KADIR HAS UNIVERSITY
SCHOOL OF GRADUATE STUDIES
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AUGMENTED VIRTUAL CROSSMATCH FOR DONOR-INDUCED ANTIBODY PREDICTION BY USING HIGH RESOLUTION HUMAN LEUKOCYTE ANTIGEN TYPING AND HUMAN LEUKOCYTE ANTIGEN EPITOPE MAPPING FOR BETTER DONOR MATCH

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DOCTOR OF PHILOSOPHY THESIS

ISTANBUL, JANUARY 2023

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ACCEPTANCE AND APPROVAL

This thesis, titled AUGMENTED VIRTUAL CROSSMATCH FOR DONOR-INDUCED ANTIBODY PREDICTION BY USING HIGH RESOLUTION HLA TYPING AND HLA EPITOPE MAPPING FOR BETTER DONOR MATCH, prepared by SEDAT TANJU KARADENIZ, in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Bioinformatics and Genetics is approved by**.**

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In addition, I acknowledge that any claim of irregularity that may arise in relation to this work will result in a disciplinary action in accordance with the university legislation.

SEDAT TANJU KARADENIZ

_____

09/01/2023

To my beloved wife,

Meltem Savran Karadeniz

To my precious children,

Deniz Karadeniz

Nevzat Acar Karadeniz

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AUGMENTED VIRTUAL CROSSMATCH FOR DONOR-INDUCED ANTIBODY PREDICTION BY USING HIGH RESOLUTION HUMAN LEUKOCYTE ANTIGEN TYPING AND HUMAN LEUKOCYTE ANTIGEN EPITOPE MAPPING FOR BETTER DONOR MATCH

ABSTRACT

The Human Leukocyte Antigen (HLA) disparity between donors and recipients is the primary driver of Donor Specific Antibodies (DSA) formation and graft rejection after transplantation. We aimed to predict the DSA by finding the HLA antigen mismatches, searching the eplets of antigens that bind to the recipient's anti-HLA antibodies, calculating the number of shared eplets between the mismatched donor HLA antigens and the recipient's pre-transplantation anti-HLA antibody-bound antigens. We have used recipient-donor HLA Typing results and the recipient's pre-transplantation and post-transplantation anti-HLA antibody detection results by Luminex single antigen bead (Luminex-SAB) assay as retrospective data for calculation in five steps. We have compared the HLA Typing results to find the mismatched antigens in the first step and searched the relevant eplets for the recipient's pre-transplantation anti-HLA antibodies in the second step. Then we calculated the shared eplets between the donor's mismatched HLA antigens and the recipient's pre-transplantation anti-HLA antibodies to find the highest number of shares, then listed the most shared anti-HLA antibodies as the most probable DSA in the fourth step. Then, we confirmed the possible epitope's peptide AA (amino acid) sequences with the IEDB Bepipred-1.0 Antibody Epitope Prediction method using the donor's HLA antigen AA sequence.

Keywords: Virtual Crossmatch, Antibody Prediction, Epitope Mapping, Donor Specific Antibody, Kidney Transplantation

DAHA İYİ DONÖR EŞLEŞMESİ İÇİN YÜKSEK ÇÖZÜNÜRLÜKLÜ İNSAN LÖKOSİT ANTİJEN TİPLEME VE İNSAN LÖKOSİT ANTİJEN EPİTOP HARİTALAMA KULLANARAK DONÖRDEN OLUŞAN ANTİKOR TAHMİNİ İÇİN ARTIRILMIŞ SANAL ÇAPRAZ EŞLEŞTİRME

