Frequency and Outcome of De novo Donor-specific Antibodies in Renal Allograft; the Role of Treatment

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Introduction:

- **Donor-specific antibodies:**

  Established biomarker predicting antibody-mediated rejection.

- **Antibody-mediated rejection (AMR):**

  Leading cause of graft loss after kidney transplant.

➢ Several phenotypes of AMR along post-transplant course determined by:

The timing and extent of humoral response

Characteristics of donor-specific antibodies, such as:

Antigen classes, Specificity, Antibody strength, IgG subclasses, and Complement binding capacity.

Complement binding capacity:

- C1q binding DSAs are closely associated with acute antibody-mediated rejection, more severe graft injuries, and early graft failure.

  when positive after treatment of ABMR, was also associated with lower clinical and histologic response to therapy*.

- C1q non-binding DSAs correlate with subclinical or chronic antibody-mediated rejection and late graft loss.

IgG subclasses:

- Complement binding IgG3 DSAs are frequently associated with acute antibody-mediated rejection and severe graft injury.
- Non-complement binding IgG4 DSAs are more correlated with subclinical or chronic antibody-mediated rejection and transplant glomerulopathy.

*Clinical recommendations for posttransplant assessment of anti–HLA (Human Leukocyte Antigen) donor-specific antibodies: A Sensitization in Transplantation: Assessment of Risk consensus document, American Journal of Transplantation 23 (2023)
Donor-Specific Antibodies in Kidney Transplant Recipients. Clin J Am Soc Nephrol. 2018

DSA timing

Preformed donor-specific antibodies (DSAs)

Alloimmune memory

Identified before kidney transplant, and/or the development of a new DSA in the first 2 weeks to 3 months posttransplant (peritransplant DSA)*

Trigger hyper-acute rejection, accelerated acute rejection, early acute antibody-mediated rejection. kidney allograft loss in both living and deceased donor recipients.

De novo donor-specific antibodies (DSAs)

Alloimmune primary or naïve response

Developed DSA >= 3 months after transplant*

Associated with late acute antibody-mediated rejection, chronic antibody-mediated rejection, and transplant glomerulopathy

*Clinical recommendations for posttransplant assessment of anti–HLA (Human Leukocyte Antigen) donor-specific antibodies: A Sensitization in Transplantation: Assessment of Risk consensus document, American Journal of Transplantation 23 (2023)

Preformed vs de novo DSAs:

- Recent studies provided additional understanding of the importance of distinguishing preformed vs de novo DSAs and their posttransplant evolution.
- Posttrans
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  3) De nov

Patients with persistent preformed DSAs displayed the highest risk of ABMR and allograft loss compared with patients with resolved preformed DSAs or DSA-negative patients.
Specifically, preformed DSAs with MFI >3000 in pretransplant sera or of DQ specificity were more likely to persist posttransplant, unlike resolved DSAs.

*Clinical recommendations for posttransplant assessment of anti–HLA (Human Leukocyte Antigen) donor-specific antibodies: A Sensitization in Transplantation: Assessment of Risk consensus document, American Journal of Transplantation 23 (2023)

Benign donor-specific antibodies (DSAs)

- “Benign” DSAs that may not be clinically relevant, because they are not associated with antibody-mediated rejection or graft failure.

❑ The development of de novo DSAs after kidney transplant was reported in 13%–30% of previously non-sensitized patients.

❑ The reported incidence of de novo DSA varies, but is about 2–10% at 1 year after renal transplantation, increases by 2% per year and reaches about 10–40% at 4–5 years after transplantation.

Donor-Specific Antibodies in Kidney Transplant Recipients. Clin J Am Soc Nephrol. 2018 Jan 6.

Clinical characteristics of renal transplant recipients who developed de novo donor-specific antigen in Kyoto University Hospital: a case series. Renal Replacement Therapy.2022

The risk factors for de novo DSA include the following:

(1) High HLA mismatches (especially DQ mismatches),

(2) Inadequate immunosuppression (especially tacrolimus trough levels <5 ng/mL)

Among patients with suboptimal Calcineurin inhibitor levels, HLA epitope mismatch load assessment may further identify patients with a higher risk of de novo DSA development.

(3) Nonadherence (missing, forgetting, or altering a dose of immunosuppressive medication at least once per month (tacrolimus fluctuation))

(4) Immunosuppression minimization (switch from CnI to mTOR inhibitors)

(5) Calcineurin inhibitor intra-patient variability.

The use of tacrolimus has been associated with decreased dnDSA development compared with cyclosporine or mTOR inhibitors*.

*Class II eplet mismatch modulates tacrolimus trough levels required to prevent donor-specific antibody development. J Am Soc Nephrol. 2017

Donor-Specific Antibodies in Kidney Transplant Recipients.Clin J Am Soc Nephrol. 2018

The risk factors for de novo DSA- continued:

(6) Graft inflammation, such as viral infection, cellular rejection, or ischemia injury, which can increase graft immunogenicity.

(7) clinical event include blood transfusions, pregnancy, homograft implantation.

Patients with de novo DSAs display:
25%-53% incidence of subclinical ABMR at the time of de novo DSA detection.
Up to 52.9% at 1 year after de novo DSA detection.

Patients with de novo DSAs also exhibit a higher risk of chronic ABMR than patients with preformed DSAs.

- In addition,
  the presence of circulating DSAs, regardless of preformed or de novo status, is associated with increased expression of ABMR-related transcripts in kidney biopsies showing no histologic signs of ABMR.

