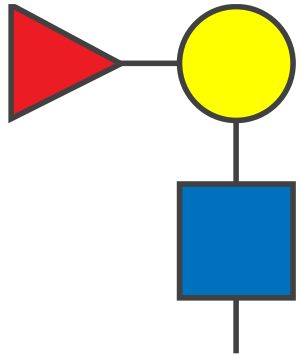


B antigen



A antigen

Anti A and Anti B Blood Group Antibodies



H antigen

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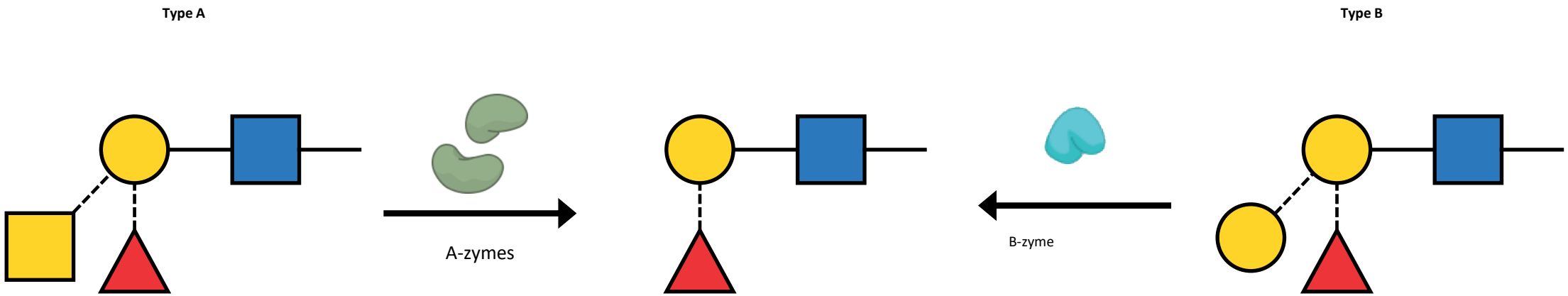
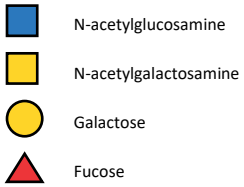
A donor-centric solution to overcome the ABO barrier

Enzyme Converted Type O (**ECO**) – convert A, B, and AB to universal Type O

Avivo Enzymes can convert A,B or AB to O





ABO conversion technology

- **Coupled to organ perfusion for real-time conversion**
- **Would expand the effective donor pool across all blood types**

Remove the one sugar – eliminate the mismatch

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Organ perfusion is revolutionizing organ donation

- Marginal donor as assessed as viable – 30-40% increase in liver use
- Increase in marginal kidney
- Surgical timing and work force mitigation strategies
- Pre – treatment of the donor whilst the kidney is on the machine

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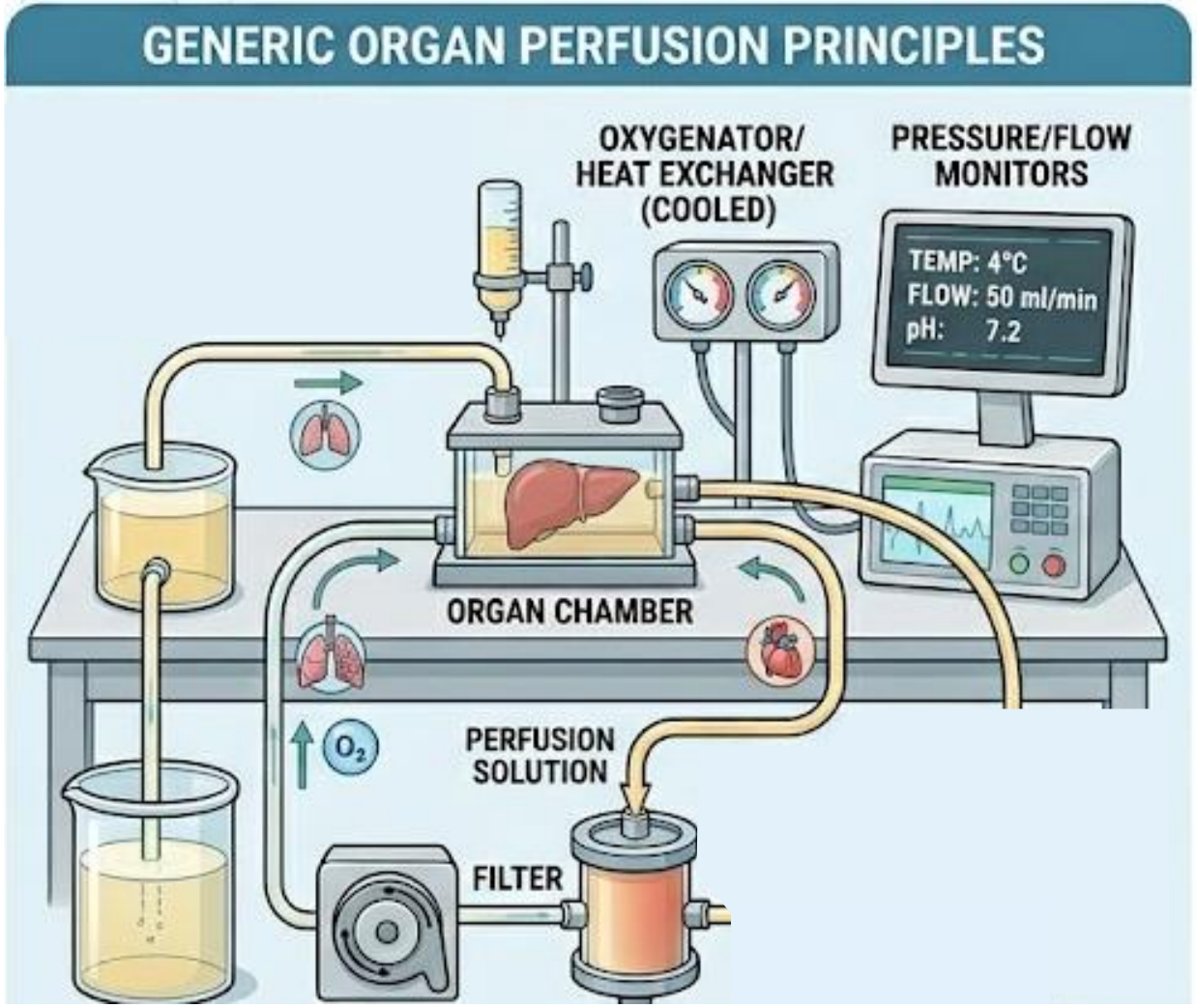