ÖZET

Donörler ve alıcılar arasındaki İnsan Lökosit Antijeni (HLA) eşitsizliği, vericiye özgü antikorların (DSA) oluşumunun ve nakil sonrası greft reddinin birincil itici gücüdür. HLA antijen uyuşmazlıklarını bularak, alıcının anti-HLA antikorlarına bağlanan antijenlerin epletlerini araştırarak, uyumsuz donör HLA antijenleri ile alıcının transplantasyon öncesi anti-HLA antikoruna bağlı antijenler arasındaki paylaşılan epletlerin sayısını hesaplayarak DSA'yı tahmin etmeyi amaçladık.. Alıcı-donör HLA Tipleme sonuçlarını ve alıcının Luminex tek antijen boncuk (Luminex-SAB) tahlili ile nakil öncesi ve nakil sonrası anti-HLA antikor tespit sonuçlarını beş adımda hesaplama için geriye dönük veriler olarak kullandık. İlk adımda uyumsuz antijenleri bulmak için HLA Tipleme sonuçlarını karşılaştırdık ve ikinci adımda alıcının transplantasyon öncesi anti-HLA antikorları için ilgili epletleri araştırdık. Daha sonra donörün uyumsuz HLA antijenleri ile alıcının nakil öncesi anti-HLA antikorları arasındaki paylaşılan eletleri hesaplayarak en yüksek payı bulduk, ardından dördüncü adımda en olası DSA olarak en çok paylaşılan anti-HLA antikorlarını listeledik. Ardından, donörün HLA antijen AA dizisini kullanan IEDB Bepipred-1.0 Antikor Epitop Tahmini yöntemiyle olası epitopun peptit AA (amino asit) dizilerini doğruladık.

Anahtar Sözcükler: Sanal Çapraz Karşılaştırma, Antikor Tahmini, Epitop Haritalama, Donöre Spesifik Antikor, Böbrek Nakli

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α : alpha domain, alpha chain

β : beta domain, beta chain

ABBREVIATIONS

ABMR : Antibody-Mediated Rejection

CDC-XM : Complement-Dependent Cytotoxicity Crossmatch

CRD : Complementarity-Determining Region

CREG : Cross-Reacting serological Groups

DNA : Deoxyribonucleic Acid

DSA : Donor-Specific anti-HLA Antibodies

FC-XM : Flow Cytometric Crossmatch

HLA : Human Leukocyte Antigens

MFI : Mean Fluorescence Intensity

MHC : Major Histocompatibility Complex

NGS : Next-Generation (Short-Read) Sequencing

PIRCHE : Predicted Indirectly ReCognizable HLA Epitopes

qPCR : Quantitative Polymerase Chain Reaction

RNA : Ribonucleic Acid

SB : Single Antigen Beads

SNP : Single Nucleotide Polymorphisms

SPI : Solid-Phase Immunoassays

SSO : Sequence-Specific Oligonucleotides

SSP : Sequence-Specific Priming

TCMR : T-Cell Mediated Rejection

TGS : Third-Generation Real-Time (Long-Read) Sequencing

XM : Cell-Based Crossmatch

1. INTRODUCTION

Transplanting donor organs to recipients with the best possible match is essential. When recipients receive a donor organ that is not correctly matched, the genetic disparities between donor and recipient may lead to cellular and humoral immune responses and may result in allograft rejection. One of the significant genetic disparities between donor and recipient targets for these alloreactive immune responses is Human Leukocyte Antigens (HLA).

A large part of solid organ transplant failures is related to rejection, caused by differences in the tissue type (antigens) between donors and recipients. Due to these differences, the recipient's immune system recognizes the donor's histocompatibility antigens as foreign, which leads to immune activation, graft inflammation (rejection), graft injury, functional graft decline, and, ultimately, graft failure. The development of immunosuppressive drugs has partly overcome this immunological barrier and enables a genetically different organ to survive in another non-identical individual. However, the immunosuppressive effects of the medicines used to prevent or treat rejection impede further increases in immunosuppression to overcome the immunological barrier due to the associated risk of infections and malignancies. The continued use of immunosuppression increases mortality risk with a functioning graft. Therefore, even in the modern era of potent immunosuppression therapies, improving long-term allograft survival without further increasing the chances and side effects is still an immediate unmet clinical need in solid organ transplantation. Understanding the histocompatibility in solid organ transplant pairs can lead to improved risk stratification, more rational donor-recipient allocation, and better-tailored immunosuppression. It can prevent premature graft failure and improve solid organ allograft survival.