In some study, Patients with de novo DSAs also had a significantly increased risk of kidney allograft loss compared with patients with both resolved or persistent preformed DSA status.

Clinical recommendations for posttransplant assessment of anti–HLA (Human Leukocyte Antigen) donor-specific antibodies: A Sensitization in Transplantation: Assessment of Risk consensus document, American Journal of Transplantation 23 (2023)

Clinical characteristics of renal transplant recipients who developed de novo donor-specific antigen in Kyoto University Hospital: a case series. Renal Replacement Therapy.2022

Anti-HLA antibodies classes

DSAs target specific epitopes in the polymorphic regions of HLA Ag.

HLA class I antigens (A, B, and C):

Expressed on all nucleated cells.

Consists of one a-chain and one β2-MG. The epitopes reside only in the polymorphic a-chain.

The β-chain of DQ is particularly polymorphic,
which adds clinical complexity of DQ antibodies.

HLA class 2 antigens (DR, DQ, DP):

Normally restricted to antigen-presenting cells (dendritic cells, B cells, and MQ)

They can be upregulated and expressed after inflammatory insults, such as ischemia-reperfusion injury, infection, rejection.

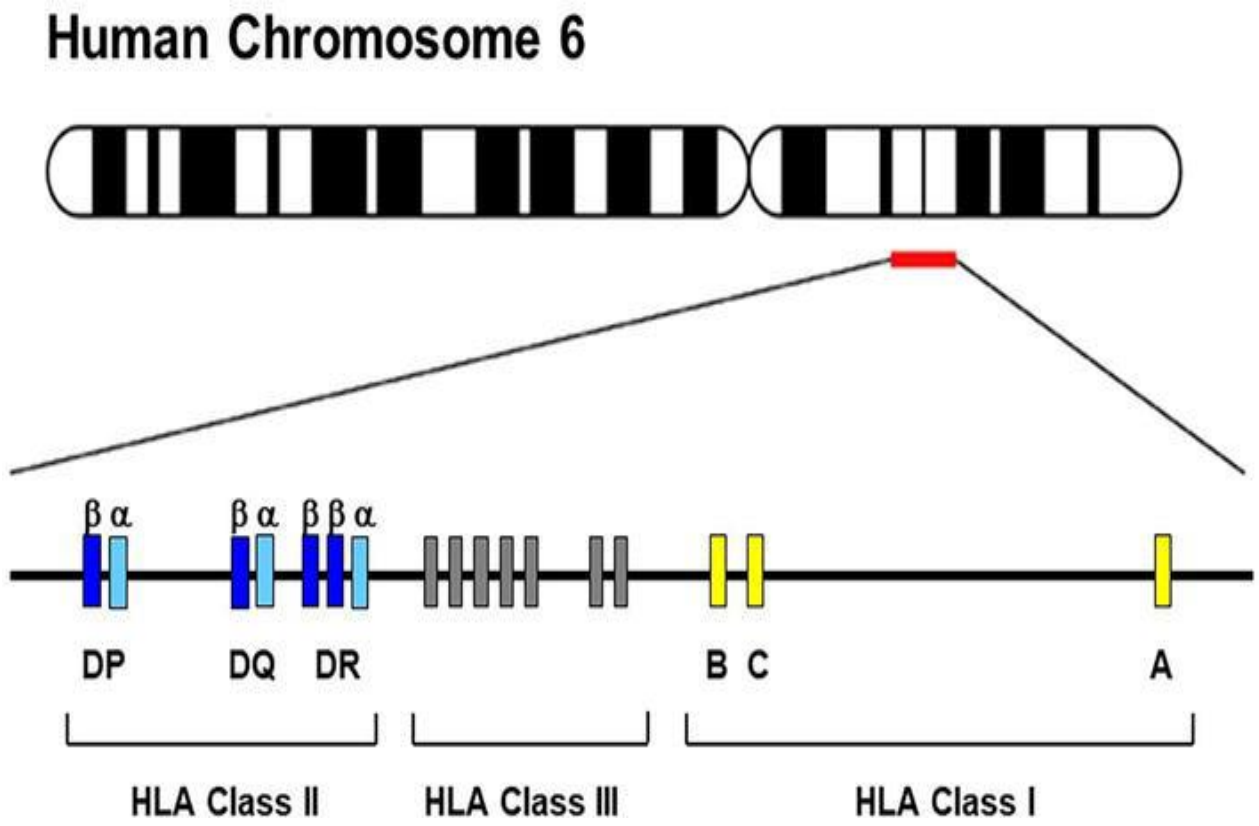
Consists of one a-chain and one *β*- chain, both chains are polymorphic

Donor-Specific Antibodies in Kidney Transplant Recipients.Clin J Am Soc Nephrol. 2018

The class III region is located between the class I and class II and contains genes encoding for molecules involved in immune function that are not targets for allorecognition.

