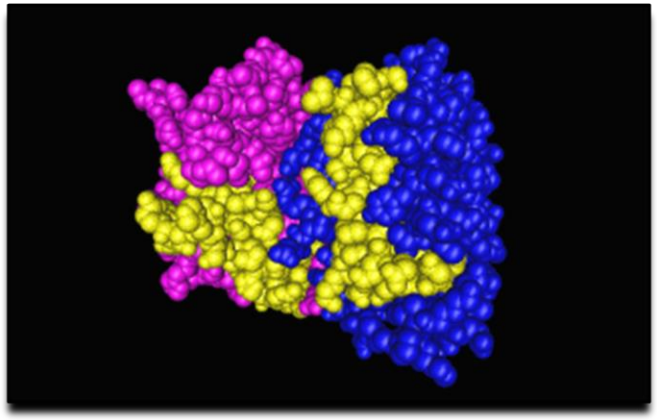


İZMİR KÂTİP ÇELEBİ ÜNİVERSİTESİ 2010

HLA EPİTOP UYUMU

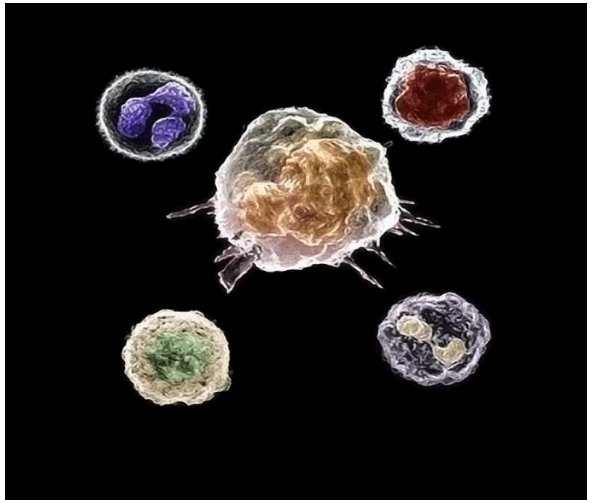
Prof.Dr.MUSTAFA SOYÖZ

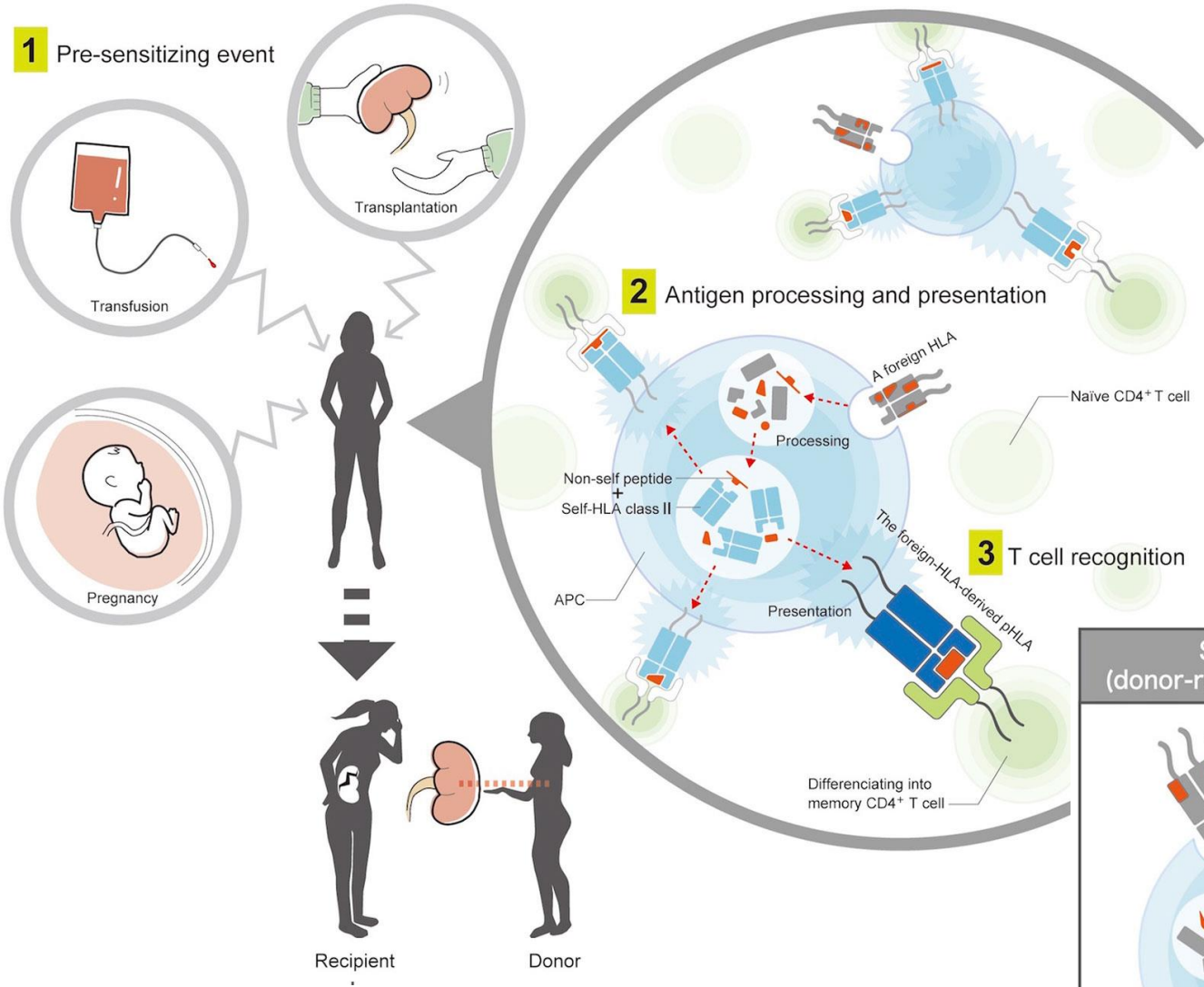
İZMİR KATİP ÇELEBİ ÜNİVERSİTESİ TIP FAKÜLTESİ

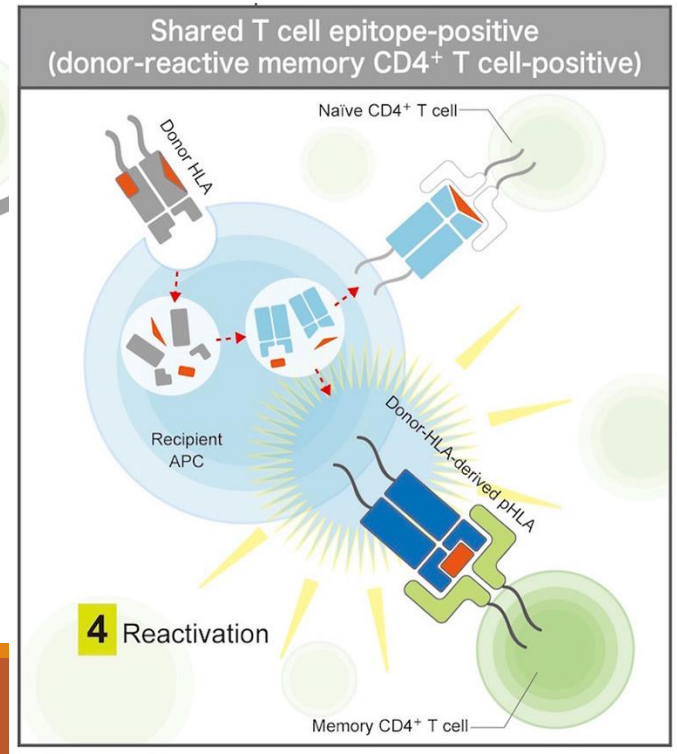
TIBBİ BİYOLOJİ AD.

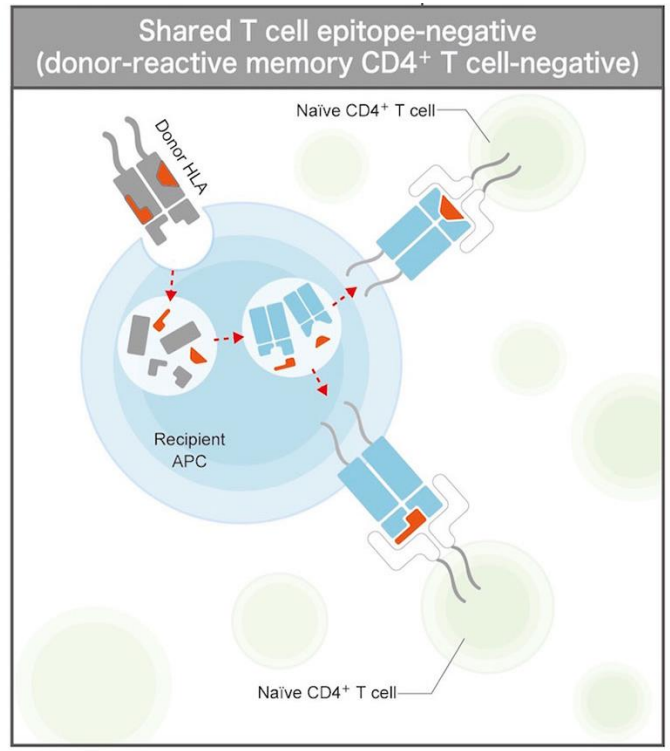
Sunum Planı

- HLA epitopları/epletler
- Transplantasyonda HLA epitopları ve epletlerin önemi
- Retrospektif çalışmalarda HLA epitop/eplet eşleştirmesinin faydaları
- Prospektif HLA epitop/eplet eşleştirmesindeki fırsatlar
- Ulusal düzeyde neler yapabiliriz, bir yerden başlamalı mı?