1.1. HLA

HLA is a set of proteins on the cell surface that can present peptides to T cells. The HLA system is tightly involved in human immune regulation by presenting these peptides to T

cells. When foreign ‘non-self’ material enters the human body, HLA can present peptides derived from this ‘non-self’ material. T-cell recognition of these ‘non-self’ peptides will eliminate ‘non-self’ material. For a proper immune defense against ‘non-self’ material, HLA diversity is needed. HLA diversity is achieved via two specific characteristics of the HLA system:

- the HLA system is polygenic; everyone has a specific set of different HLA molecules, consisting of HLA Class I and HLA Class II molecules. These different HLA molecules have different peptide-binding specificities.
- the HLA system is highly polymorphic; multiple variants of each HLA gene exist at the population level.

The enormous amount of identified HLA alleles reflects the highly polymorphic character of the HLA system. Nowadays, 25,019 HLA Class I alleles and 10,201 HLA Class II alleles have been found. The polymorphisms between different HLA antigens result in differences in the peptide-binding groove or are located at positions interacting with the T cell. Thus, foreign HLA antigens can have a specific peptide-binding groove and present a unique repertoire of ‘non-self’-derived peptides to T cells. Via the high diversity of HLA at the individual and population levels, the human immune system has ensured that an adaptive immune response can be elicited against a diverse repertoire of antigens. The HLA gene complex is in the 6p21.3 region of the short arm of chromosome 6. It encodes the Major Histocompatibility Complex (MHC) proteins, which figure out the tissue type of an individual. This HLA complex plays a leading role in antigen recognition and regulating the immune response to specific foreign pathogens and neoplastic cells. It prevents the development of autoimmune diseases in the human body. The most critical MHC proteins are the products of the HLA Class I (A, B, C) and Class II (DR, DQ, DP) loci. The HLA Class I molecule is a monomer consisting of a polymorphic α chain, while the HLA Class II molecule is a dimer composed of two polymorphic chains, the α, and the β chain. An international HLA nomenclature has been developed to name each HLA allele. An HLA allele encodes only one α or β chain of the complete HLA molecule. Already 35,220 different HLA alleles have been described by the end of April 2022 (IMGT/HLA database v3.50.0), which illustrates that these genes are highly polymorphic,

related to their primary function in the immune response. Each HLA allele is uniquely defined by the name of the locus followed by an asterisk and up to 4 fields of numbers, separated by a colon. The 1st field HLA result represents the serological antigen group or allele family, defined as a group of closely related alleles that share similar serological behavior. The 2nd field defines one HLA protein and represents a non-synonymous difference in the exons, the 3rd field represents a synonymous difference in the exons, and the 4th field represents differences outside the exons, the non-coding parts of the gene.

1.1.1. HLA Class I and HLA Class II Structure and Function

Due to the polygenic character of the HLA system, everyone expresses a range of different HLA molecules on the cell surface. These different HLA molecules belong to two HLA classes: HLA Class I and HLA Class II (Figure 1.1). HLA Class I and HLA Class II have variable extracellular domains and a constant transmembrane and cytoplasmic domain. HLA Class I molecules (HLA-A, HLA-B, and HLA-C) are expressed on all nucleated cells and consist of two polypeptide chains: a polymorphic alpha chain encoded by chromosome 6 and a non-polymorphic β2-microglobulin that is encoded by chromosome 15. The polymorphic alpha chain consists of several domains. The leader peptide is encoded by exon 1, the alpha -1, -2, and -3 domains are encoded by exon 2, 3, and 4, the transmembrane domain is encoded by exon 5, the cytoplasmic domain is encoded by exon 6, and 7, and the 3' untranslated region is encoded by exon 8. HLA Class II molecules (HLA-DR, HLA-DQ, and HLA-DP) are generally expressed on professional antigen-presenting cells and consist of a potentially polymorphic alpha chain and a polymorphic beta chain, which are also encoded by chromosome 6. Since everyone inherits a maternal and a paternal variant of the alpha and beta chains, four potential proteins can be generated. The alpha and the beta chains consist of four domains: an alpha/beta-1 domain, an alpha/beta-2 domain, a transmembrane domain, and a cytoplasmic domain. The alpha-1 and the beta-1 domains are encoded by exon 2 and are involved in antigen presentation to T cells. The alpha-1 and the alpha-2 domains of HLA Class I molecules resemble the cleft to which peptides can bind: thus, these domains present peptides to T cells. HLA Class I molecules can present small peptides of 8-10