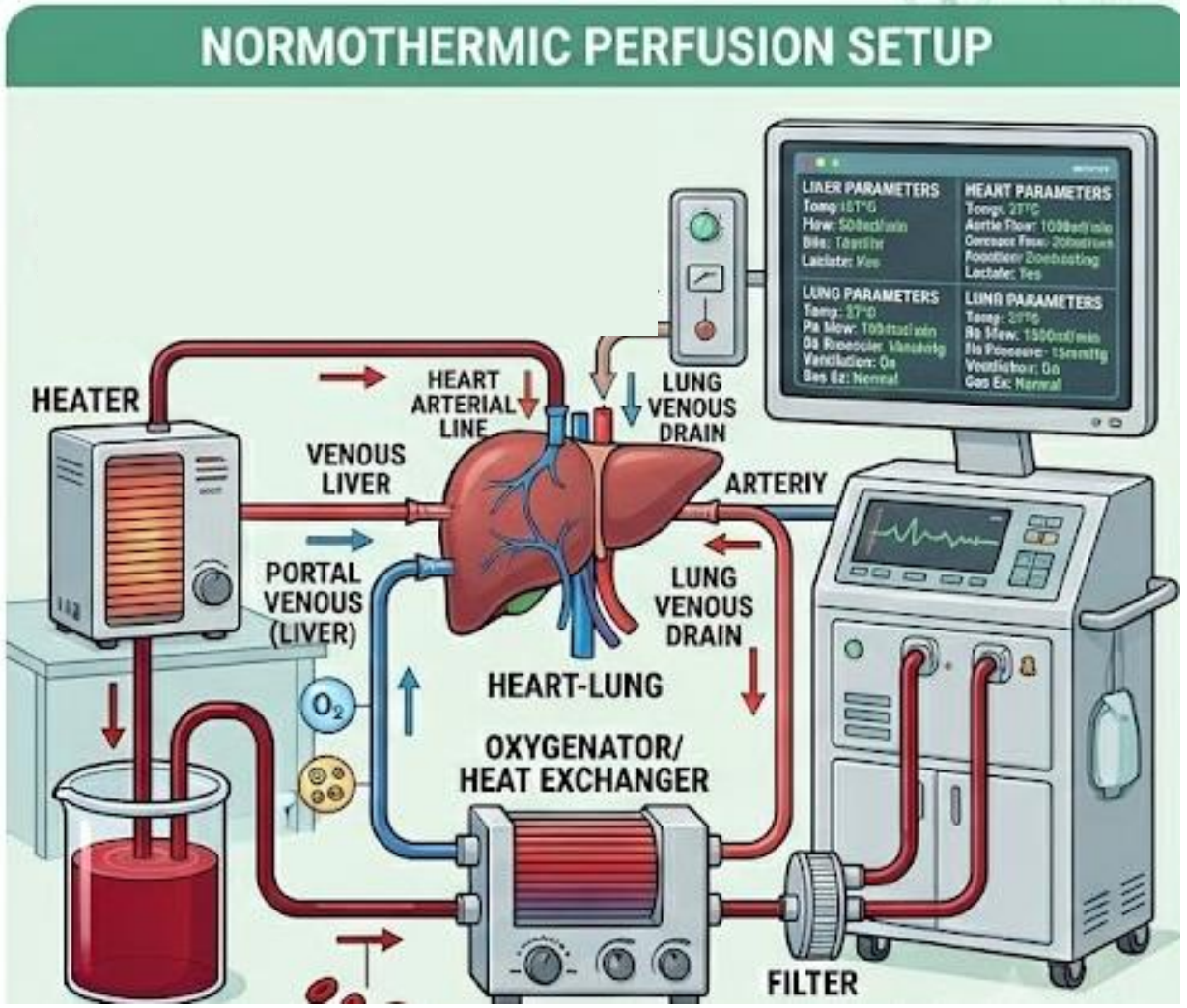

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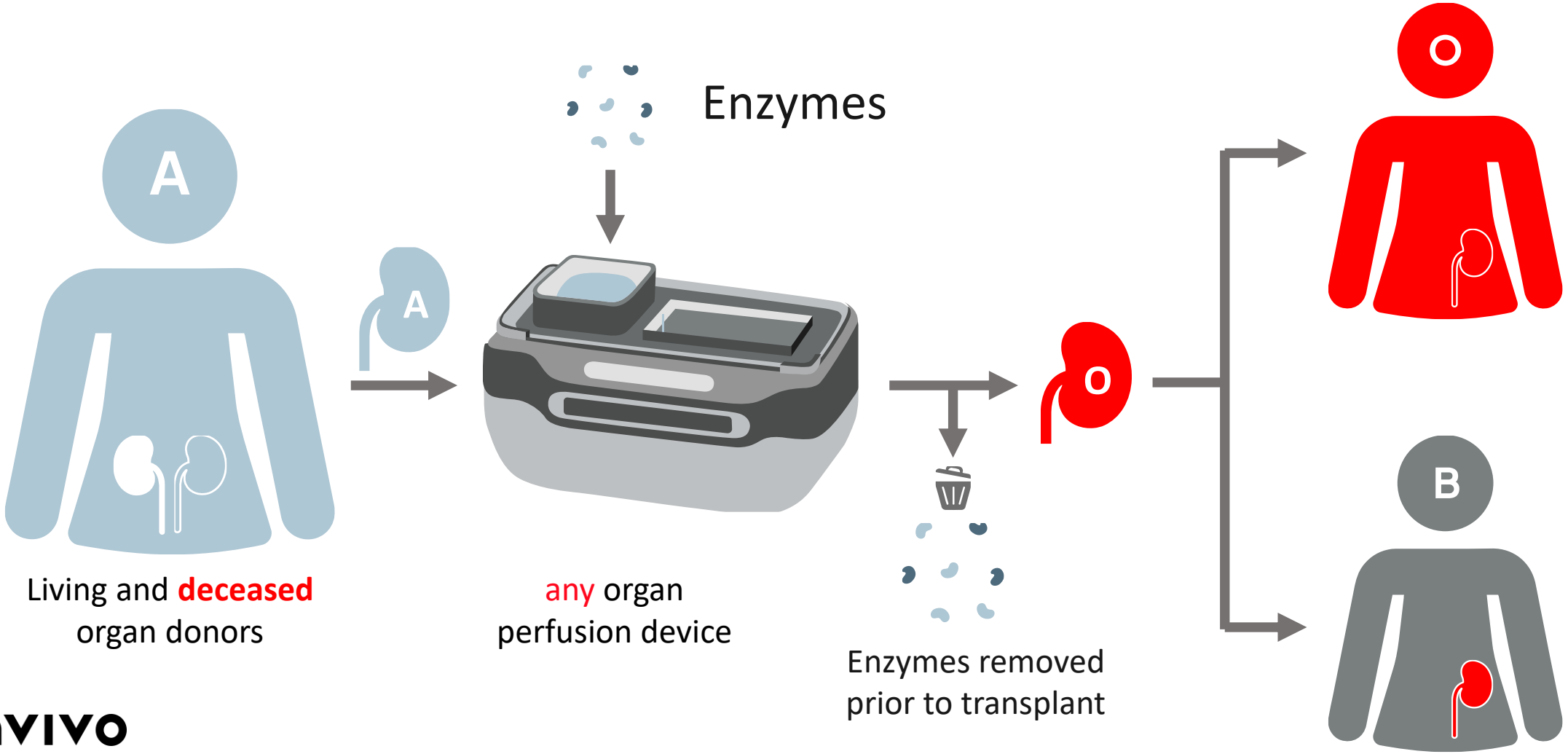
Enzymatic converted O (ECO) transplantation



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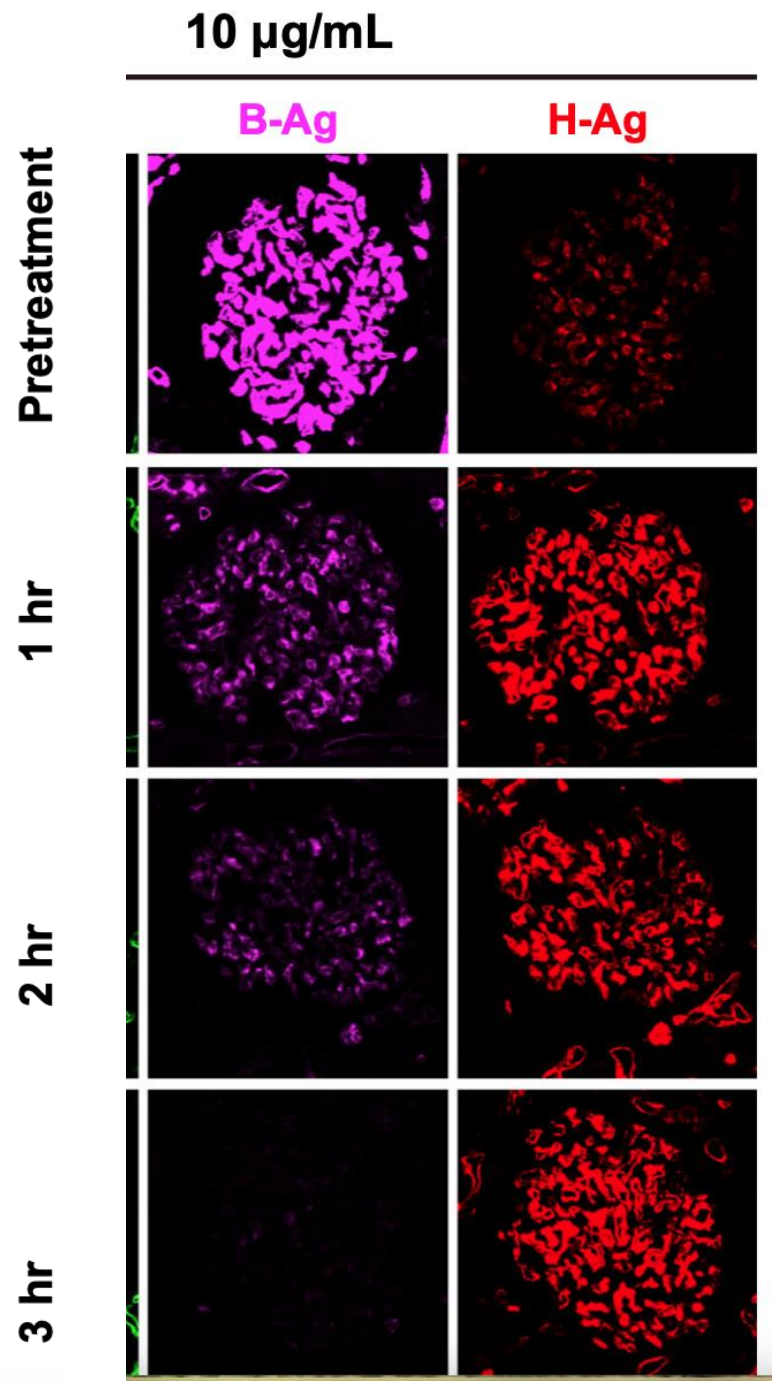
3 hour perfusion to remove Blood Group B sugars from a kidney

Microscopic view of a kidney filtration unit losing Blood Group B (purple) and revealing H antigen (group O in red)



Enzymatic **conversion** of **blood group** B **kidney** prevents hyperacute antibody-mediated injuries in ABO-incompatible **transplantation**.Nat Commun. 2025 Feb 10;16(1):1506. doi: 10.1038/s41467-025-56563-w.