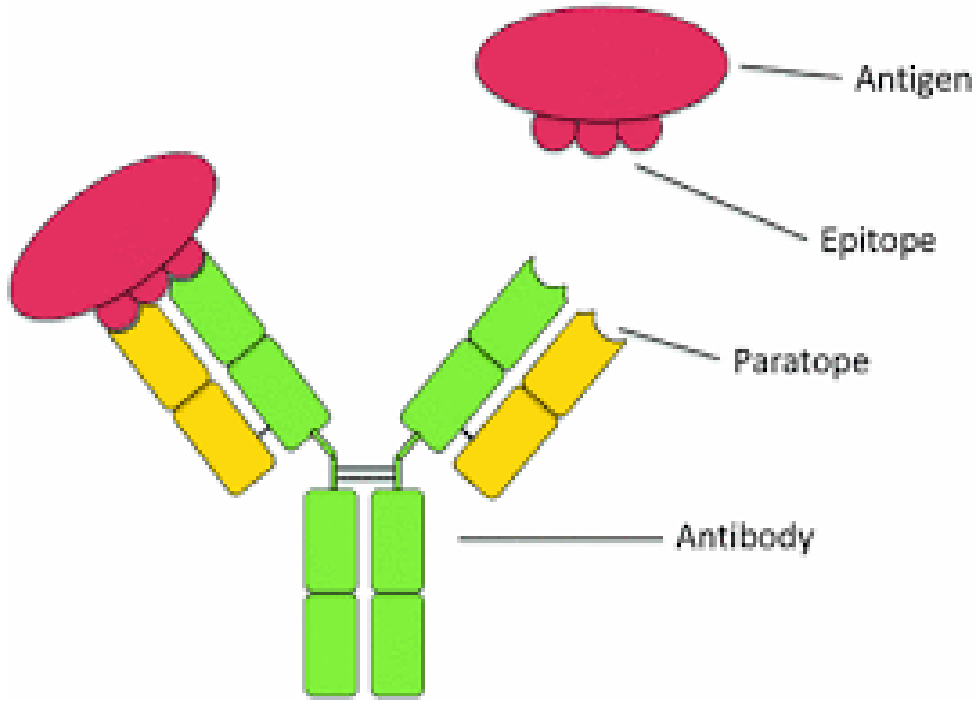
Several cytokine genes such as tumor necrosis factor (TNF) are found in the class III region.

The HLA class III is not part of the polymorphic HLA system.



Epitope (antigenic determinant)

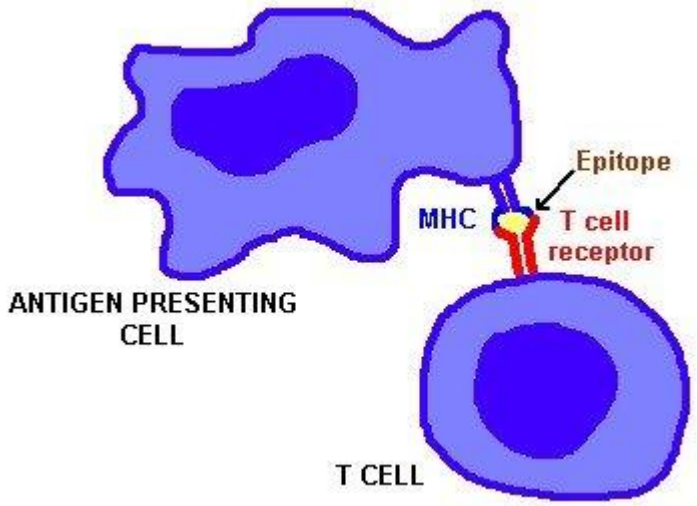
- A portion of a foreign protein, or antigen, that is capable of stimulating an immune response.
- In adaptive immune, epitopes can be divided into T-cell epitope and B-cell epitope, which can be recognized by the receptor on the surface of T cells or B cells.
- Binding between the receptor and epitope occurs only if their structures are complementary. It is necessary to activate B-cell production of antibodies.

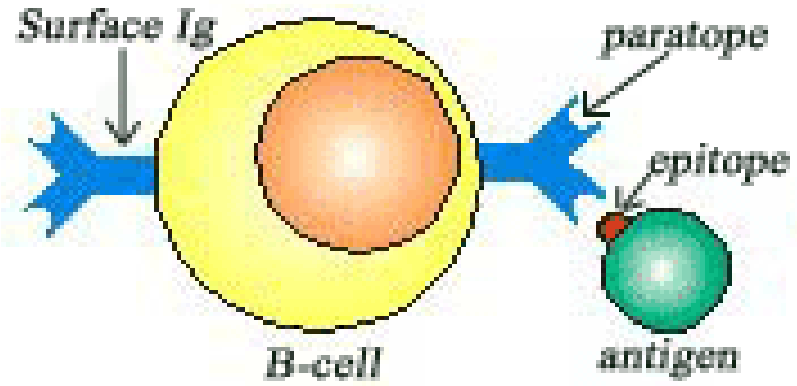


https://www.sciencedirect.com/science/article/pii/S0924224420306580

"epitope". Encyclopedia Britannica, 11 Nov. 2022, https://www.britannica.com/science/epitope. Accessed 7 August 2024.

- B cells can recognize an epitope alone but T cells can recognize an epitope only when it is associated with an MHC molecule on the surface of a self-cell (either an antigen-presenting cell or an altered self-cell).





https://microbeonline.com/epitope/

Terasaki epitopes, also known as TerEps

- Terasaki epitopes are defined as
understanding the immune response to HLA mismatches between donors and recipients.

Eplets and Their Role

- A significant aspect of Terasaki
- Research has shown that many Terasaki epitopes correspond to individual Eplets or pairs of Eplets, highlighting their importance in the immunogenicity of HLA molecules.