amino acids in length. The peptides presented by HLA Class I molecules are endogenously derived; these proteins can be cleaved intracellular into peptides by proteasome degradation and then transported into the endoplasmic reticulum via the TAP transporter, where the peptides are loaded on HLA Class I molecules. Once loaded on HLA Class I molecules, the presented peptide can be recognized by CD8+ T cells. HLA Class II molecules can present larger peptides than HLA Class I molecules (i.e., 13-25 amino acids in length) due to a more open peptide-binding groove structure. The peptides presented on HLA Class II molecules are generally exogenously derived; these proteins can be internalized into endosomes and processed via hydrolytic enzymes into peptides. These peptides are then loaded on HLA Class II molecules. Once loaded on HLA Class II molecules, the presented peptides can be recognized by CD4+ T cells (Cruz-Tapias P, Castiblanco J, 2013).

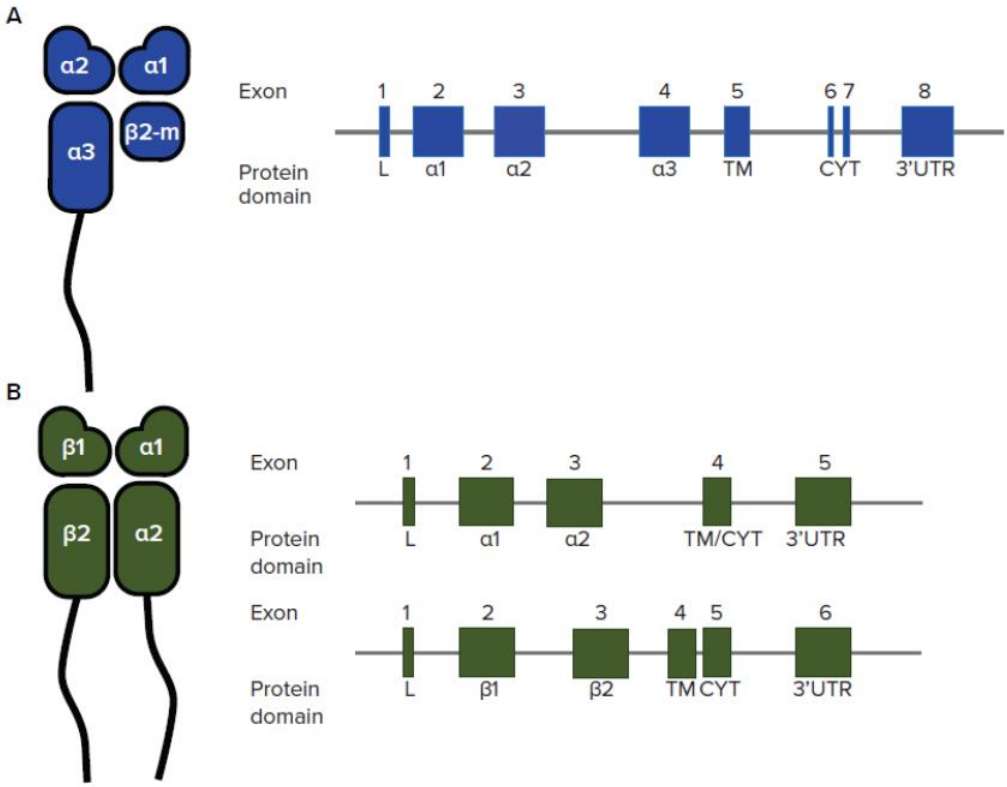

Figure 1.1 Molecular structure and exon organization of HLA. HLA Class I molecules (A) consist of a polymorphic alpha chain and a non-polymorphic beta 2-microglobulin. 8 exons encode the alpha chain of HLA Class I molecules. HLA Class II molecules (B) consist of a potentially polymorphic alpha-chain and a polymorphic beta-chain and are encoded by five or six exons. L = leader peptide; α1/2/3 = alpha-1/-2/-3 domain; β1/2 = beta-1/-2 domain; TM = transmembrane domain; CYT = cytoplasmic domain; 3'UTR = 3' untranslated region.