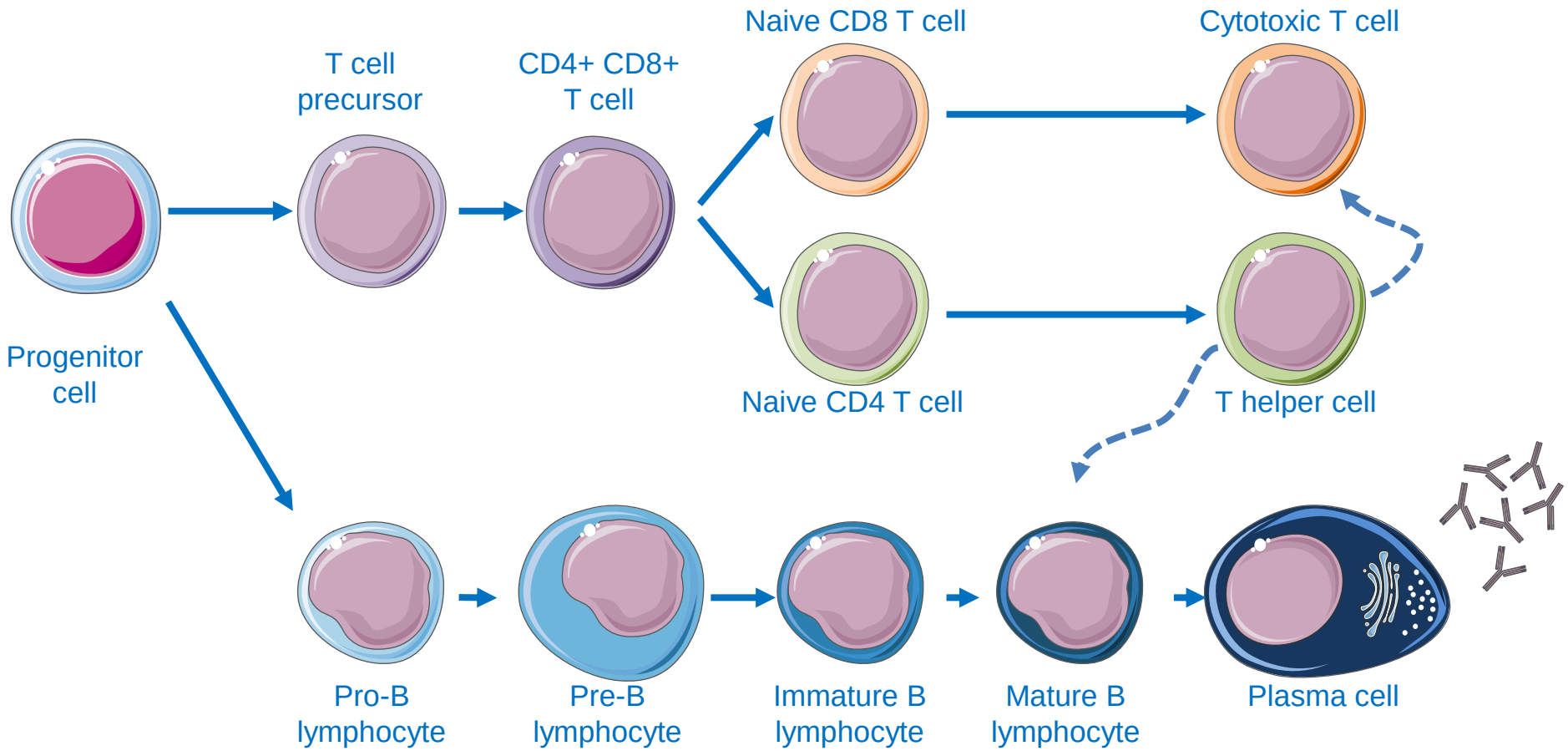






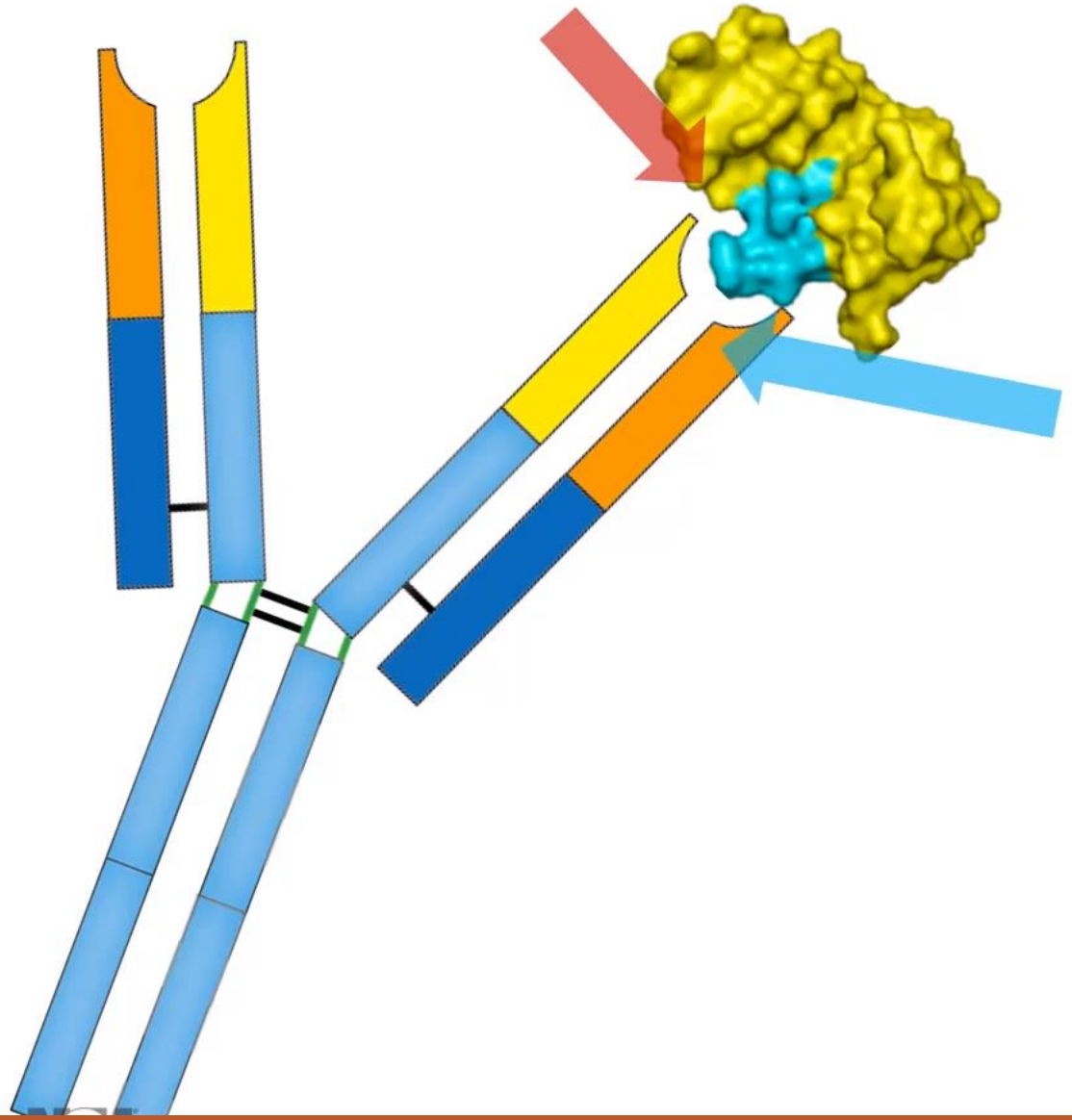
Tomosugi et al. Front.Immunol. 2021

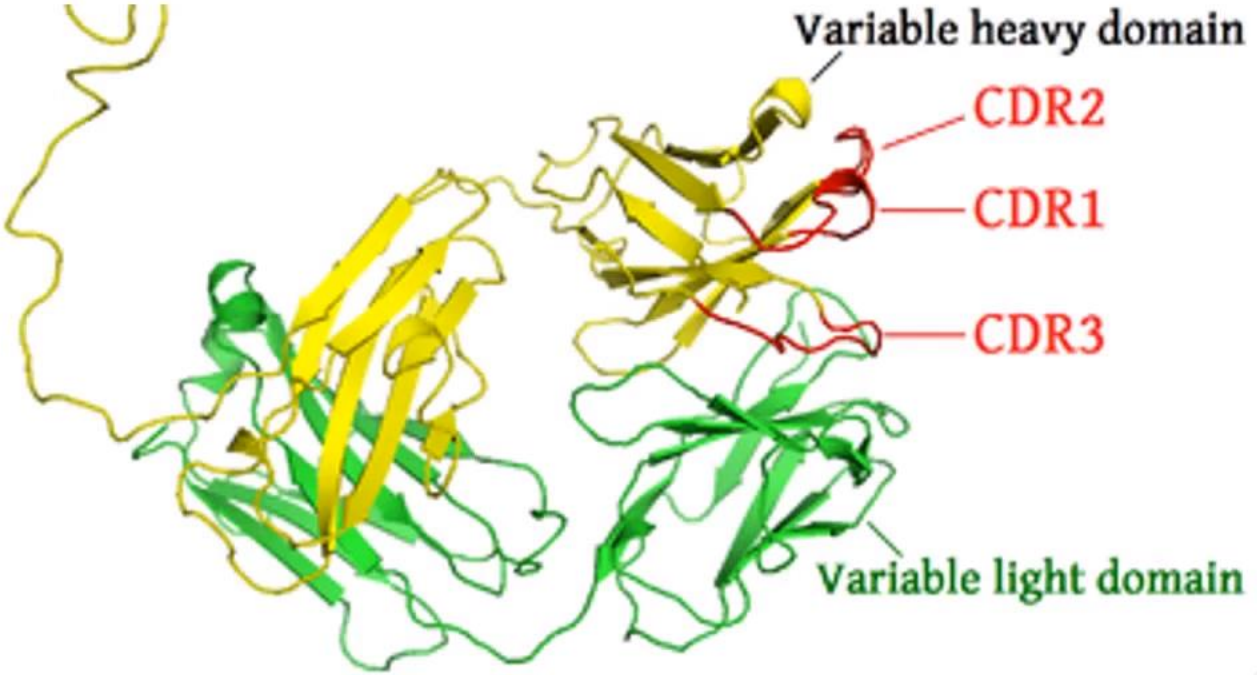
T ve B Hücrelerin İşbirliği



epitope

Paratope





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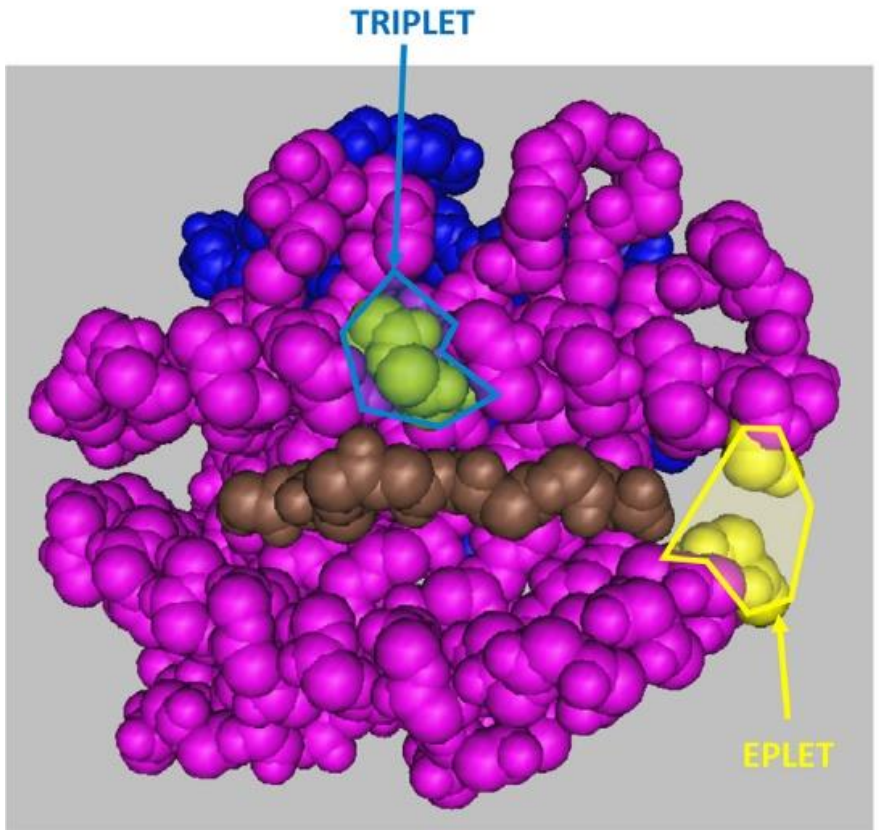