The understanding of these Eplets enhances the ability to predict the risk of developing donor-specific antibodies (DSA) in transplant recipients, thus improving transplant outcomes.

Terasaki Epitope Mismatch Burden Predicts the Development of De Novo DQ Donor-Specific Antibodies and are Associated With Adverse Allograft Outcomes. Transplantation. 2018

Clinical Applications

- Evaluating the epitope mismatch burden, predict DSA development better, which is a significant factor in graft rejection.
- Alternative strategy for assessing transplant compatibility beyond traditional HLA matching methods.
- There are two strategies to determine the HLA epitope repertoire:

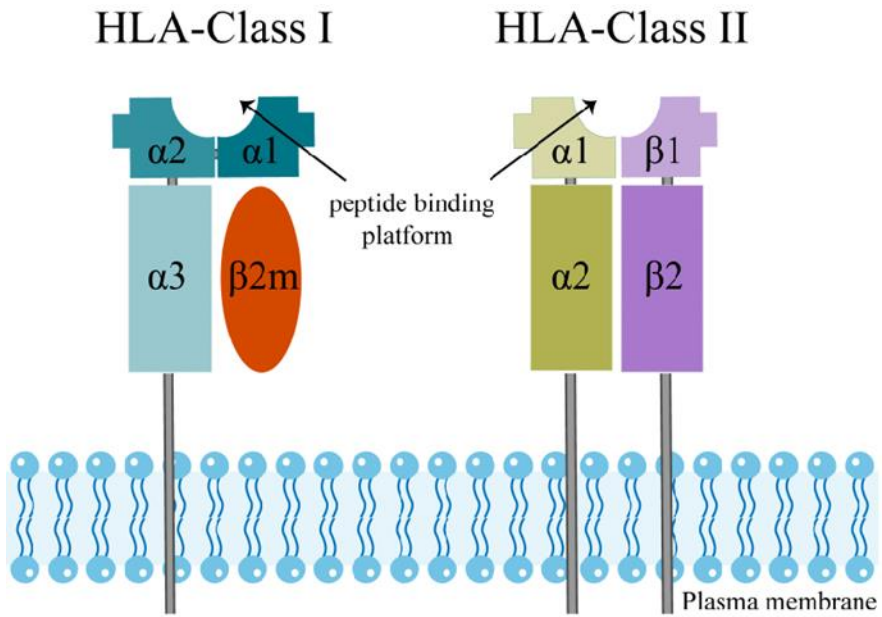
Empirical Methods Using Luminex Panels:
Analyzing the reactivity of single allele Luminex panels with mouse monoclonal antibodies (mAbs).
Establishing a comprehensive list of Terasaki's HLA class I epitopes, to understanding immune responses in transplantation contexts.

Theoretical Prediction Using Algorithms: HLAMatchmaker
A theoretical approach, predicts HLA epitopes based on stereochemical modeling of the HLA molecular surface. Identifies potential epitopes by analyzing the structural features of HLA molecules and their interactions with antibodies.

HLA Epitopes as Viewed by Antibodies: What Is it All About? American Journal of Transplantation 2015

STAR 2017 working group recommendation:

Anti–HLA antibody assessment would be performed using a solid-phase assay and includes all major HLA class I and II loci (HLA-A, -B, -C, -DRB1, -DRB3/4/5, -DQA1/DQB1, -DPA1/DPB1).



Clinical recommendations for posttransplant assessment of anti–HLA (Human Leukocyte Antigen) donor-specific antibodies: A Sensitization in Transplantation: Assessment of Risk consensus document, American Journal of Transplantation 23 (2023)

De novo DSAs classes:

- Class 1 *de novo* DSAs

  Usually detected sooner after transplant

  More likely IgG1 and IgG3 subclasses.

  Associated with acute antibody-mediated rejection and early graft loss.

- Class 2 *de novo* DSAs

  Appear later

  Commonly non-complement binding IgG2 or IgG4 subclass.

  Tend to be persistent and associated with chronic antibody-mediated rejection and transplant glomerulopathy.

Donor-Specific Antibodies in Kidney Transplant Recipients.Clin J Am Soc Nephrol. 2018

- The majority of de novo DSAs after kidney transplant are class 2 antibodies, especially DQ, usually occur during the first year of kidney transplant, but they can appear anytime, even several years later.

- Trying aggressively to eliminate class 2 DSA, especially the DQ, may not be successful, and it can put patients at great risk of excessive immunosuppression without much benefit .

Donor-Specific Antibodies in Kidney Transplant Recipients.Clin J Am Soc Nephrol. 2018

Comparison of the dominant characteristics of classes 1 and 2 DSAs

	Class 1 Donor-Specific Antibodies	Class 2 Donor-Specific Antibodies
HLA		
Antigens	A, B, and C	DR, DQ, and DP
Epitopes location	α-chain	α- and *β*-chains
Expression	All nucleated cells	Antigen-presenting cells
Preformed donor-specific antibodies		
Important	Very	Less
Positive crossmatch	T cells	B cells
Transplant decision	No transplant	Permissible
***De novo* donor-specific antibodies**		
Detection	Sooner	Later
IgG subclasses	IgG1, IgG3	IgG2, IgG4
Complement binding	Strong	Weak/no
Frequency	Fewer	Common, especially DQ
Antibody-mediated rejection		
Phenotypes	Acute	Chronic, subclinical
Presentation	Early	Later
Graft dysfunction	Rapidly	Slowly
C4d deposit	Positive	Negative
Treatment	More responsive	Less responsive
Graft loss	Early	Later