1.1.2. HLA Nomenclature and HLA Typing

A reliable and uniform HLA nomenclature was needed with the rising numbers of identified HLA alleles. Over the past decades, the HLA nomenclature has enormously evolved based on the methods used for HLA typing. Initially, different HLA alleles were shown using serological phenotyping. Since HLA antibodies can bind to different epitopes on different HLA molecules, there is serological phenotyping. In serological phenotyping, the reactivity of HLA on lymphocytes towards sera having HLA antibodies is measured, thereby finding different HLA antigens. A serological nomenclature was set up to describe the serologically defined HLA antigens. However, serologically defined HLA antigens are a broad definition of varying HLA alleles, as HLA alleles with the same serological specificity may differ in their amino acid sequence. Since allelic variation between different HLA alleles can be serologically undetectable, serological phenotyping is not a proper method to show all polymorphisms between different HLA alleles. With the rise of DNA genotyping methodologies, the resolution of HLA typing improved dramatically. DNA genotyping methods currently allow the identification of the HLA locus and individual HLA alleles by figuring out their exact nucleotide sequence. These DNA typing methodologies have resulted in the development of a different nucleotide-based HLA nomenclature (Figure 1.2). In this nucleotide-based HLA nomenclature, the specific HLA locus is written down, followed by a unique, allele-specific number of up to four fields. The first field of this terminology refers to the allele group, which often is composed of the underlying serological specificity of the HLA allele, and the second field refers to a specific nucleotide sequence difference. This terminology can be substituted with a third and a fourth field, which shows synonymous nucleotide substitutions in the coding regions and nucleotide differences in non-coding regions, respectively. Since serological HLA phenotyping and DNA genotyping are currently simultaneously used in clinical practice, both the serological nomenclature and the DNA-based nomenclature are still being used. Serological terminology is used to describe HLA alleles at a low-resolution level. In contrast, the DNA-based nomenclature is used to describe HLA alleles at the higher- or allelic-resolution level. (Geneugelijk, 2017)

1.2. HLA Matching

Minimizing the number of HLA mismatches between donor and recipient is a classical and powerful method to avoid B cell- and T cell-mediated alloreactivity after transplantation. Although the number of HLA mismatches is a potent indicator of post-transplantation complications, recent studies suggest that this method may be further refined by assessing the immunogenicity of individual HLA mismatches. The