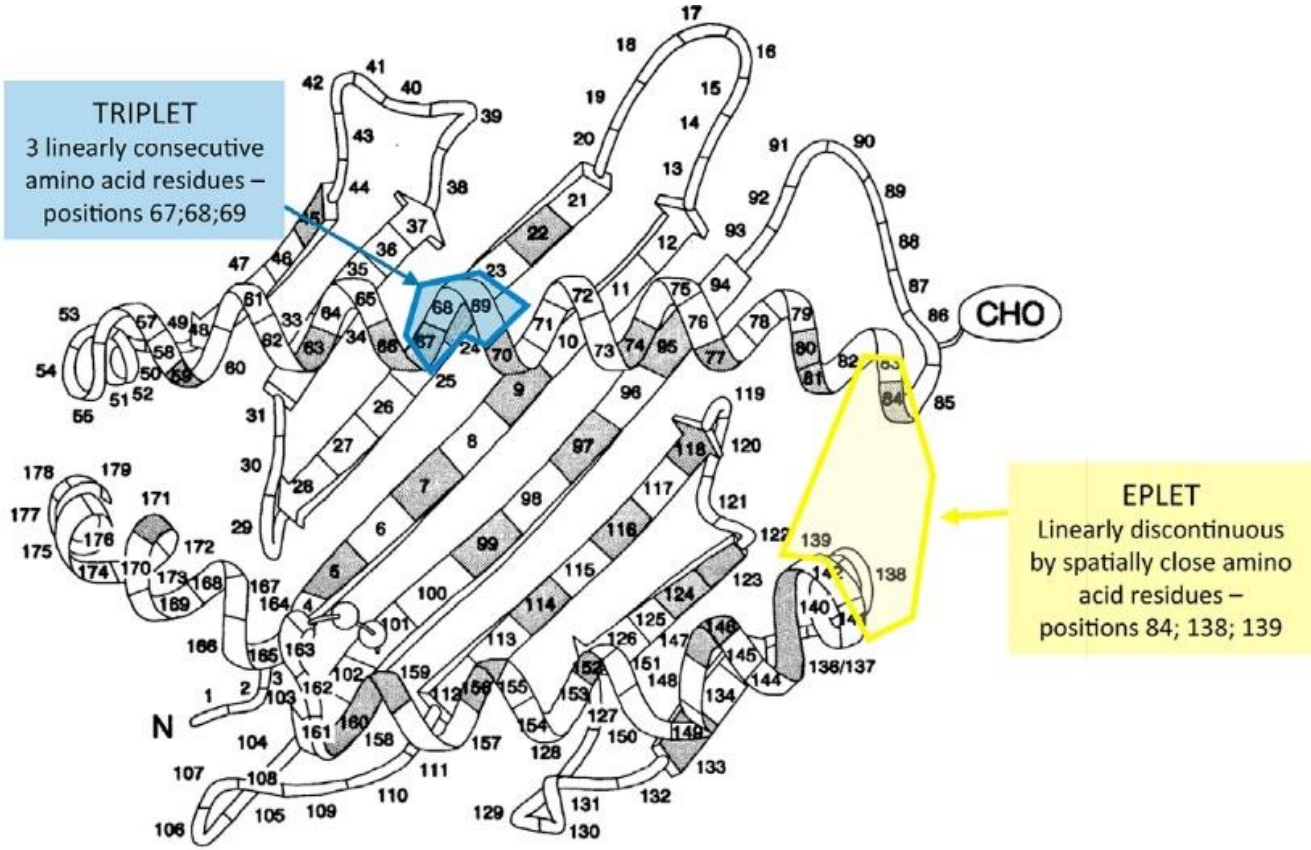
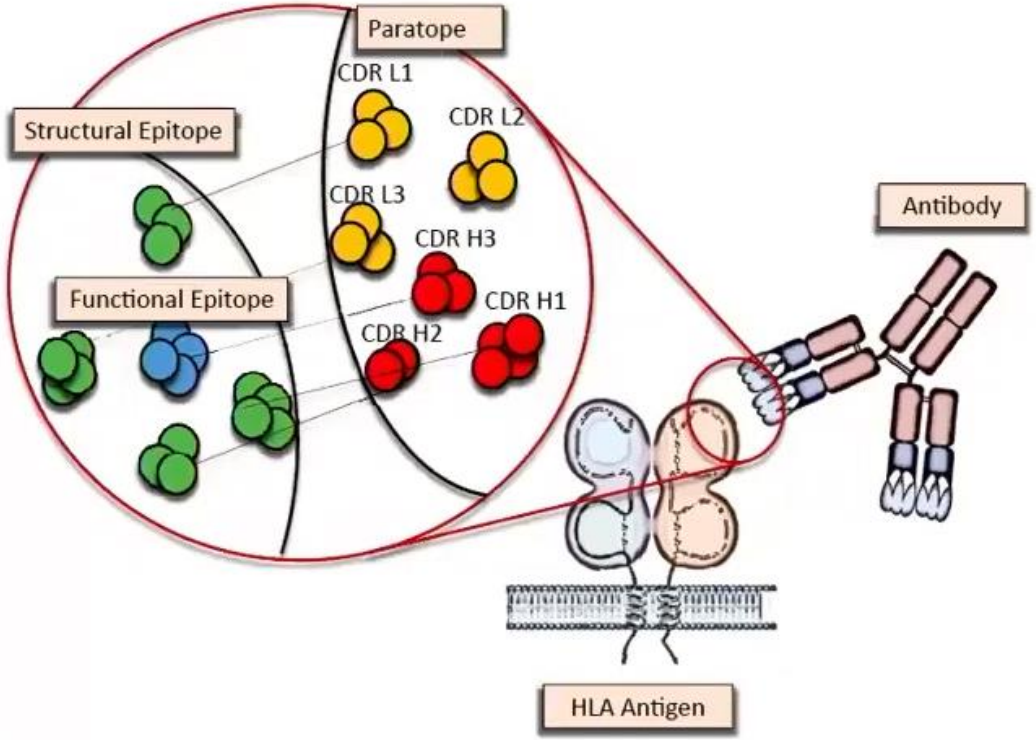
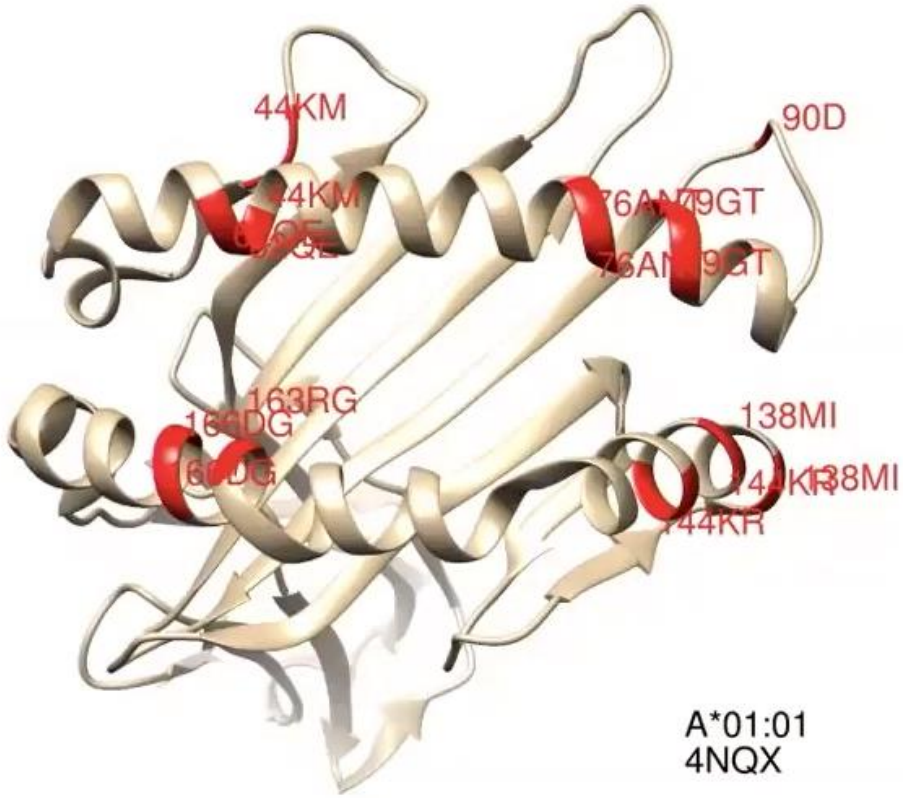


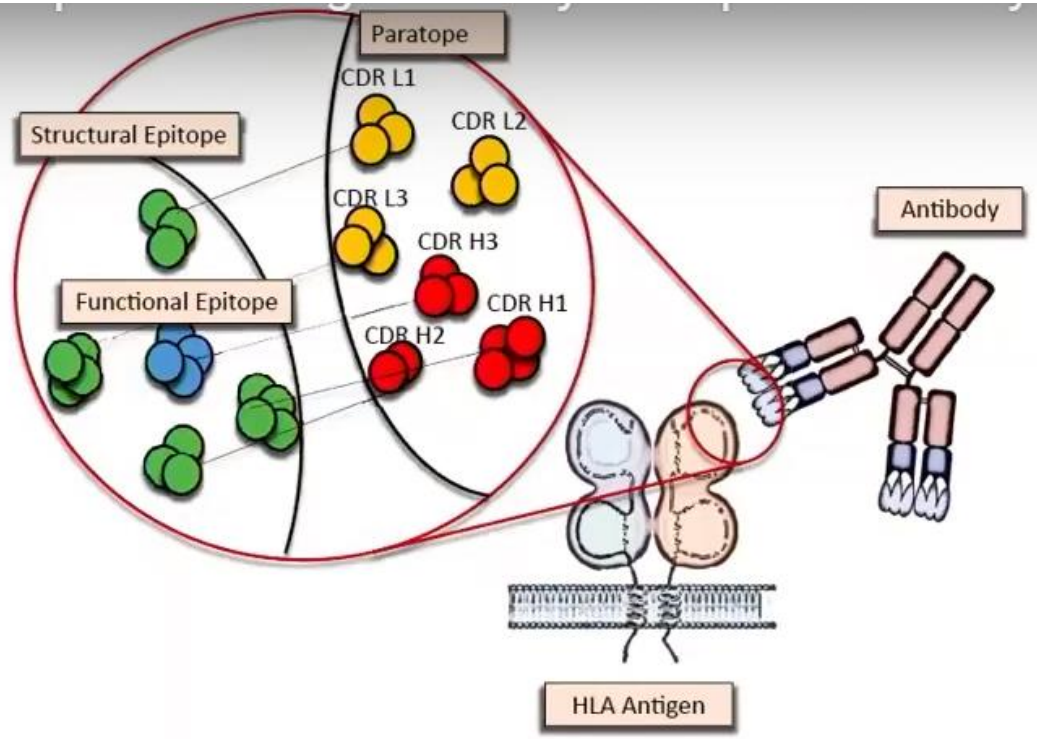


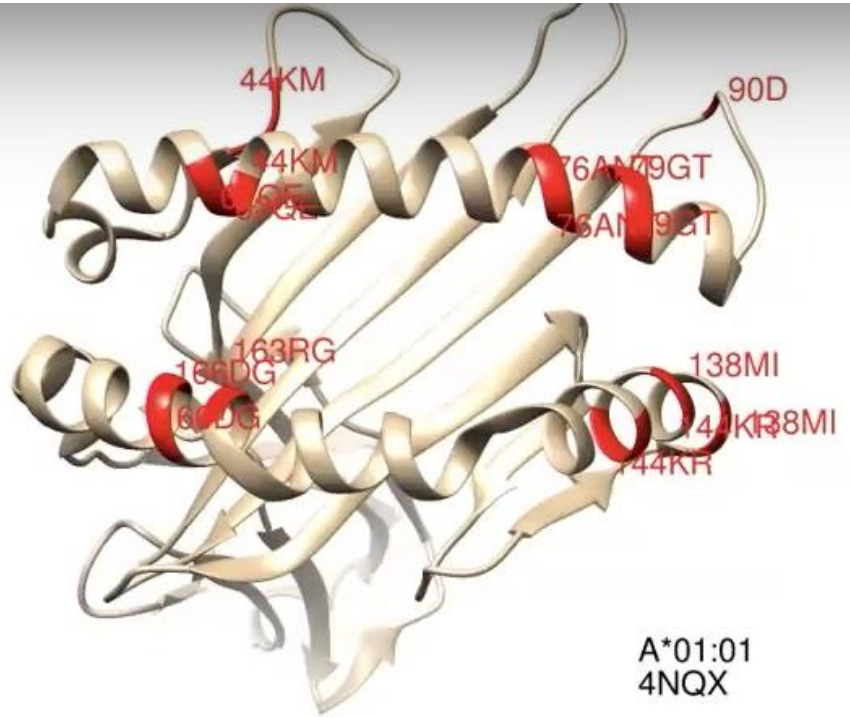
Tambur AR, Claas FH. Am J Transplant. 2015 May;15(5):1148-54. doi: 10.1111/ajt.13192.