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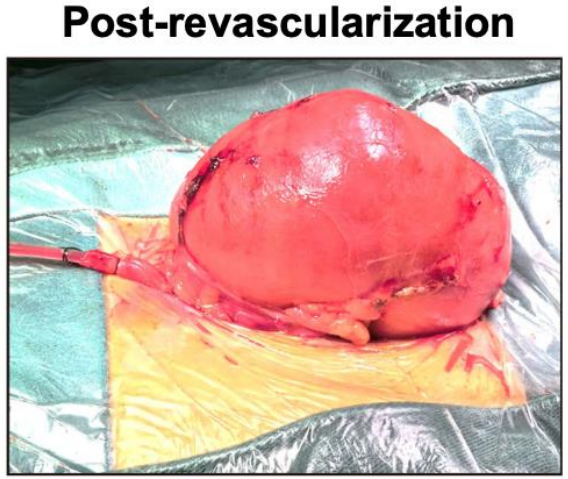
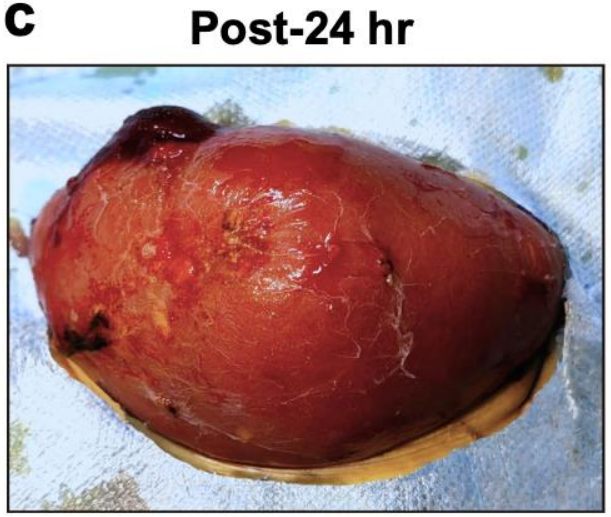
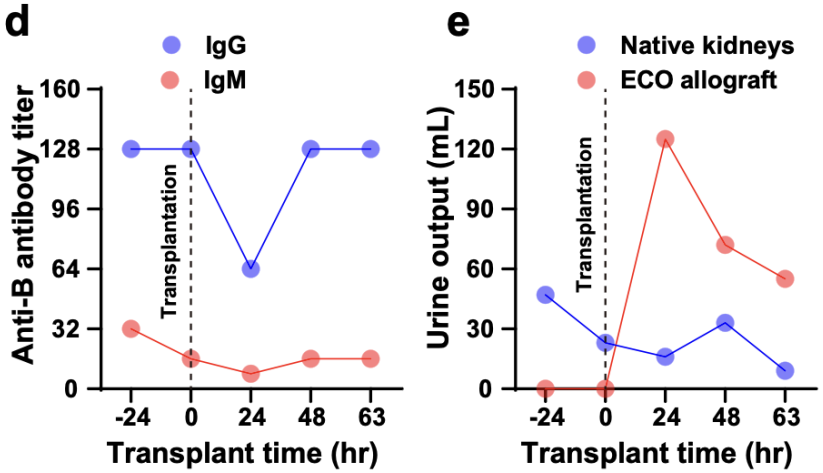
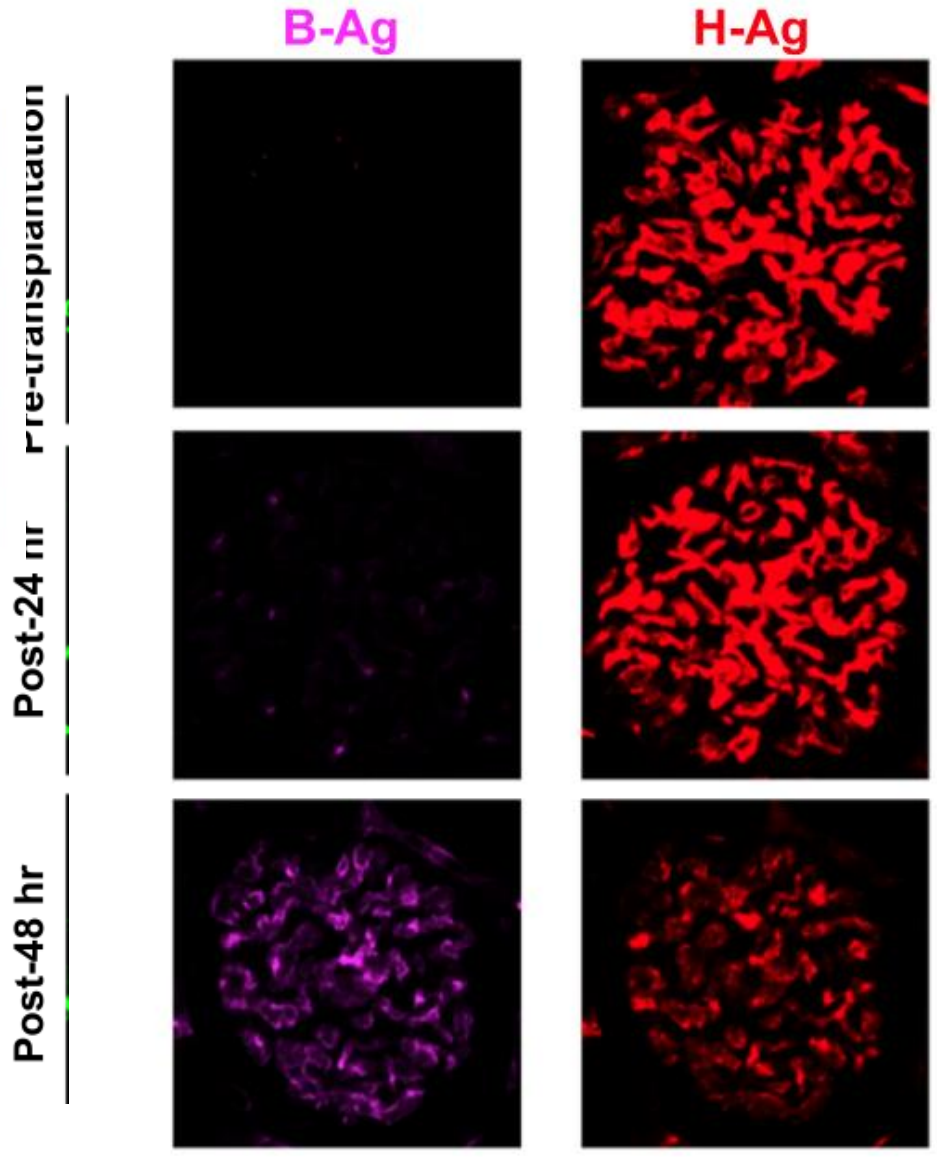
B Antigen regeneration - occurs in vivo