DSA Strength (or Titer)

- Usually expressed as the Mean Fluorescence Intensity (MFI) by Luminex solid-phase assay.
- STAR 2017 working group, also defined MFI thresholds for anti–HLA antibody positivity of 1000 to 1500 MFI to be used as universal cutoff values for normalized values with excellent consistency between manufacturers.
- The workgroup provided guidance for a biologically significant change in antibody quantity based on the semi quantitative readout of MFI (>25%-50% change)

Clinical recommendations for posttransplant assessment of anti–HLA (Human Leukocyte Antigen) donor-specific antibodies: A Sensitization in Transplantation: Assessment of Risk consensus document, American Journal of Transplantation 23 (2023)

DSA Strength- continued

However, the correlation between DSA strength and clinical outcome is far from perfect.

DSAs with similar mean fluorescence intensity do not always activate the complement cascade.

The ability of DSAs to bind on beads may not be the same as that to bind on HLA antigens of endothelial cells.

There are patients with transplants with high levels of circulating DSAs who escape rejection or graft dysfunction.

Donor-Specific Antibodies in Kidney Transplant Recipients.Clin J Am Soc Nephrol. 2018

DSA Strength- continued

- False positive or high titers:

  Due to the presence of antibodies to denatured HLA molecules.

  DSAs targeting one of the shared epitopes may be diluted across the beads

- False negative or low titers:

  In the presence of inhibitors or “prozone effects,” affecting the assay of very high levels of DSAs.

  Serial dilution of sera before assay provided more accurate measure of DSA strength.

Donor-Specific Antibodies in Kidney Transplant RecipientsClin J Am Soc Nephrol. 2018 Jan 6.

The three proposed pathogeneses of DSA in antibody-mediated rejection

- Binding of DSA to antigen expressed on allograft endothelial cells can activate classic complement pathway, a key pathologic process of **acute antibody-mediated rejection phenotypes**
- Some DSAs can cause graft damage through antibody-dependent cellular cytotoxicity; innate immune cells, including neutrophils, macrophages, and natural killer cells, can bind to Fc fragments of DSAs, trigger degranulation, and release lytic enzymes, which cause tissue injury and cell death.

  smoldering damages to the endothelial cells; proposed as an important pathogenesis in **subclinical and chronic antibody-mediated** rejection phenotypes.

The three proposed pathogeneses of DSA in antibody-mediated rejection-continued

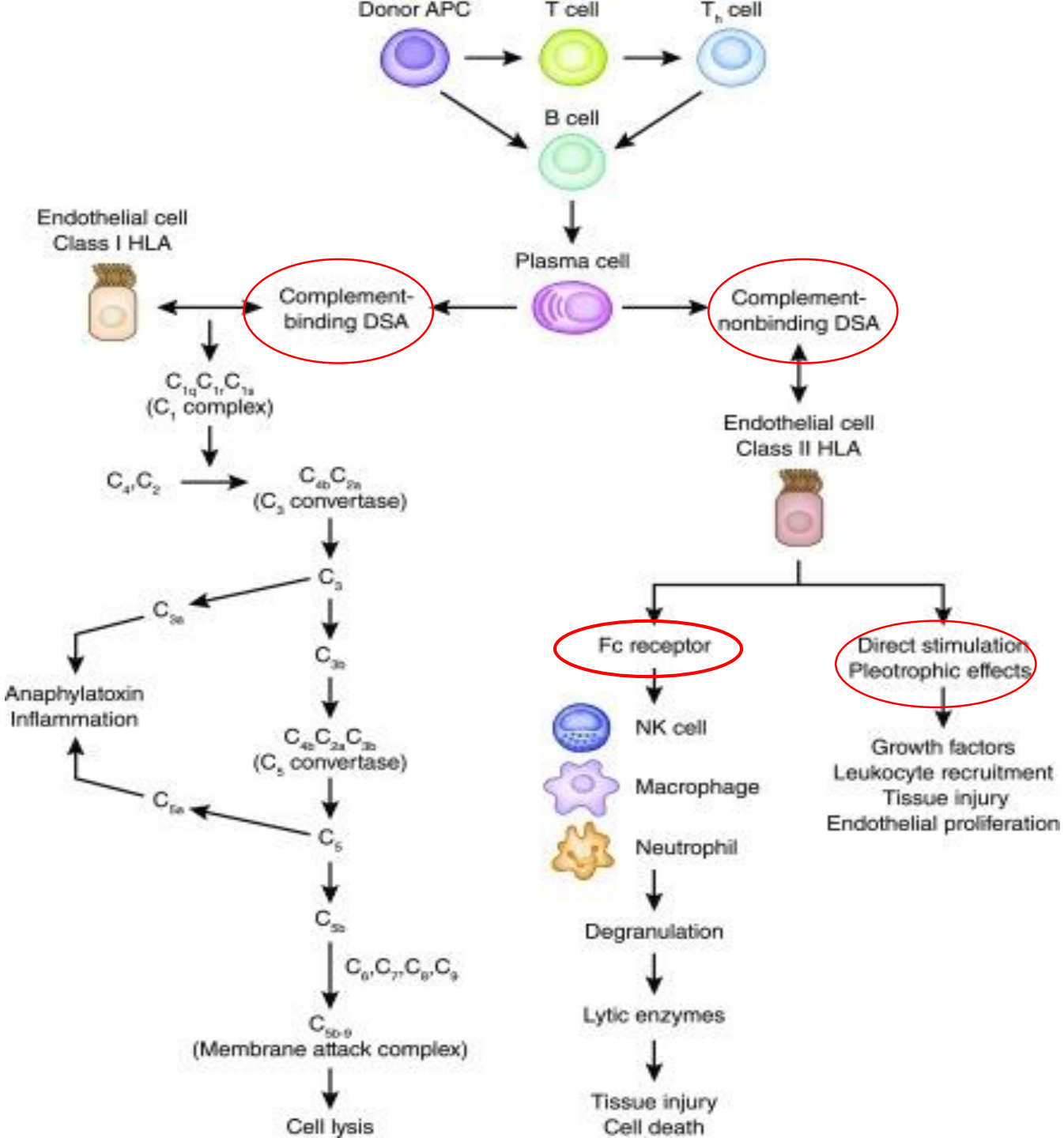
- DSAs can cause graft injury by direct activation of endothelial proliferation through increasing vascular endothelial growth factor production, upregulating fibroblast growth factor receptor, and increasing its ligand binding as well as other signaling pathways for cellular recruitment.