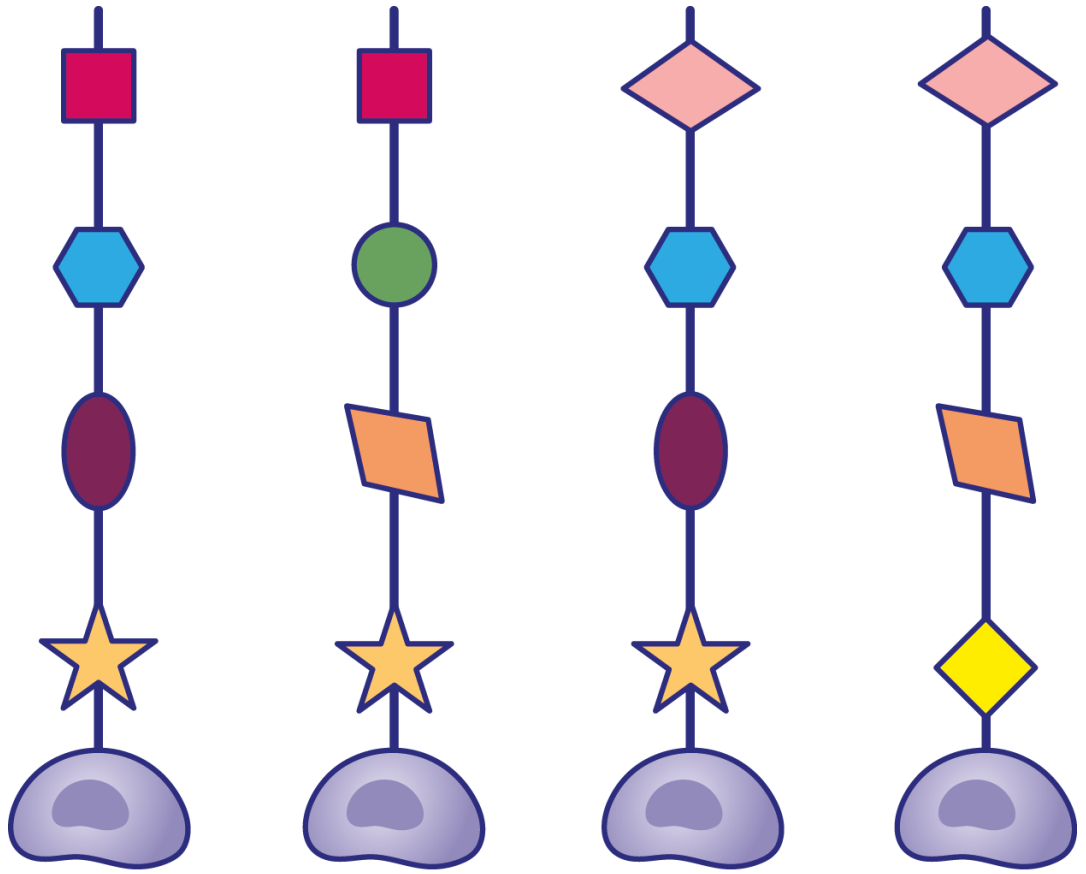
Recipient B*7		
Donor 1	B*8	1 mismatch
Donor 2	B*35	1 mismatch
Donor 3	B*44	1 mismatch



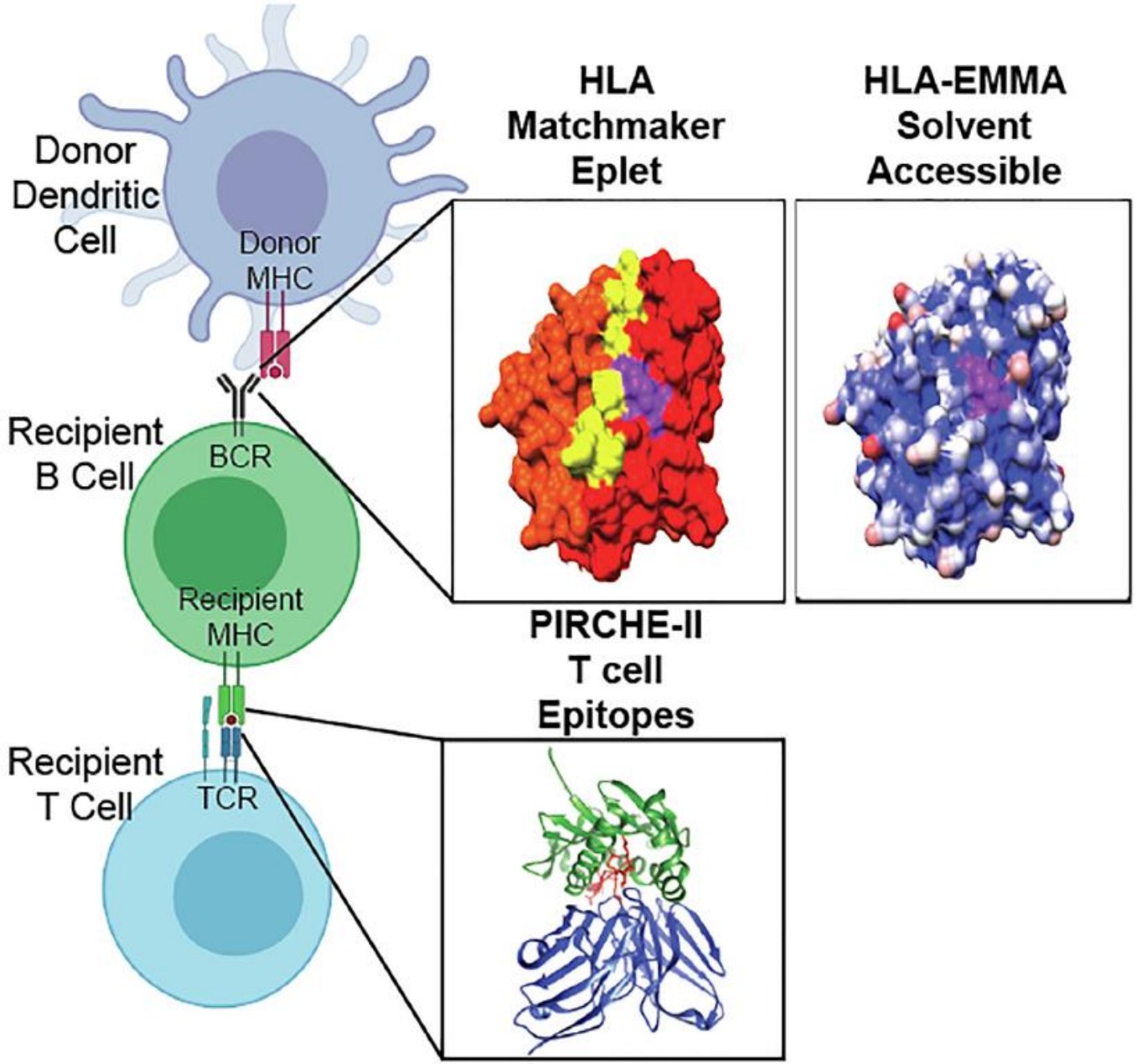


		80 90
Recipient	B*7	AQTDRESLRN LRGYYNQSEA
Donor 1	B*8	T--------- ----------
Donor 2	B*35	T--Y------ ----------
Donor 3	B*44	T--Y--N--T ALR-------

HLA Antijenlerinin Kendilerine Özgü Epitop Kombinasyonu Var, Ama…



Tambur AR, Claas FH. Am J Transplant. 2015 May;15(5):1148-54. doi: 10.1111/ajt.13192.



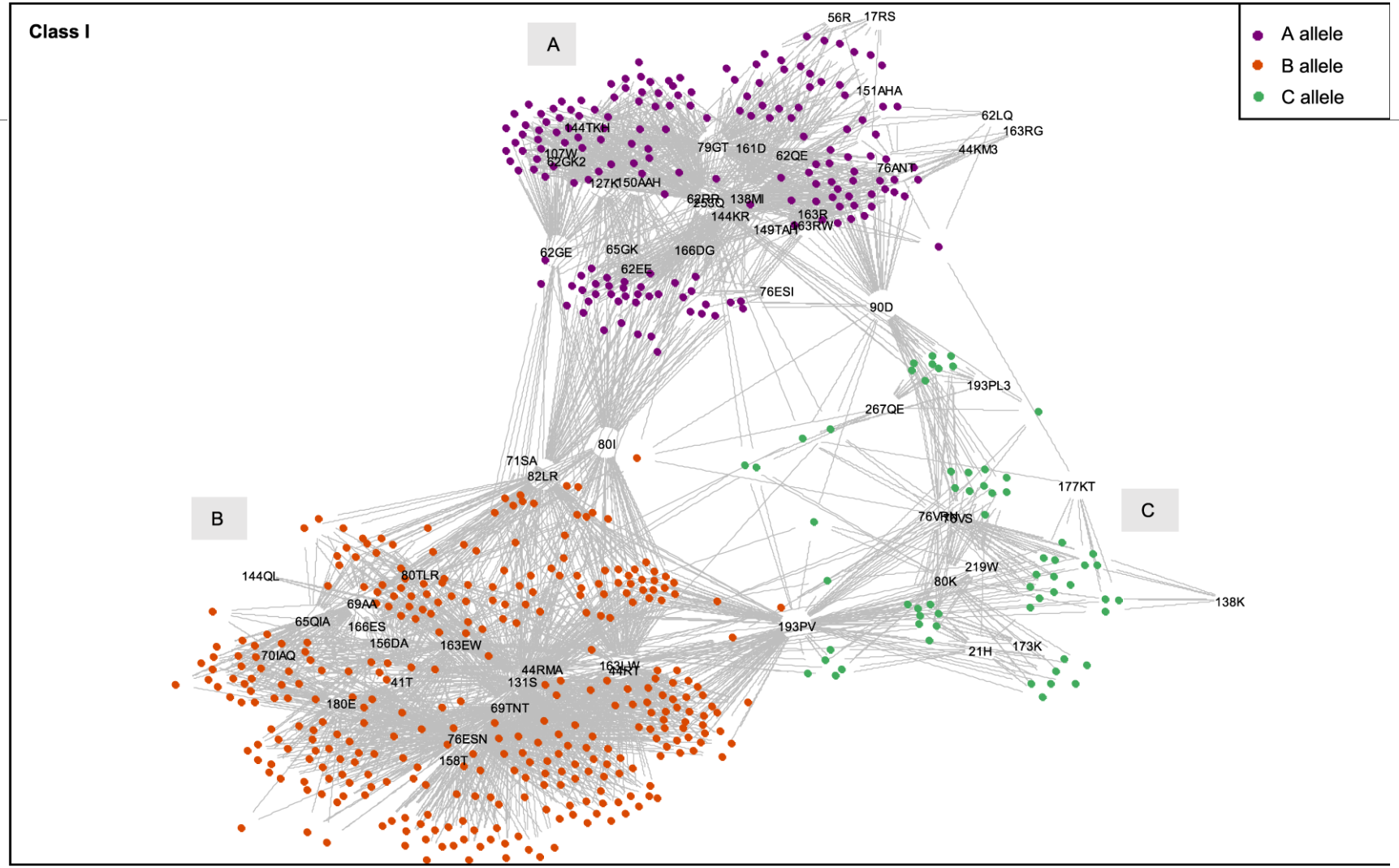
UNIVERSITY OF CAMBRIDGE
Immunogenicity Algorithms