Nat Commun. 2025 Feb 10;16(1):1506

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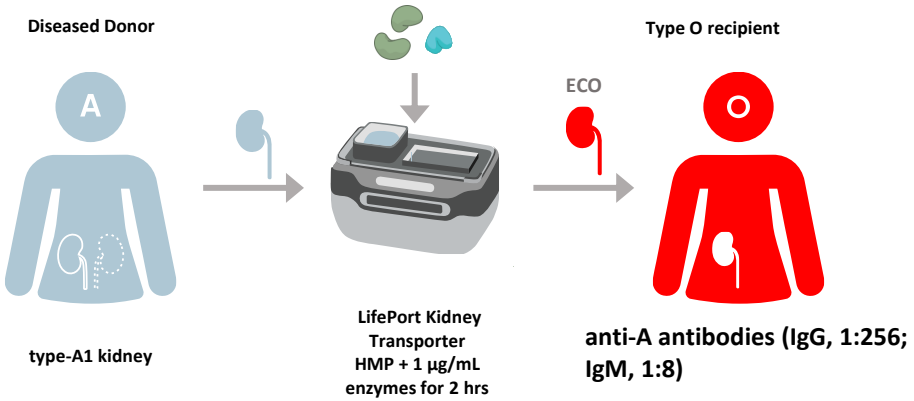
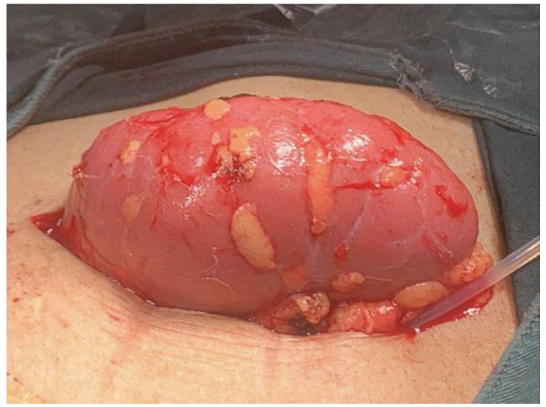
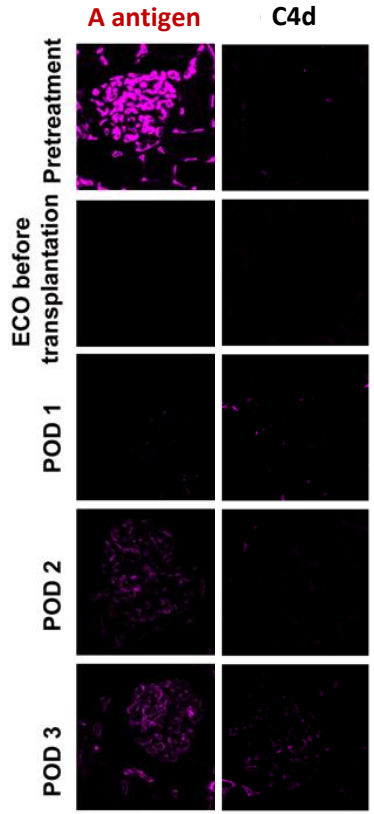
A → ECO kidney transplant a human decedent

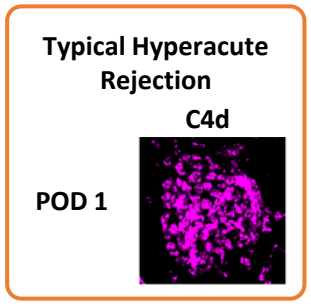




ECO kidney after transplant



A antigen expression and complement levels after transplant



- **Managed as ABO-compatible transplant**
- No hyperacute rejection (72 hrs)
- Normal early graft function