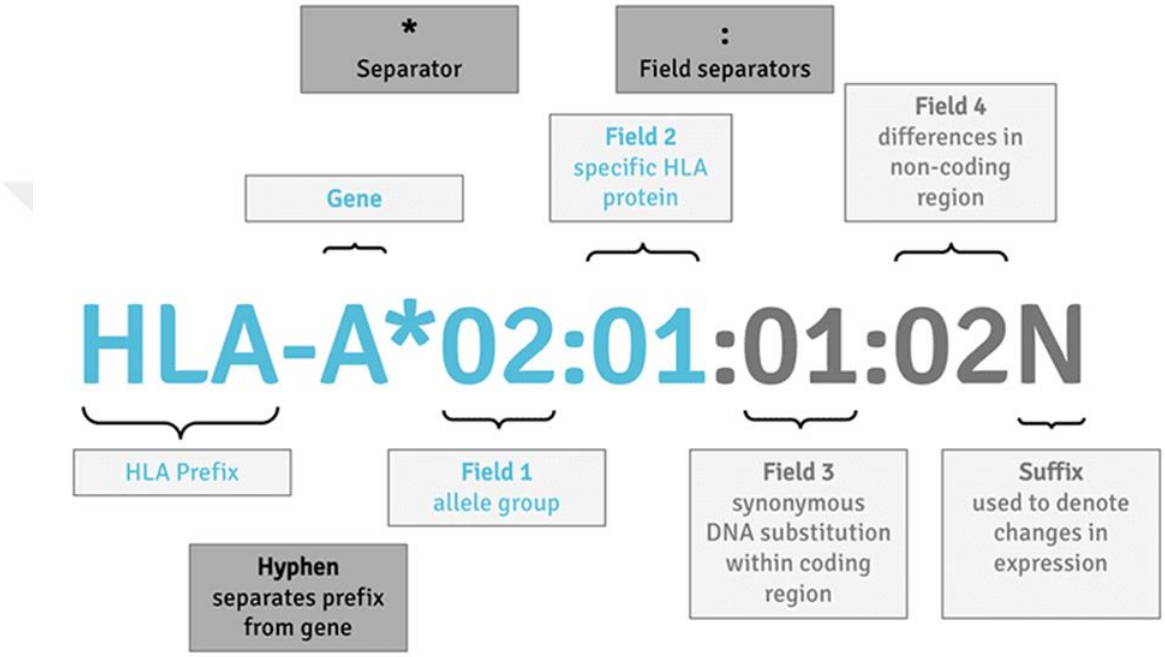

Figure 1.2 HLA Nomenclature

immunogenicity of individual HLA mismatches is highly diverse; a group of HLA mismatches can be classified as high-risk (unacceptable or non-permissible) and lead to severe clinical alloreactivity, while other HLA mismatches are well-tolerated (defined as acceptable or permissible HLA mismatches). This variable immunogenicity of individual HLA mismatches has been described for both hematopoietic cell transplantation and solid organ transplantation settings, showing that knowledge about the permissibility of individual HLA mismatches can be used to avoid B cell- and T cell-mediated alloimmune responses and thus further improve transplant outcome after solid organ transplantation. Over the last decades, HLA alleles have been extensively characterized by their three-dimensional structure and exact amino acid sequence. This extensive characterization

allowed the identification of functional epitopes on HLA that take part in the alloimmune response after transplantation. An enormous number of these epitopes can be present on multiple HLA antigens. Epitopes shared between the donor and recipient will not induce alloimmune responses, while epitopes mismatched between donor and recipient may induce alloimmune responses. Therefore, quantifying the epitope load between donor and recipient (i.e., the number of mismatched epitopes) instead of counting the total number of HLA mismatches may be a more sophisticated method to figure out donor-recipient compatibility as this method allows the definition of the permissibility of individual HLA mismatches. The concept in which epitopes are used for recipient-donor matching, rather than the number of HLA mismatches, is designated epitope-based HLA matching.

1.2.1. Epitope, Eplet, and Triplet

Epitope: The HLA epitope can be described using the functional and the structural epitope. The functional epitope determines the specificity of the antibody through its interaction with the complementarity-determining region 3 (CDR3) of the heavy chain of the antibody. The structural epitope comprises all amino acids of the HLA-molecule that are involved in the binding to the antibody paratope and spans a radius of approximately 15 Angstrom (Bezstarosti, Bakker, *et al.*, 2022).

Eplet: The definition of an eplet resembles the functional epitope and comprises the minimal amino acid configuration on the HLA molecule needed to induce an antibody response. Active residues must be within 3 -3.5 Angstrom (Bezstarosti, Bakker, *et al.*, 2022) (Figure 1.3).

Triplet: Like eplet but continuous in sequence and already within 3-3.5 Angstrom.

Initially, epitope-based HLA matching focused on differences in B cell epitopes between donor and recipient. B cell epitopes are small polymorphic amino acid patches on the molecular surface of HLA, which serve as antibody-antigen recognition sites. These polymorphic amino acid patches, called eplets, can be predicted using the HLAMatchmaker algorithm. More recently, the PIRCHE algorithm (Predicted Indirectly

ReCognizable HLA Epitopes) was proved to show mismatched HLA-derived epitopes that can be recognized by T cells via the indirect T cell recognition pathway (Bezstarosti, Kramer, *et al.*, 2022) (Figure 1.3).