PyMOL

HLA Eplet Registry

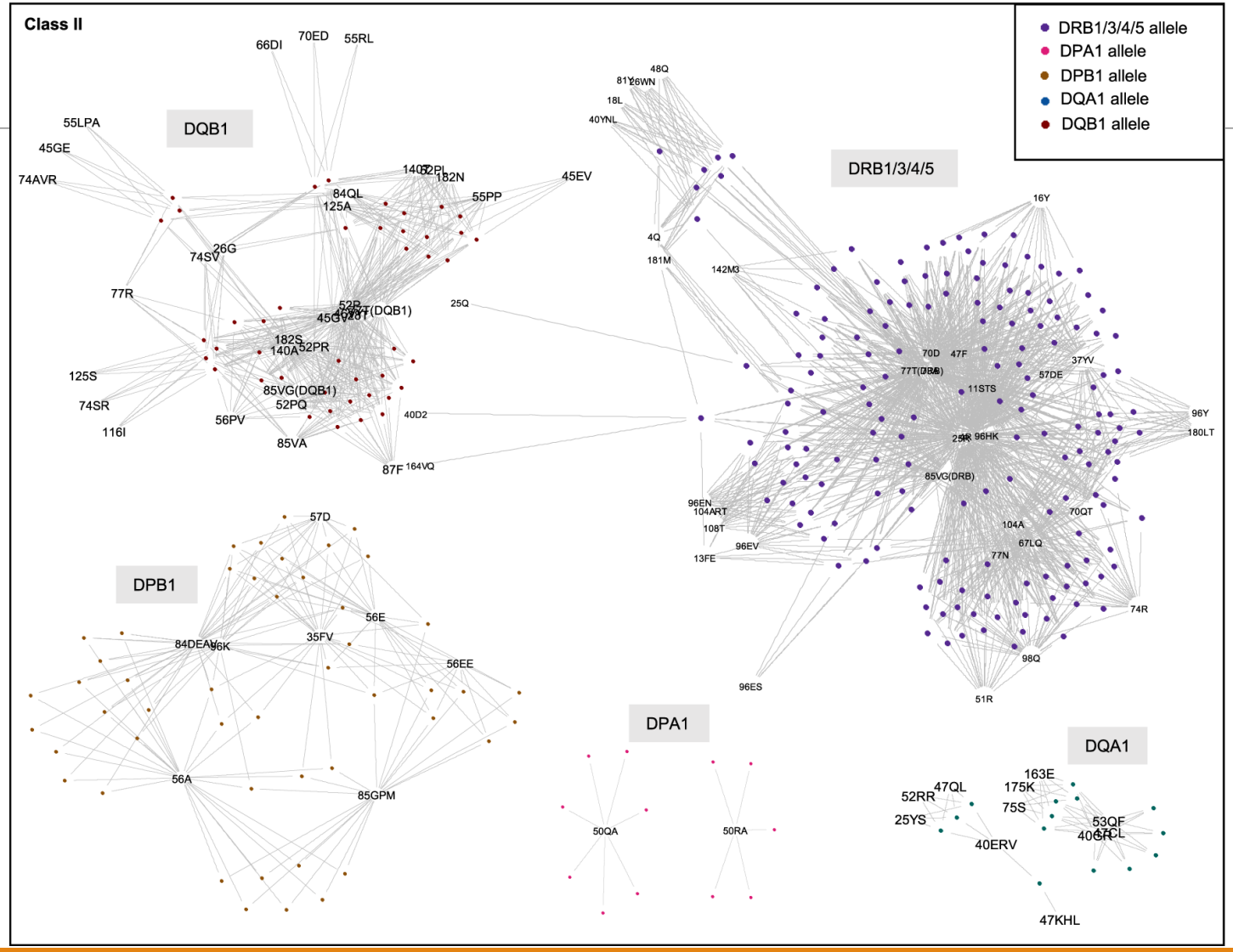
Ladowski JM et.al. Human Immunology, 2021

HLA sınıf I genleri için HLAMatchmaker v02'de mevcut olan HLA alellerinin ve bunlarla ilişkili epletlerin tam kütüphanesinin ağları

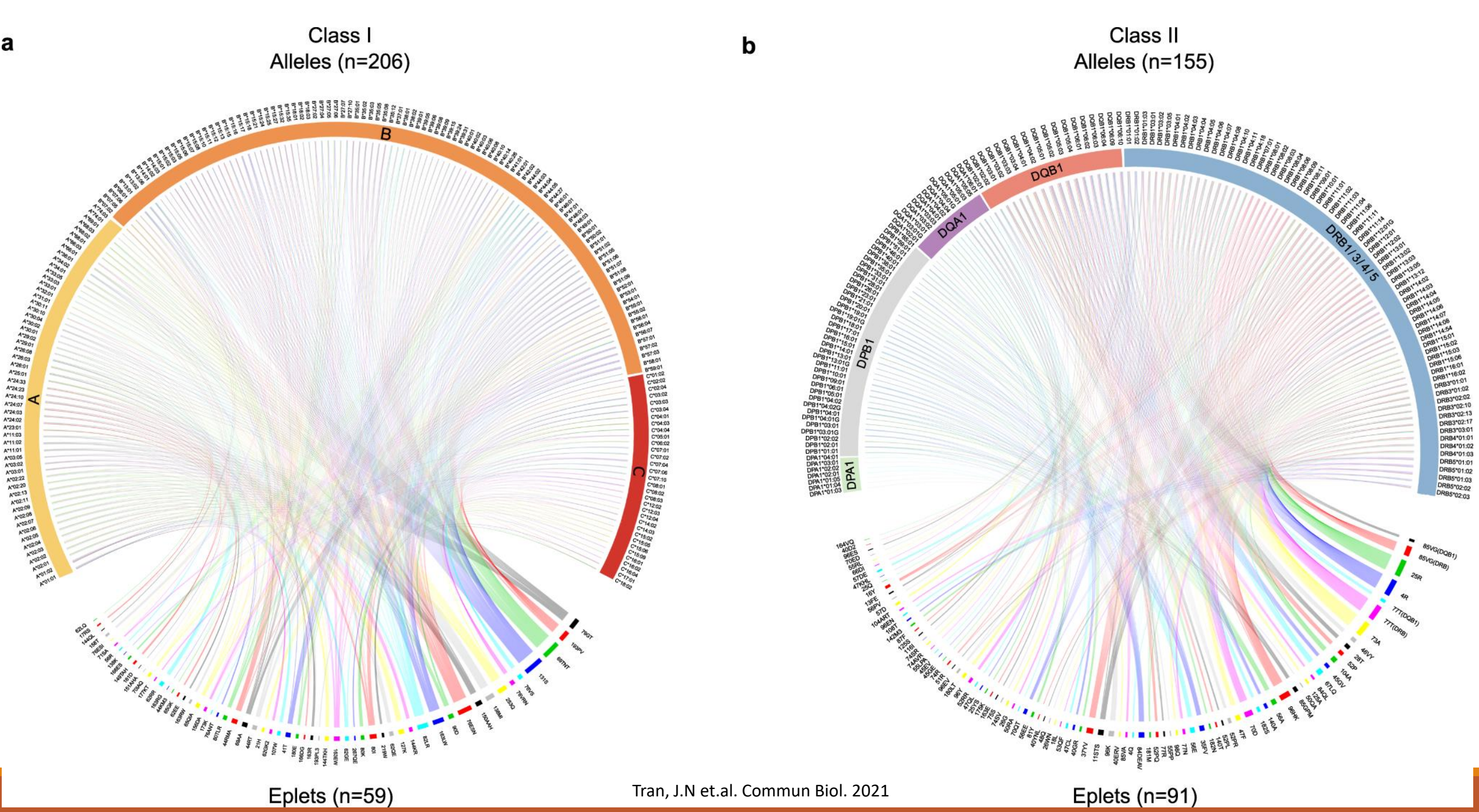


Tran, J.N et.al. Commun Biol. 2021

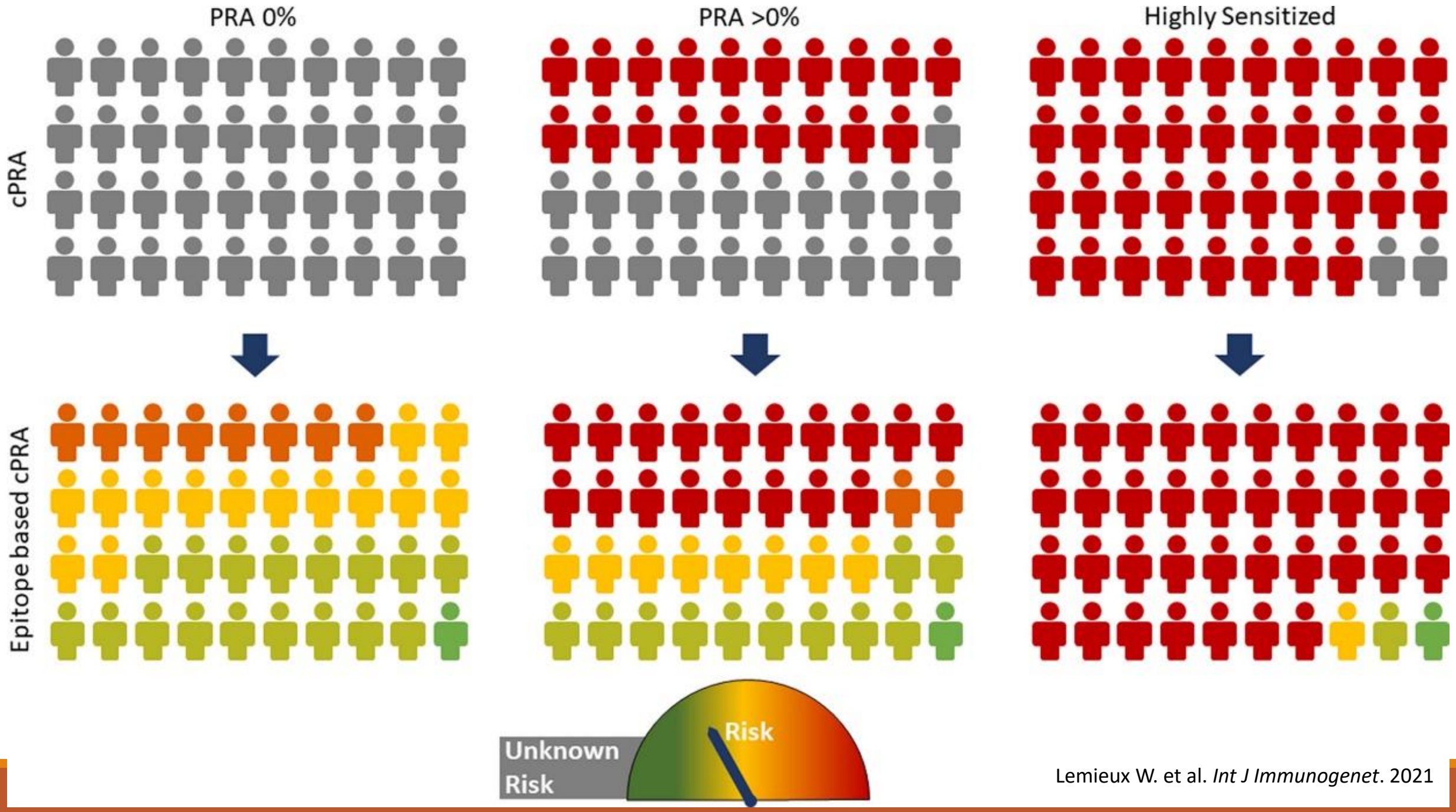
HLA sınıf II genleri için HLAMatchmaker v02'de mevcut olan HLA alellerinin ve bunlarla ilişkili epletlerin tam kütüphanesinin ağları