  contribute to **transplant glomerulopathy and vasculopathy**.

Donor-Specific Antibodies in Kidney Transplant RecipientsClin J Am Soc Nephrol. 2018 Jan 6.

The three proposed pathogeneses of DSAs in antibody-mediated rejection:

- complement-independent mechanisms can explain the clinical phenotypes of antibody-mediated rejection with negative C4d staining in peritubular capillaries.



De novo donor-specific antibody (DSA) to human leukocyte antigen (HLA) remains difficult to treat and is a major cause of transplant renal dysfunction.
The association between the development of de novo DSA and ABMR is unclear, as not all DSA-positive patients develop ABMR.
No standard treatment for ABMR due to de novo DSA has been established.

Patients with de novo DSA develop ABMR later than patients with preformed DSA and have a reduced long-term survival rate .
The average time of de novo DSA appearance is reportedly 3.8–68 months after transplantation.

Monitoring for DSA in patient with tacrolimus fluctuates greatly and when the trough value of tacrolimus is 8 ng/ml or less, may improve the prognosis of the transplanted kidney through early diagnosis and treatment at the subclinical ABMR stage before the clinical appearance of renal damage.

Clinical characteristics of renal transplant recipients who developed de novo donor-specific antigen in Kyoto University Hospital: a case series. Renal Replacement Therapy.2022

371 recipients were classified into low(n = 180), moderate (n = 108), high (n = 83) immunological risk groups.
Patients were followed for a mean of 3.3 (SD 2.1) years.
dnDSA were detected in 78 recipients: 21 (27%) Class I Ab,
43 (55%) Class II Ab,
14 (18%) Class I+ Class II.
The median time to first detection was 61 days posttransplant.
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dnDSA development, only TCMR remained significant on multivariable analysis.
TCMR was also associated with development of dnDSA in the subgroup of recipients with pretransplant DSA.
There was a trend toward increased risk of dnDSA in patients of higher immunological risk on univariable analysis; however, this was nonsignificant on multivariable analysis.

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In conclusion, dnDSA developed at a rate of 16% in low-risk recipients, 30% in moderate-risk recipients, and 29% in high-risk recipients by 1 year posttransplant.
Denovo DSA significantly increased the risk of ABMR (HR: 2.2) but were not an independent risk factor for death-censored graft survival.
TCMR is a risk factors for dnDSA development.
Although we do not currently know whether treatment of dnDSA can reduce the incidence of ABMR or late graft loss.

frontiers | Frontiers in Medicine

TYPE Original Research
PUBLISHED 16 September 2022
DOI 10.3389/fmed.2022.943502

The total population: 3,344 transplanted patients in the period from March 2000 until May 2021.
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Patients with
lower long-term allograft survival compared to patients without dnDSA (Control group, n = 2,752).

Annual DSA screening was performed for more than18 years , with a median number of 1.6 DSA determinations per patient/year.

Median time from the last negative sample to the first positive dnDSA was 11.3 months.

The biopsies of allograft kidneys were performed by clinical indication (rise in creatinine and/or proteinuria), and 72.0% of patients had at least one biopsy. About 35.0% of patients had at least one episode of T-cell mediated rejection(TCMR) before the first appearance of dnDSA.
All episodes of ABMR appeared at the time and/or after the first occurrence of dnDSA.

Patients with at least one rejection episode, either TCMR or ABMR, had significantly lower graft survival compared to those patients without rejection.

rlin, Germany

The relationship between MFI evolution and graft loss:

Doubling and fluctuating MFI was higher in the graft loss group ($p < 0.001$),

Patients with ≥50% MFI reduction and stable negative MFI of dnDSA (10% of patient) were significantly associated with less graft failure.

The MFI evolution was associated with 5-year death-censored allograft survival post-dnDSA:

74.0% in patients with MFI reduction ≥ 50%,

62.4% with fluctuating MFI (MFI reduction ≥ 50% and doubling),

52.7% with doubling MFI (log-rank $p < 0.001$)

Proteinuria and eGFR before and after dnDSA appearance:

The eGFR was already decreased at the time of the first appearance of dnDSA (rejection in 6.5% of patients), with a negative slope after this date (-11.9 ml/min/10 years). There was 24.8% rejection over follow up period.