Antigen regeneration and immune activation began POD 2/3 and POD 4, respectively

Zeng et al 2025

nature biomedical engineering

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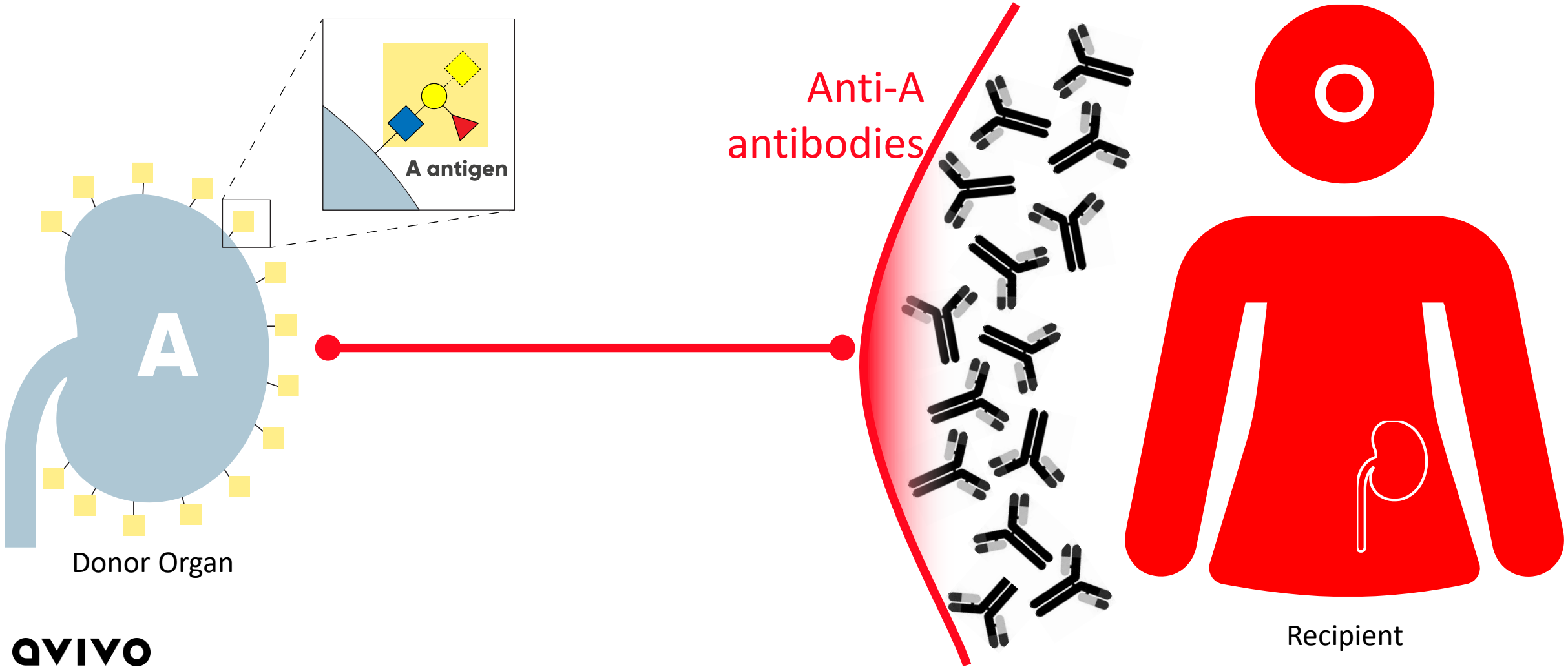
Breaking the blood group barrier



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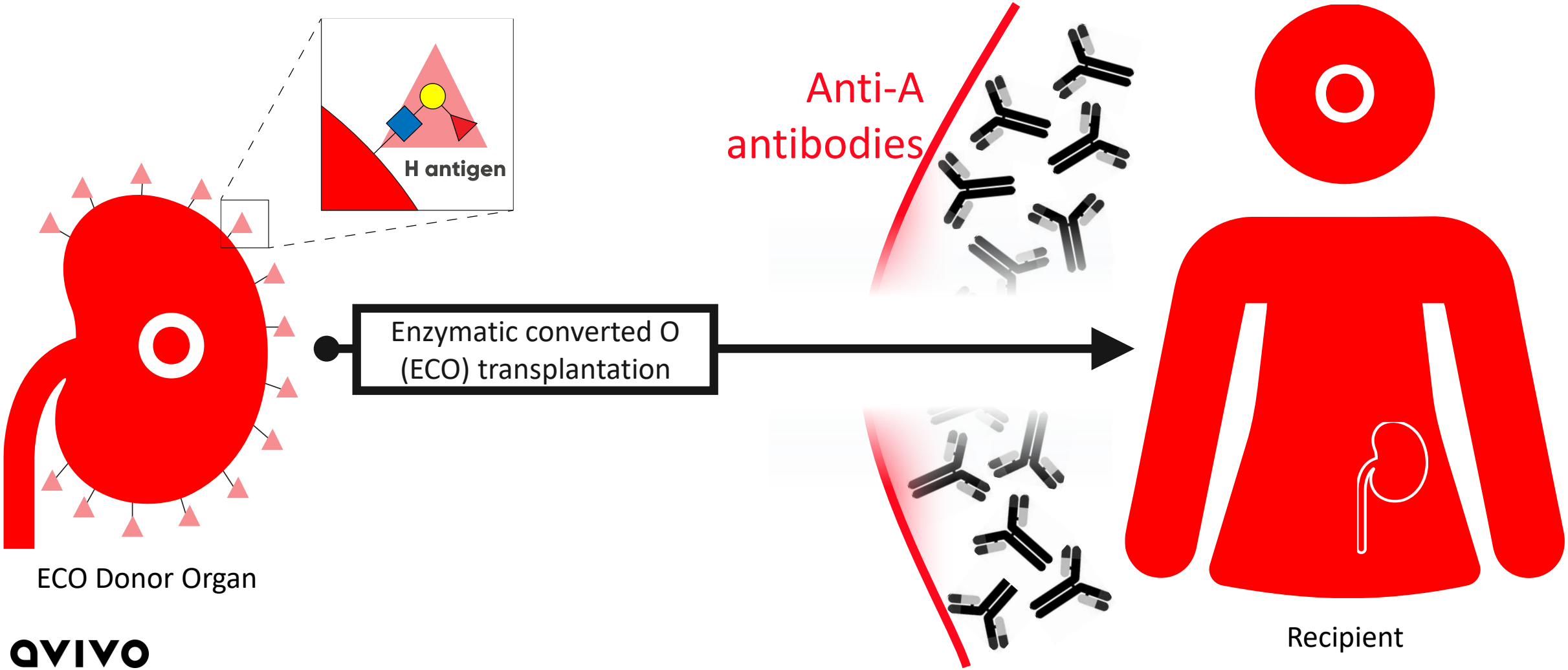
If the antigen is not there does not matter about the antibodies!