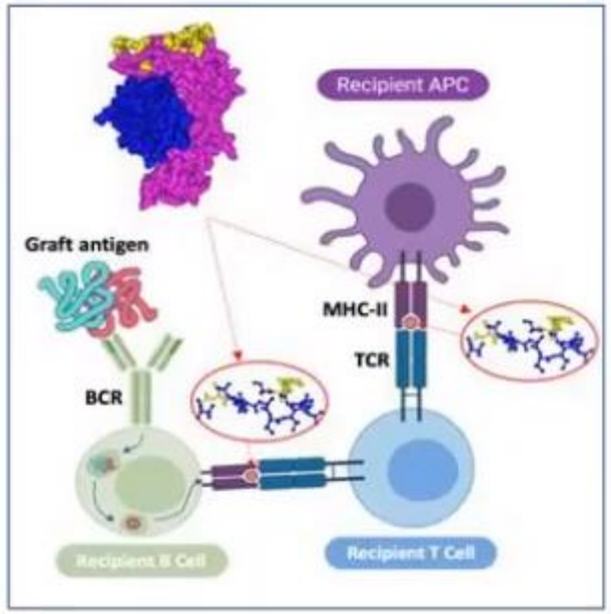
Tran, J.N et.al. Commun Biol. 2021

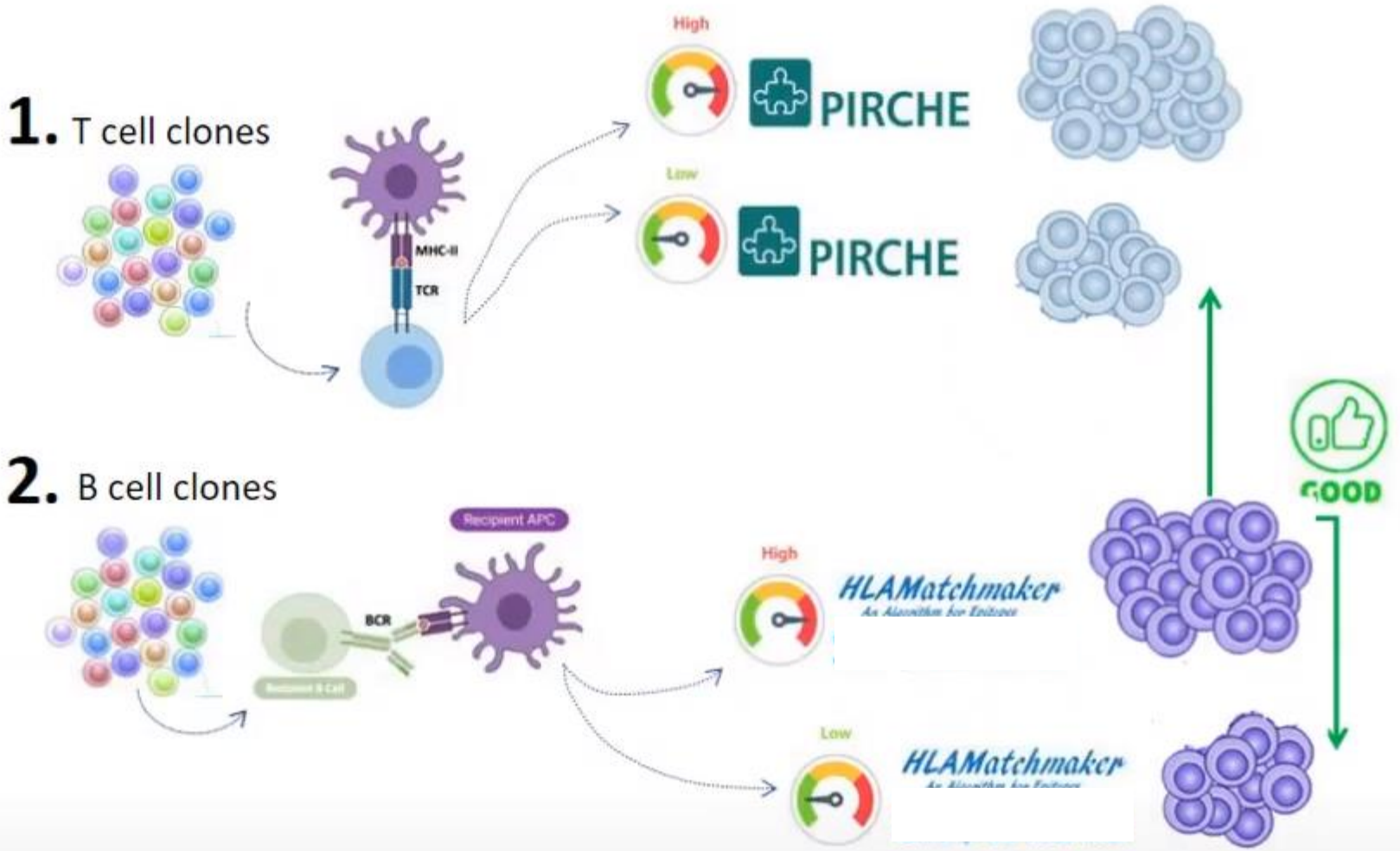


Tran, J.N et.al. Commun Biol. 2021

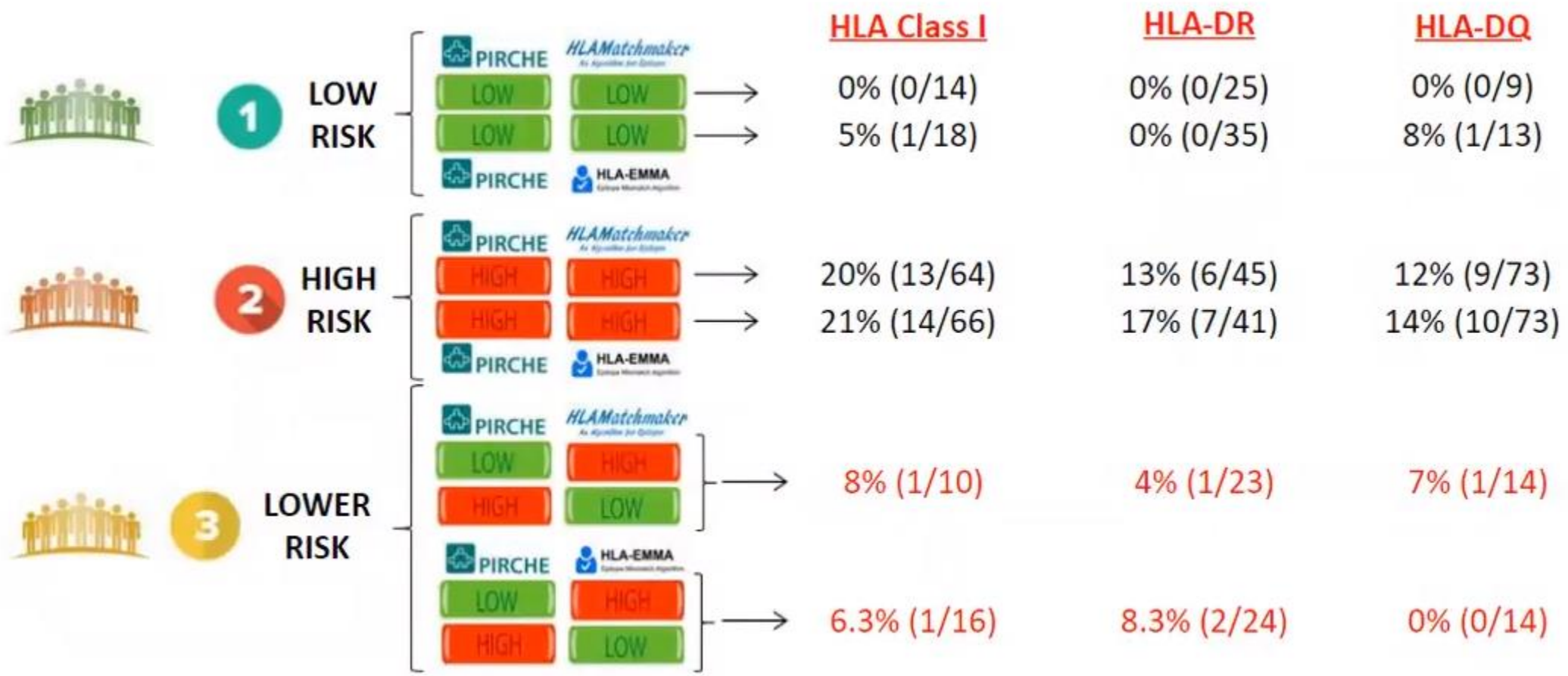


Lemieux W. et al. *Int J Immunogenet*. 2021


Recipient APC
Graft antigen
MHC-II
TCR
BCR
Recipient B Cell
Recipient T Cell

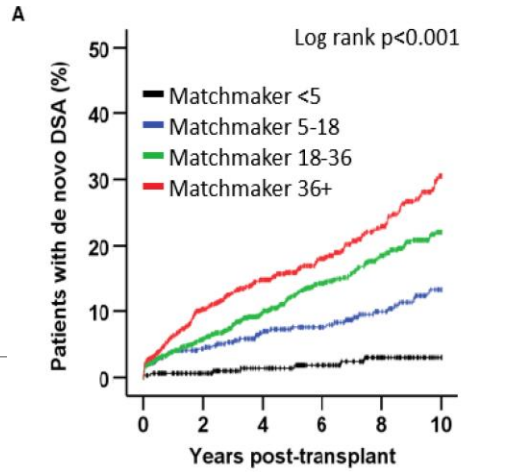

1. T cell clones
MHC-II
TCR
High
PIRCHE
Low
PIRCHE
2. B cell clones
Recipient APC
BCR
High
HLAMatchmaker
Low
HLAMatchmaker
GOOD

Algoritmalarla Risk Değerlendirmesi (DSA)



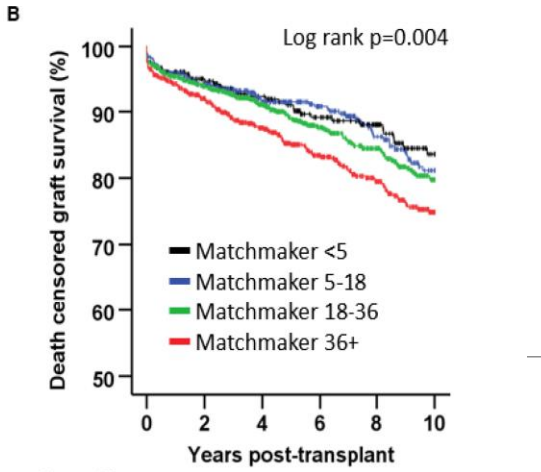
n= 2787

dnDSA&greft sağkalımı



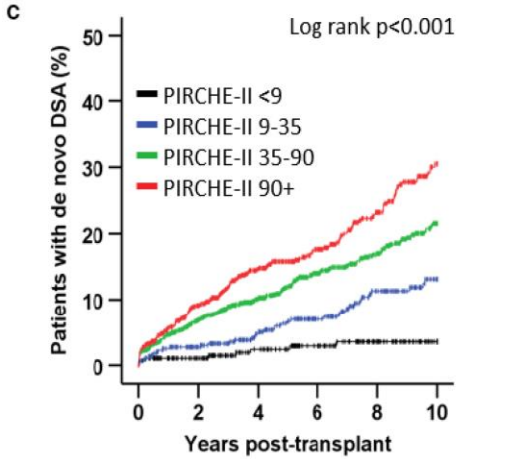
Number at risk

Years post-transplant	0	2	4	6	8	10
Matchmaker <5	323	280	236	193	145	101
Matchmaker 5-18	476	397	326	263	201	150
Matchmaker 18-36	1136	917	683	510	388	249
Matchmaker 36+	852	644	495	371	265	162



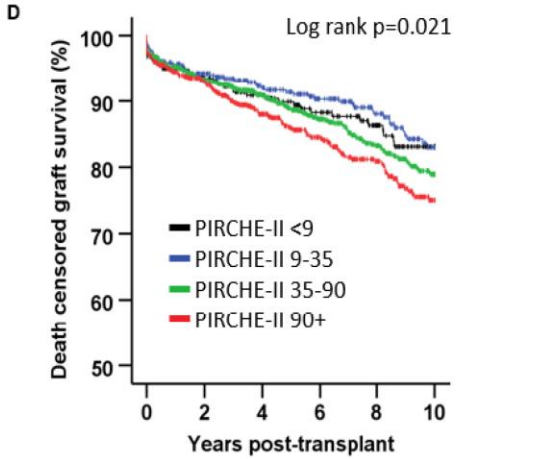
Number at risk

Years post-transplant	0	2	4	6	8	10
Matchmaker <5	323	268	222	179	136	90
Matchmaker 5-18	476	391	320	255	190	138
Matchmaker 18-36	1136	926	703	524	399	250
Matchmaker 36+	852	672	523	388	278	168



Number at risk

Years post-transplant	0	2	4	6	8	10
PIRCHE <9	285	246	203	168	126	87
PIRCHE 9-35	446	378	311	245	182	131
PIRCHE 35-90	1222	984	763	578	451	301
PIRCHE 90+	834	630	463	346	240	143