Proteinuria increased at the time of the first occurrence and over time.

Patients with class II dnDSA had significantly less graft loss ($p = 0.007$)

both class I + II dnDSAs was significantly associated with graft failure ($p < 0.001$).

Patients with ≥ 4 dnDSA experienced significantly more frequent graft loss ($p < 0.001$)

DQ dnDSA:

They confirm the high frequency of DQ dnDSA, presenting with higher MFI at the time of appearance and being more persistent, but seem less harmful to the graft or produce insidious and progressive chronic damage with late graft failure as described in some studies.

The proportion of DQ was significantly lower in the graft loss group (53.7 vs. 43.3%, p = 0.006).

They support and highlight the

Graft inflammation, such as TCMR, can increase immunogenicity and can also precipitate the formation of dnDSA. We can confirm this strong association, as around one-third of our patients had experienced TCMR before the appearance of dnDSA.

Further studies are needed to distinguish those dnDSA which are harmful from those dnDSA with an uneventful clinical course AND need to expand knowledge about DQ-dnDSA and improve HLA-DQ matching strategies.

A better knowledge of relevant HLA epitopes or the use of novel biomarkers of graft dysfunction, such as cell-free DNA, may provide additional information to identify patients at risk.

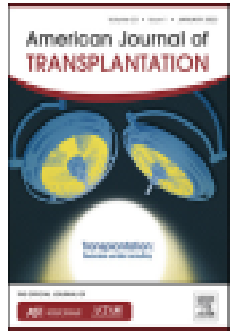
The natural history of denovo donor-specific HLA antibodies after kidney transplantation.frontier in medicine.2022

American Journal of Transplantation 23 (2023) 115–132

Contents lists available at ScienceDirect

American Journal of Transplantation

journal homepage: www.journals.elsevier.com/american-journal-of-transplantation



Meeting report

Clinical recommendations for posttransplant assessment of anti–HLA (Human Leukocyte Antigen) donor-specific antibodies: A Sensitization in Transplantation: Assessment of Risk consensus document☆

The attribute group from STAR 2022 developed organ specific recommendations based on the literature review and expert assessment of the strength of evidence.

First author: Senev
Journal: J Am Soc Nephrol
Year: 2020
Number of patient: Adult 926
DSA: de novo
DSA attribute: MFI
Threshold: >500
EDTA pretreatment: reported not
Time point of DSA assessment: at day 0, at 3 month post transplant, yearly post transplant, and at time of an indication biopsy
Object: To evaluate the effect of number of eplet mismatches (mismatch load) on de novo DSA development, rejection and allograft loss, using high-resolution genotyping of HLA loci.
Main conclusion: **Eplet mismatches in HLA-DQ** confer substantial risk for de novo DSA formation, graft rejection, and graft failure after kidney transplantation. Mismatches in other loci seem to have less effect.
Limitation: Single center study

First author: Davis
Journal: Am J Transplant
Year: 2021
Number of patient: Adult 444
DSA: de novo
DSA attribute: MFI
Threshold: >500
EDTA pretreatment: No
Time point of DSA assessment: during first year of post transplant
Object: To evaluate HLA-DR/DQ molecular mismatch to predict de novo DSA and how difference in tacrolimus exposure may modulate this risk.
Main conclusion: Intermediate- and high-risk patients (according to defined mismatch thresholds) with a mean tacrolimus <6 ng/ml versus >8 ng/ml had **increased risk of DR/DQ de novo DSA** at 1 year post transplant
Limitation: DSA assessment limited to the first year post transplant

First author: Snanoudj
Journal: Kidney Int
Year: 2019
Number of patient: Adult 89
DSA: de novo
DSA attribute: positive detection
Threshold: not reported
EDTA pretreatment: Not reported
Time point of DSA assessment: pretransplant, at -3 and -12 months post transplant, yearly post transplant
Object: To evaluate whether the number of mismatched epitopes, or ("epitope load") would identify patients at the highest risk of developing de novo DSA following minimization of immunosuppression
Main conclusion: After conversion from **cyclosporine to everolimus** (at 3-months post transplant), 32.6% developed de novo DSA. Compared to the number of HLA mismatches, epitope load was more strongly associated with the development of de novo DSA. **Assessing epitope load before minimizing immunosuppression may be a more efficient tool to identify patients at the highest risk of allosensitization.**
Limitation: Limited sample size

First author: Willicombe
Journal: Transplantation
Year: 2018
Number of patient: Adult 1003
DSA: de novo
DSA attribute: positive detection
Threshold: >500
EDTA pretreatment: Not reported
Time point of DSA assessment: in the first week, at 1-, 3-, 6- and 12-months post transplant and yearly post transplant
Object: To analyze the immunogenicity of the different HLA antigens, DQB1 alleles and DQB1 Terasaki epitopes (TerEp), by comparing patient mismatches with de novo DSA development
Main conclusion: Patients **mismatched at a DQB1 allele** were at significantly higher risk of developing de novo DSA compared with other mismatched HLA antigens. For patients mismatched at a **single DQB1 allele**, the risk of de novo DQ DSA development increases with **the number of TerEp mismatches**. Patients who develop antibodies against TerEps are at increased risk of ABMR.
Limitation: single center study

First author: Bertrand
Journal: Transplantation
Year: 2020
Number of patient: Adult 123
DSA: de novo
DSA attribute: MFI
Threshold: >1000
EDTA pretreatment: Not reported
Time point of DSA assessment: not reported
Object: To investigate the prevalence of subclinical ABMR in patients without allograft dysfunction biopsied because of the presence of de novo DSA
Main conclusion: There were 51 (41.4%) subclinical ABMR, of which 32 (26%) were active and 19 (15.5%) chronic active ABMR.
Predictive factors associated with diagnosis of **active subclinical ABMR** were **MFI of immunodominant DSA >4000**, **MFI of the sum of DSA >6300**, **age** of the recipient **<45** years old, and the **absence of steroids** at biopsy.
Limitation: Limited sample size and retrospective nature of study design

Table 5

Organ specific recommendations.