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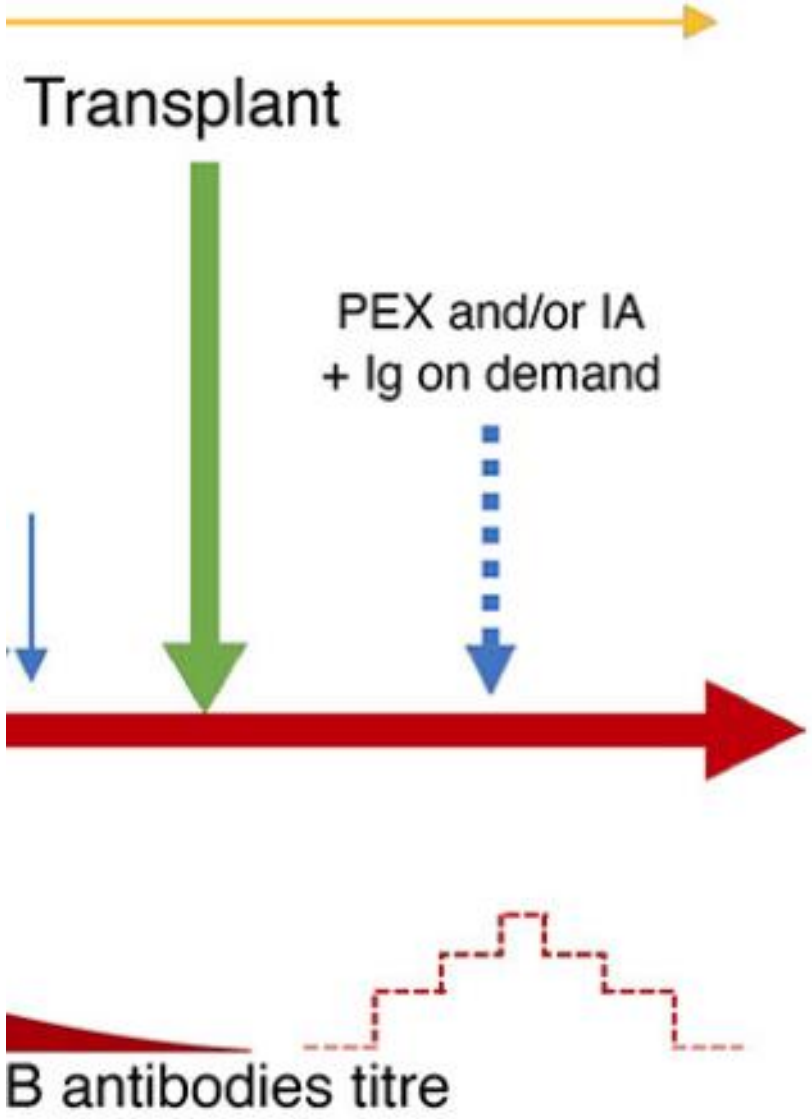
Enzyme cleavage technology - only manage the antibodies post op



Current Perspectives in ABO-Incompatible Kidney Transplant
Pages 3095-3103 | Published online: 25 May 2022 Journal of inflammatory research

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Do we have alternatives to post op PLEX?

- IDES – imlifidase – Hansa Biopharma

RESEARCH ARTICLE | BIOCHEMISTRY |

Structure of the streptococcal endopeptidase IdeS, a cysteine proteinase with strict specificity for IgG

Katja Wenig, Lorenz Chatwell, Ulrich von Pawel-Rammingen, +2 , and Peter Sondermann Authors Info & Affiliations

December 1, 2004 | 101 (50) 17371-17376 | https://doi.org/10.1073/pnas.0407965101