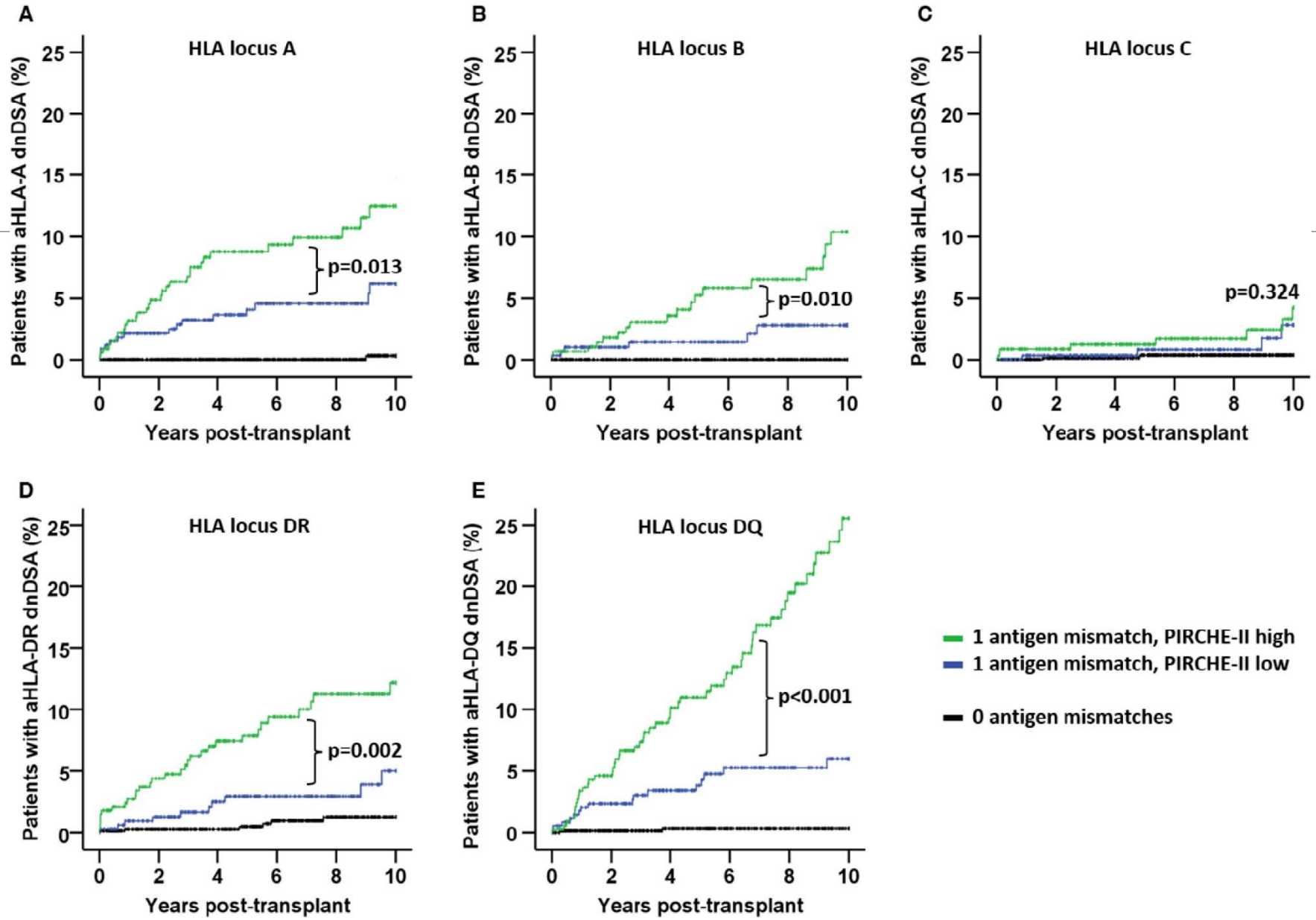
Number at risk

Years post-transplant	0	2	4	6	8	10
PIRCHE <9	285	234	190	155	116	77
PIRCHE 9-35	446	370	301	238	179	123
PIRCHE 35-90	1222	1001	787	590	450	299
PIRCHE 90+	834	652	490	363	258	147

Lachmann et al. American Journal of Transplantation 2017 173076-3086DOI: (10.1111/ajt.14393)

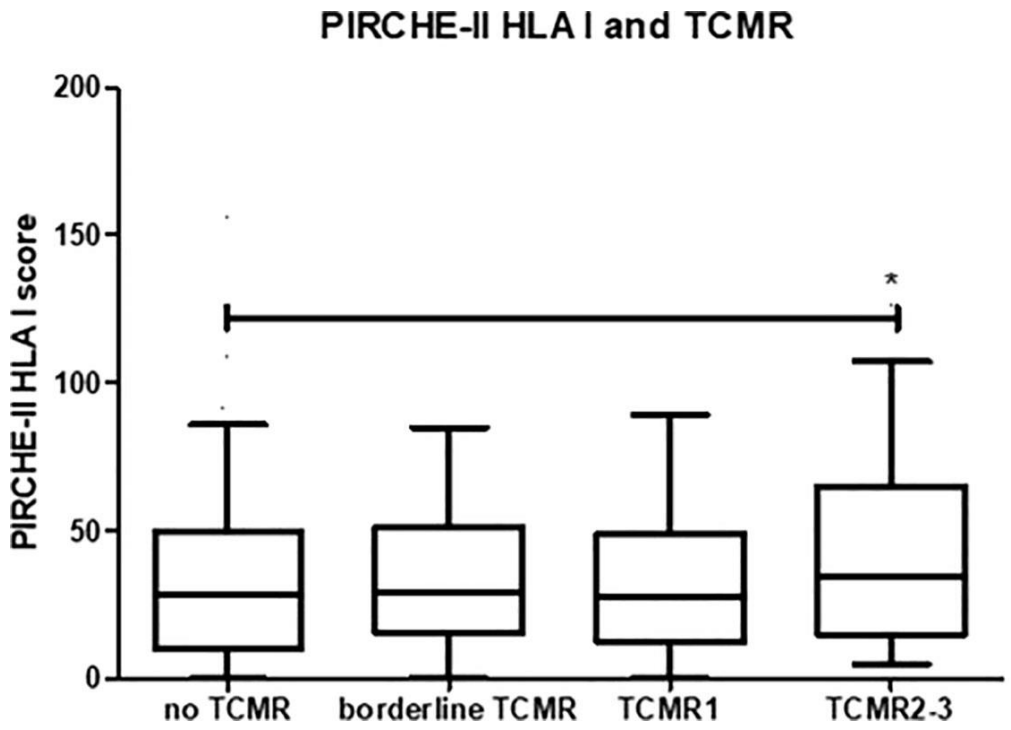
n= 2787

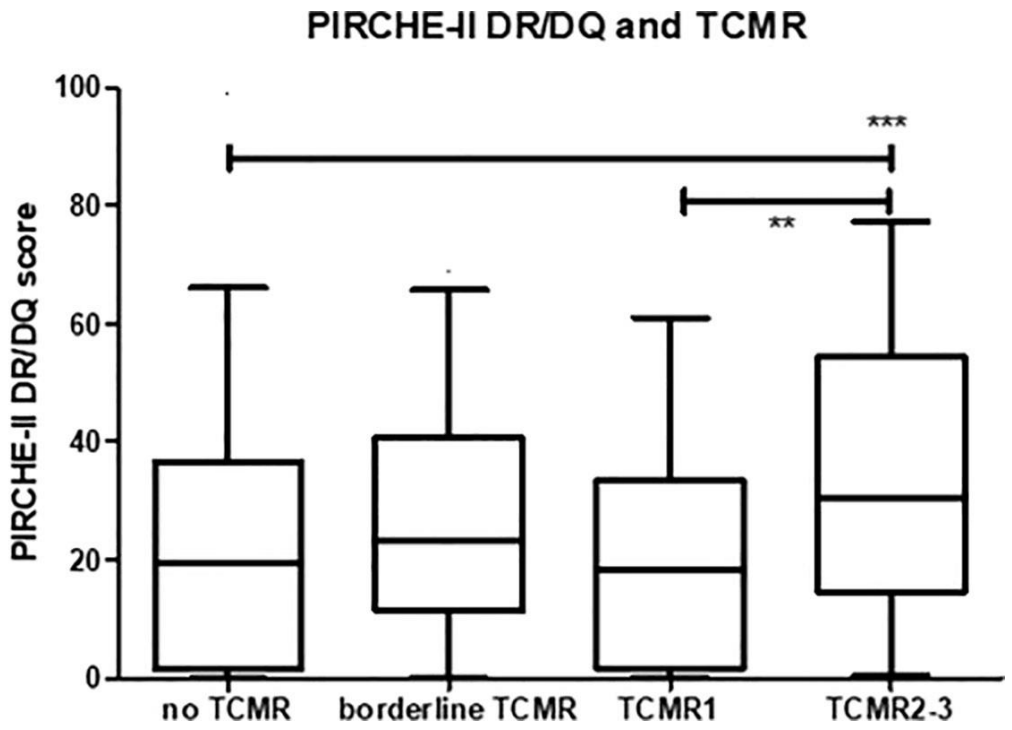
dnDSA



Lachmann et al. American Journal of Transplantation 2017 173076-3086DOI: (10.1111/ajt.14393)

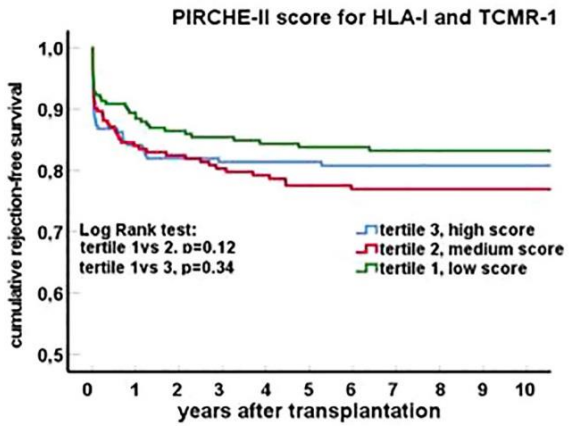
PIRCHE-II Skorlaması ve T-Hücre Aracılı Ret

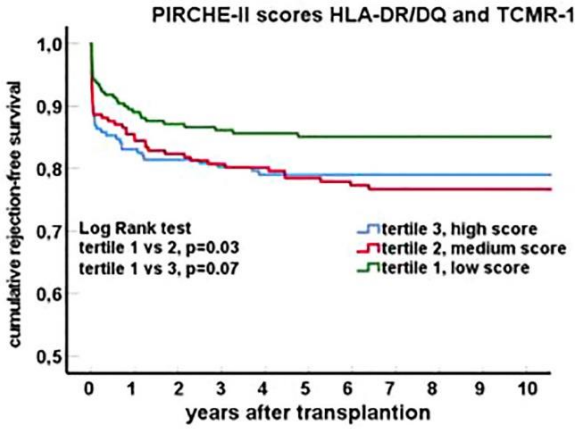


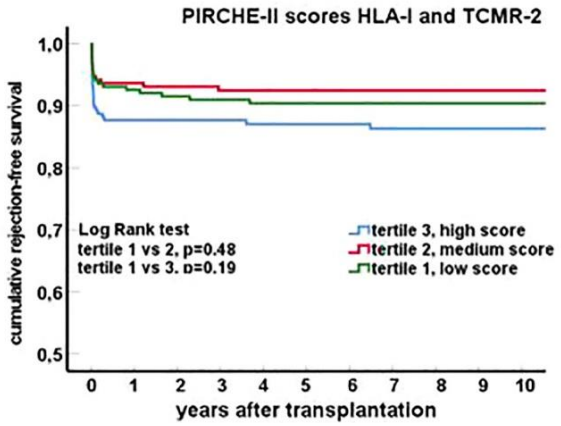


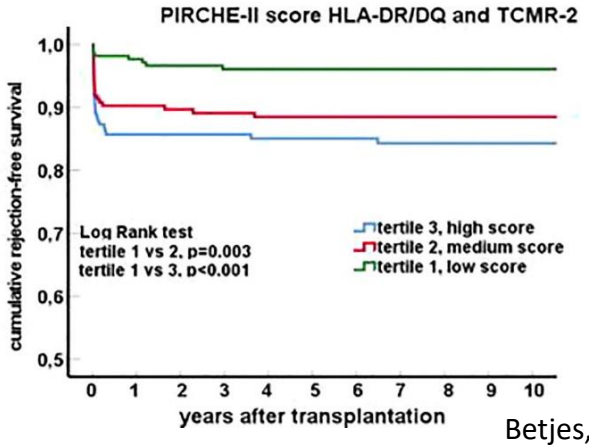
Betjes, M. et al.(2022) *Frontiers in Immunology*, *13*.