1.2.2. HLA Antigen Matching

Since the first successful kidney transplantation between monozygotic identical twins, it became clear that organs could not be transplanted randomly. Besides the ABO blood group barrier, it was revealed that the leukocytes carry antigens on their surface that elicit immune reactions (rejection) and prohibit transplantation between non-identical individuals, the highly polymorphic HLA antigens. Soon after the initiation of clinical transplantation, HLA matching strategies were installed to maximally avoid rejection of

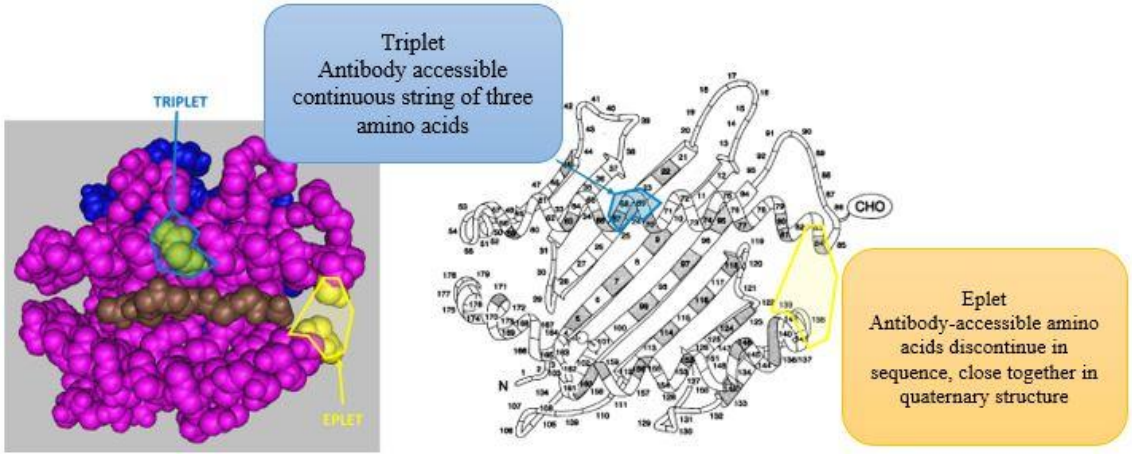

Figure 1.3 Eplet Triplet definition.

the transplanted organ based on HLA typing. The ability to react with a series of specific antisera was used in the first method for HLA typing described by Paul Terasaki and John McClelland in 1964. The 'microdroplet' cytotoxicity test made it possible to determine the HLA antigens of an individual serologically. HLA antigens were defined by evaluating the lymphocytes of an individual with a panel of sera containing well-characterized HLA-specific alloantibodies. The requirements of only small volumes of antisera for this method made it possible to type many individuals and to study the HLA antigens in detail (Aleksandar SENEV, 2020). It was soon discovered that HLA antigens are genetically determined. Although the HLA antigens vary from individual to individual, there is some cluster reactivity with antisera. The HLA-A and B loci are the

first two HLA clusters described. Matching the donors and recipients for HLA-A and -B serotypes correlated with better kidney allograft survival. This clinical relevance made the micro lymphocytotoxicity assay the worldwide standard technique for HLA serotyping. Another advancement in our knowledge was the development of the mixed lymphocyte culture (MLC) reaction. The HLA antigen repertoire detected by the MLC test had some discrepancies with the antigen repertoire detected by micro lymphocytotoxicity testing. This discrepancy could be explained by the discovery of additional HLA antigens present on B lymphocytes that remained undetected by the micro lymphocytotoxicity test. Later, it was demonstrated that these antigens represent a different serological subgroup, HLA-DR, significantly impacting post-transplant allograft survival. Since the 1970s and today, HLA antigen matching for the HLA-A, -B, and -DR loci have been integrated into deceased donor kidney allocation algorithms. The main aim of these matching algorithms is to minimize donor/recipient HLA disparity to improve transplant outcomes. In addition to the use in kidney allocation, these three HLA loci, defined at antigen level (i.e., 1st field typing), are sometimes used for rejection risk assessment and to guide medical decisions on post-transplantation immunosuppression. Some HLA antigen groups share reactivity patterns across HLA serotypes. Although HLA-A, -B, -DR serotype matching is still used in clinical routine, the discovery of this phenomenon, initially called CREG (Cross-Reacting serological Groups), challenged the initial HLA antigen categorization. It is known that shared epitopes cause this cross-reactivity on different HLA antigens (1st field serological level). This CREG principle explained the confirmed HLA reactivity and how one mismatched HLA antigen could lead to the development of antibodies reactive, not only to that specific mismatched antigen but also to a broader range of HLA antigens across distinct HLA serologically defined antigens. For instance, a recipient transplanted with an HLA-A2 mismatched kidney graft can develop reactive antibodies, not only with HLA-A2 but also with different 1st field HLA groups, like A28 and/or B17, depending on the own antigens of the recipient. Despite the elegant principle, the CREG algorithms failed to fulfill the enormous expectations, mainly due to a lack of clinical support for matching the CREG groups over the traditional HLA antigen matching approach. However, although not incorporated in current matching strategies and allocation algorithms, the knowledge of cross-reactivity between HLA antigens led to fine-tuning these antigens by improving the