Indication	Kidney
Posttransplant assessment of DSAs and clinical implications	
High-resolution HLA genotyping for correct assessment of anti–HLA antibody specificity to donor	2D
Anti–HLA antibody testing of the sample used at the time of transplant	1A
Anti–HLA antibody testing in the posttransplant period	
In case of allograft dysfunction	1B
In situations at risk of anti-HLA alloimmunization	
After minimization of immunosuppression or CNI avoidance protocols	1A
Nonadherence	1A
In the absence of clinical events	1C
Modulation of clinical management in a patient with positive DSA detection considering clinical situations	
Repeated measures of anti–HLA antibody testing to appreciate kinetics posttransplant	1C
Allograft biopsy in patients with allograft dysfunction	1C
Allograft biopsy in patients without allograft dysfunction	2C
Posttransplant DSA assessment for diagnosis, clinical phenotype identification, and treatment of ABMR	
Anti–HLA antibody testing in patients with histologic lesions of ABMR	1B
Anti–HLA antibody testing to modulate management and treatment of ABMR	2C
Ancillary HLA diagnostic assays (titer, complement, or isotype assays) to better characterize and help decide on optimal therapeutics	2C
Posttransplant assessment of DSAs for allograft prognosis and risk stratification	
Integration of anti–HLA antibody testing to clinical, functional, and histologic parameters to evaluate allograft prognosis and improve risk stratification	1B
Integration of ancillary anti–HLA antibody testing (titer, complement, or isotype assays) to evaluate allograft prognosis and improve risk stratification	2B

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of CABMR.

Allograft outcome (graft and patient survival rates) in the dnDSA (+) group was similar to that of the dnDSA (–) group.
There was no significant difference in the allograft outcome between the C4d (+) and C4d (–) subgroups in the dnDSA (–) or dnDSA (+) groups.
There was no significant difference in the death-censored graft survival rate between the two groups, regardless of the treatment

The pathologic findings were more severe in the dnDSA (+) group than in the dnDSA (–) group.
Used the same protocol, irrespective of the presence of dnDSA or C4d, the treatment r
(+) group than in the

In this study, 21 KTRs
KTRs received treatm
The MFI values of six
dnDSA did not result
period. Six KTRs had
statistically significan

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KOREAN JOURNAL OF TRANSPLANTATION
pISSN 2671-8790
eISSN 2671-8804

The prognosis of the allograft kidney was found to be related more to the amount of proteinuria than the presence of dnDSA. In other words, the death-censored graft survival rate was lower in the high-proteinuria group than in the low-proteinuria group in both the dnDSA (–) group and dnDSA (+) groups.

There was no significant difference in allograft function within 12 months after the diagnosis of CABMR between the dnDSA (–) and dnDSA (+) groups, the eGFR at 12 months after the diagnosis of CABMR was the risk factor associated with graft failure, regardless of the presence or absence of dnDSA.

HIGHLIGHTS

In conclusion, although the effect of dnDSA on the prognosis of CABMR is not clear, it would be important not to neglect treatment for CABMR even without dnDSA in the case of risk factors such as heavy proteinuria, low allograft function, and deceased donor KT.

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t, there was
no difference of prognosis between the two groups.

- Continuous and rigorous surveillance of DSA and allograft function is needed in patients with CABMR.

Clinical significance of de novo donor-specific antibody in kidney transplant recipients with chronic antibody-mediated rejection. Korean J Transplant 2021.

American Journal of Transplantation 23 (2023) 1882–1892

Contents lists available at ScienceDirect

American Journal of Transplantation

ELSEVI

De novo donor-specific antibody (dnDSA) after renal transplantation has been shown to correlate with antibody-mediated rejection and allograft loss. However, the lack of proven interventions and the time and cost associated with annual screening for dnDSA are difficult to justify for all recipients.

Original Ar

A rational approach to guide cost-effective de novo donor-specific antibody surveillance with tacrolimus immunosuppression

A rational approach to guide cost-effective de novo donor-specific antibody surveillance with tacrolimus immunosuppression

Could a risk-based approach to de novo DSA (dnDSA) surveillance minimize testing costs?

Single center prospective study (Jan '99–Apr 22')

949 kidney Tx recipients without preTx DSA

+ tacrolimus
+ dnDSA monitoring

HLA DR/DQ imputed eplet molecular mismatch scoring

Statistical analysis of risk factors and stratification

Younger age

Recipient age + HLA-DR/DQ mMM

identified recipients most likely to develop dnDSA

independent predictors

52% of recipients were deemed "low-risk"

and therefore unlikely to benefit from testing

median subclinical dnDSA-free survival at 5 and 10 years, 98% and 97%,

Inadequate immunosuppression

was also a factor for increased risk of dnDSA development

AJT

Thank you for your attention