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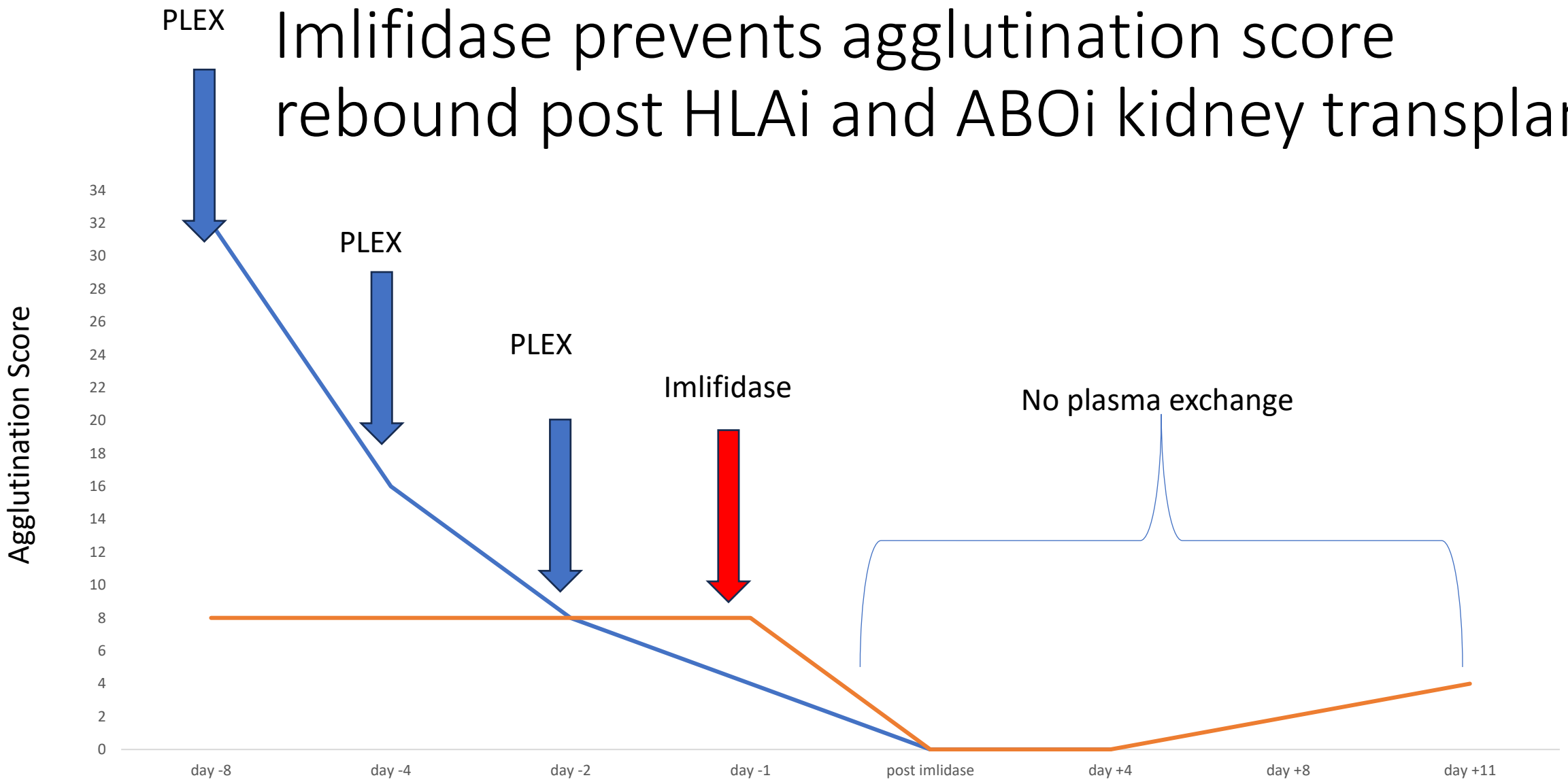
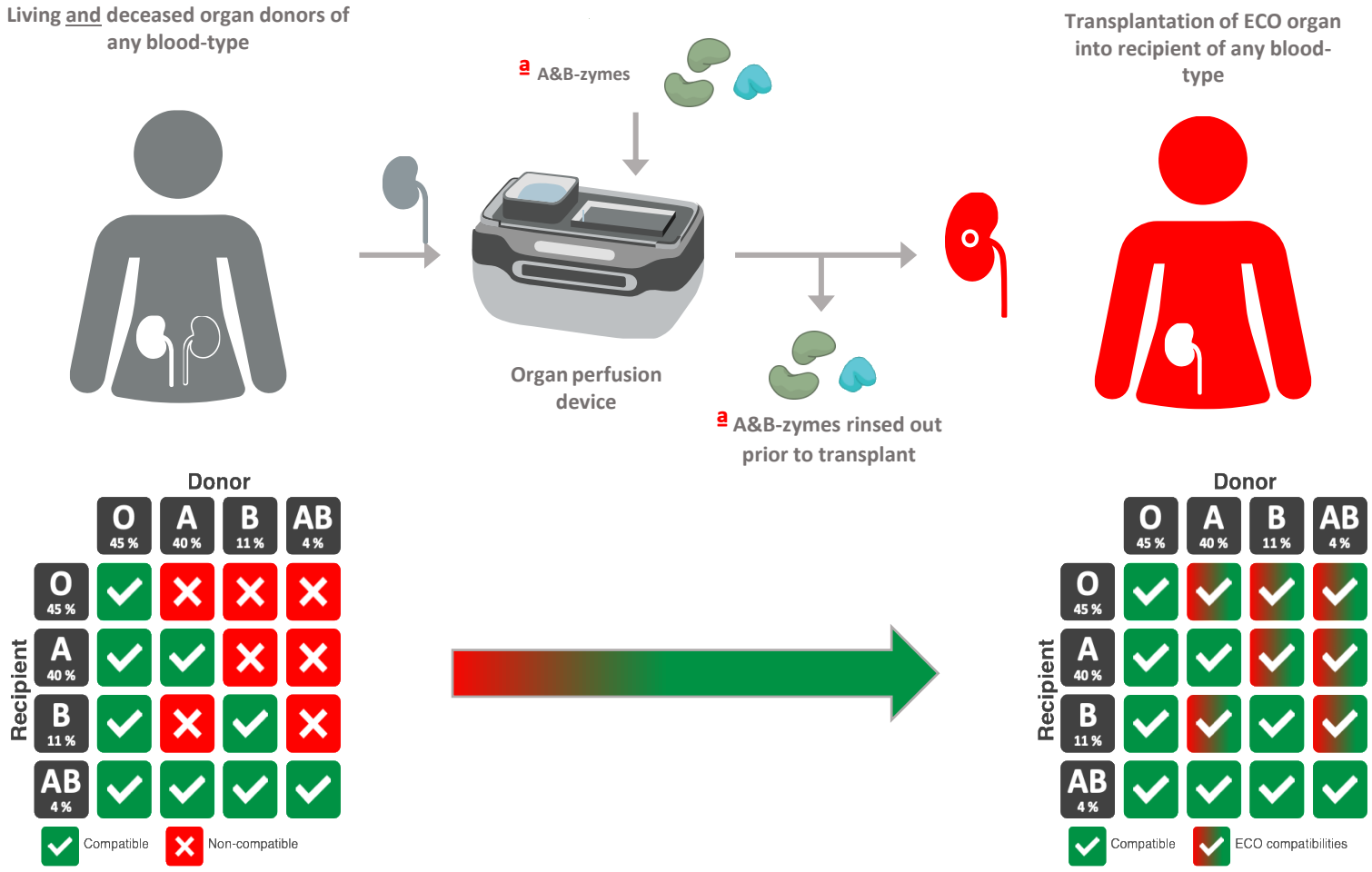
Imlifidase prevents agglutination score rebound post HLAi and ABOi kidney transplant



Any organ to any recipient – better matching – less rejection – longer organ survival …..?



All organ can go to all recipients

Double the chance of HLA match

Longer organ/patient survival

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Summary

- Universal A1 or B to O group can be generated with enzyme technology
- Antigen regeneration at 48-72 hours (in vivo)
- Optimal post operative management yet to be determined
- Integration of ECO – into the organ allocation – framework.