PIRCHE-II Skorlaması ve T-Hücre Aracılı Ret

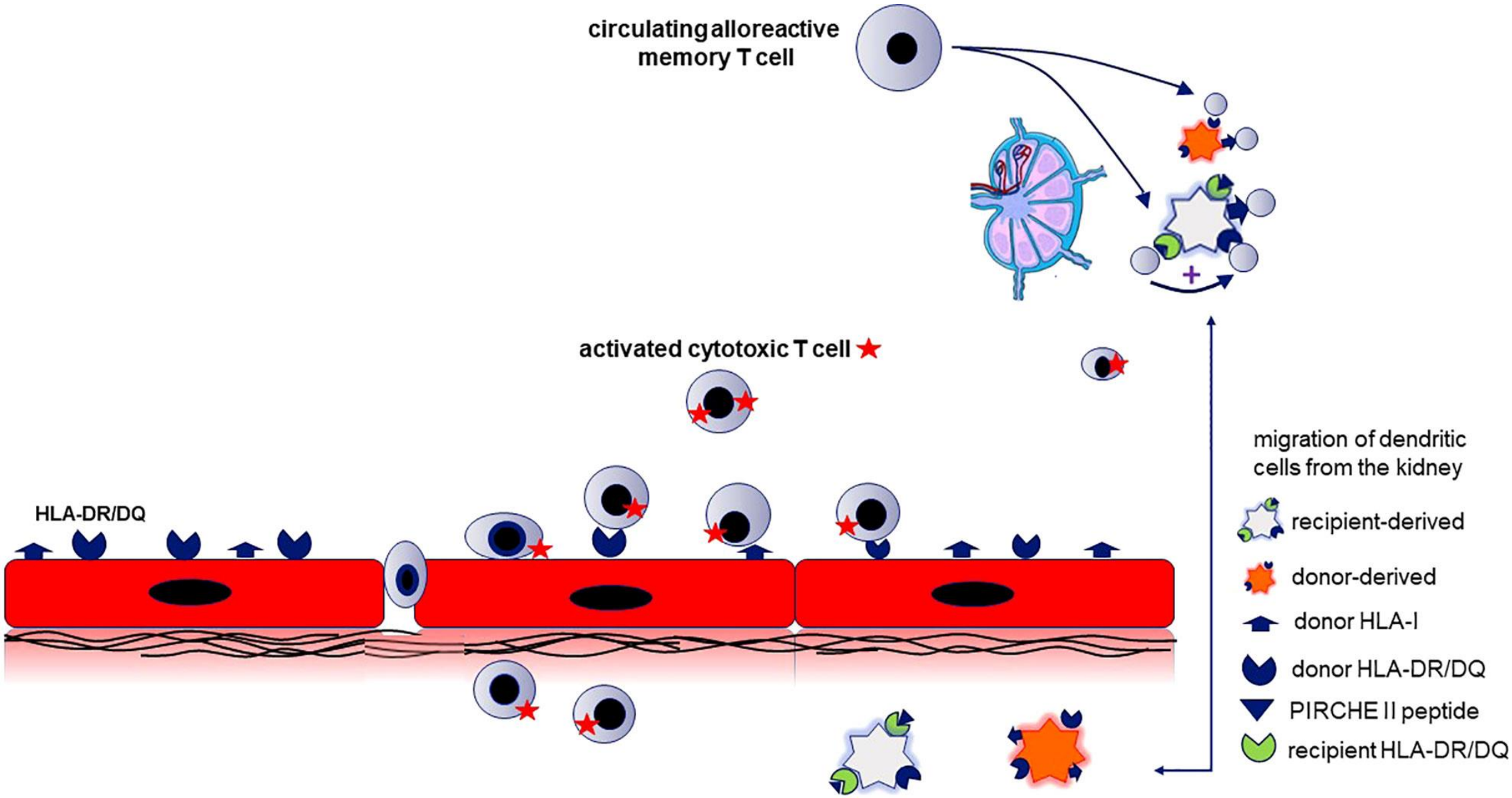








Betjes, M. et al.(2022) *Frontiers in Immunology*, *13*.



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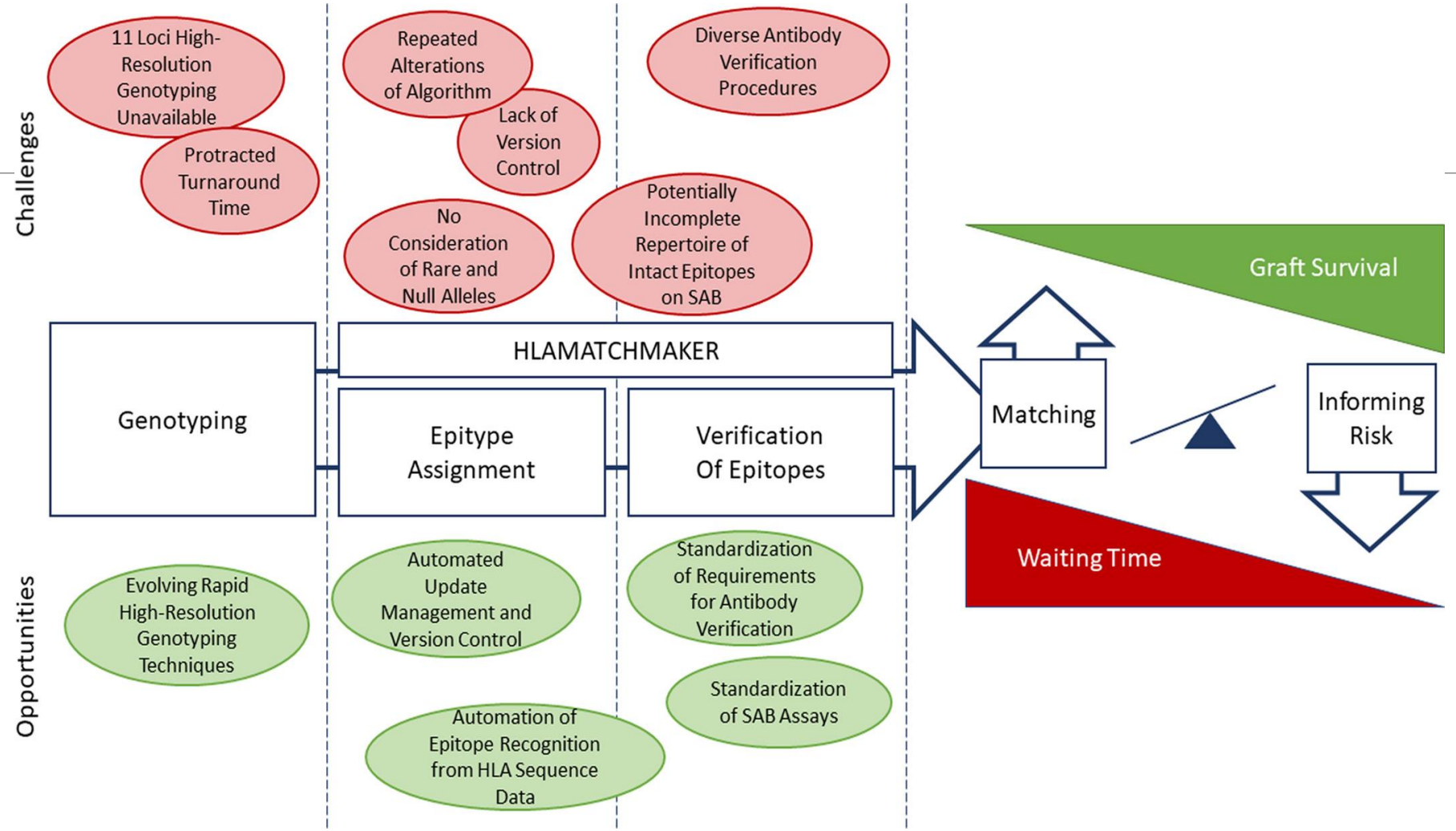


Int J Immunogenetics, Volume: 48, Issue: 2, Pages: 135-144, First published: 10 January 2021, DOI: (10.1111/iji.12525)

Nerden Başlamalı?

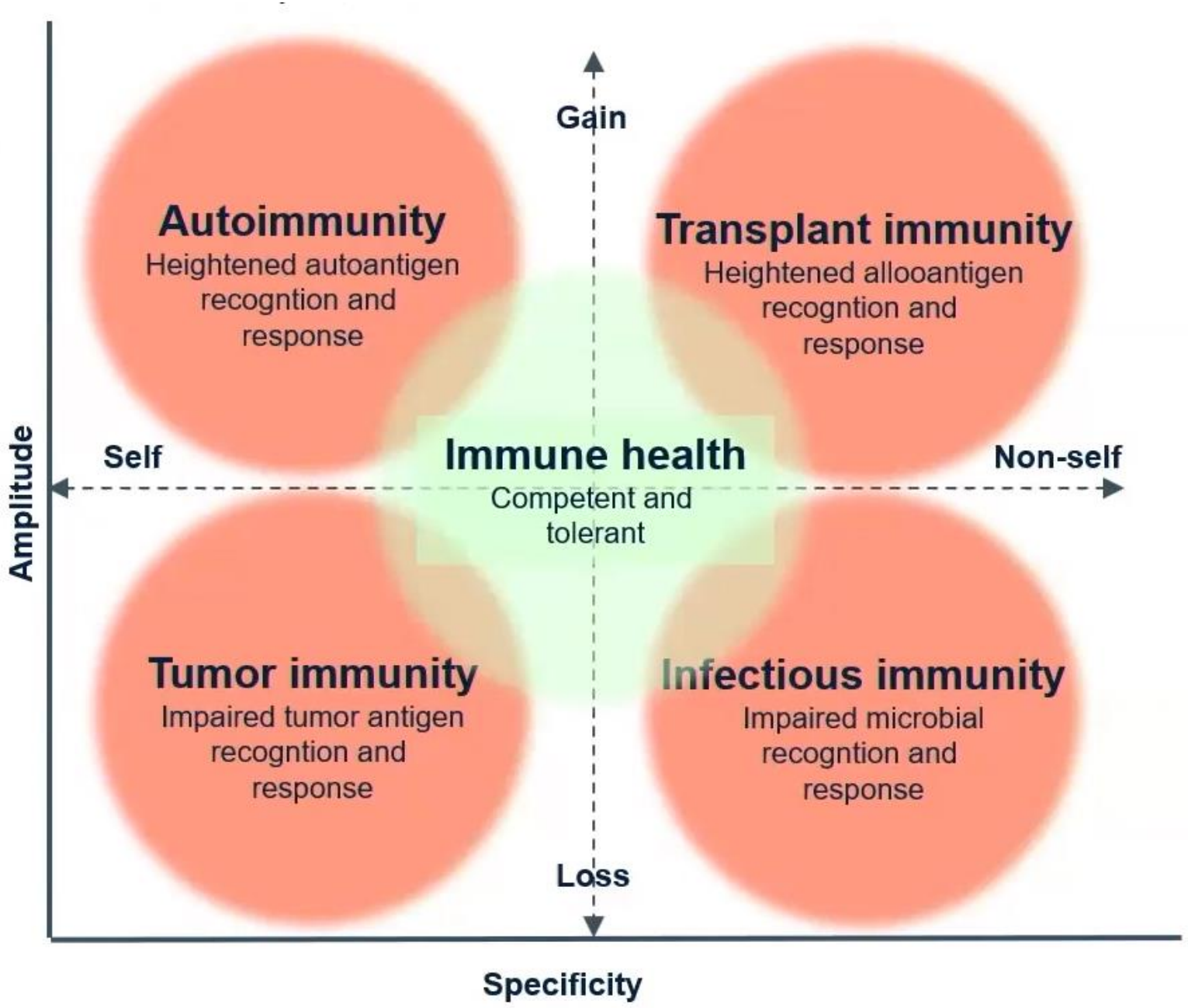
1
- Çalışma Grubu

2
- Yüksek çözünürlüklü HLA Tiplemesi
- Eplet/Epitop MM Algoritmaları
- Düşük ve Yüksek Risk Tanımlamaları

3
- Biopsi Skorları
- Klinik Veriler

İstatistiksel Analizler

Multidisipliner Bakış Açısı...



Tran, J.N et.al. Commun Biol. 2021

Özet

Moleküler uyumluluk immünolojik riski daha iyi tanımlar

Hasta/Donör moleküler uyumu; HLA Matchmaker, HLA-EMMA ve PIRCHE algoritmaları ile tahmin edilebilir

Moleküler uyumluluk mükemmel bir prognostik belirteçtir

Adaptif bağışıklık yanıtındaki T/B hücrelerinin işbirliği nedeniyle T hücre peptit uyumsuzluğunu ve B hücre epitop uyumsuzluğu ile birleştirip değerlendirmek daha ayrıntılı ve kesin risk tanımlanmasına olanak tanır

Ükemizde bu alanda yapılacak çalışmalara ihtiyaç var…