HLA antibody analysis of recipients. The clinical benefit of HLA antigen matching in kidney transplantation is extensively documented, demonstrating that increased numbers of mismatched HLA-A, -B, or -DR antigens are associated with decreased graft survival, despite the universal use of intense immunosuppression to prevent immune activation. Thus, one could argue that to improve outcomes after transplantation, complete HLA matching strategies could significantly improve outcomes and reduce immunosuppression. However, the polymorphism of the HLA antigens, with 114 different HLA-A, -B, and -DR antigens, must be balanced with other factors, like urgency, waiting time, age, risk profiles, and equity balances. Although desirable from the immunologic point of view, complete HLA matching cannot be achieved. It would lead to longer waiting times and inequity in access to transplantation, especially for people with rare HLA antigen profiles. Therefore, despite some HLA antigen matching included in the allocation algorithms, most recipients receive a mismatched graft on the HLA antigen level of the "classic" HLA-A, -B, and -DR loci. Although some level of HLA antigen serotype matching is meant to minimize rejection and alloimmunization after transplantation, the HLA antigen mismatch does not accurately reflect the individual immunologic risk.

1.2.3. Anti-HLA Antibody Detection

Next to the relevance of HLA antigen mismatches for transplant outcomes, circulating anti-HLA antibodies in the recipient's serum play a crucial role in evaluating HLA histocompatibility between donors and recipients. The importance of donor-specific anti-HLA antibodies (DSA) was first shown by Patel and Terasaki in their report on the high incidence of hyperacute graft failure when kidneys are transplanted in recipients with donor-specific anti-HLA antibodies. Two assays are commonly used to monitor recipient's circulating HLA antibodies: cell-based crossmatch (XM) assays and solid-phase immunoassays (SPIs). In crossmatch assays, the recipient's serum is incubated with the donor's T and B lymphocytes to assess antibody reactivity with the donor's cell surface antigens. In SPIs, the recipient's serum is incubated with soluble HLA antigens bound to beads. XM results must be correlated with and supported by SPI results to rule out non-HLA or HLA antibodies that may not be relevant to the outcome. SPIs provide

specificity and sensitivity and crossmatch assays aid antibody strength assessment. In its basic version, without the addition of anti-human globulin, the complement-dependent cytotoxicity crossmatch (CDC-XM) detects complement-activating antibodies. In the more sensitive flow cytometric crossmatch (FC-XM), fluorophore-conjugated antihuman immunoglobulin G (IgG) detects all cell-bound antibodies (Figure 1.4). The degree of cytotoxicity or fluorescent signal measures the relative strength of donor-reactive antibodies. It is important to remember that IgM and non-HLA IgG antibodies can affect these assays, and the correlation between antibody relative strength (MFI) obtained by SPI and the outcome of the cell-based assay is paramount. DSAs, detected by complement-dependent lymphocytotoxicity crossmatching (CDC-XM), have been demonstrated to associate with graft rejection and failure. From these early experiences, a positive CDC-XM was and is still considered an absolute contraindication for kidney transplantation unless desensitization strategies to negativize the CDC-XM are implemented. Since then, they have been evaluating anti-HLA antibodies, and assessing their donor specificity is required for pretransplant immune risk stratification. For several decades, the CDC-XM test was the only test used to investigate the anti-HLA antibodies in a recipient's serum and to guide allocation based on predefined unacceptable HLA antigens from the CDC HLA antibody profiles (Bettinotti, 2022).

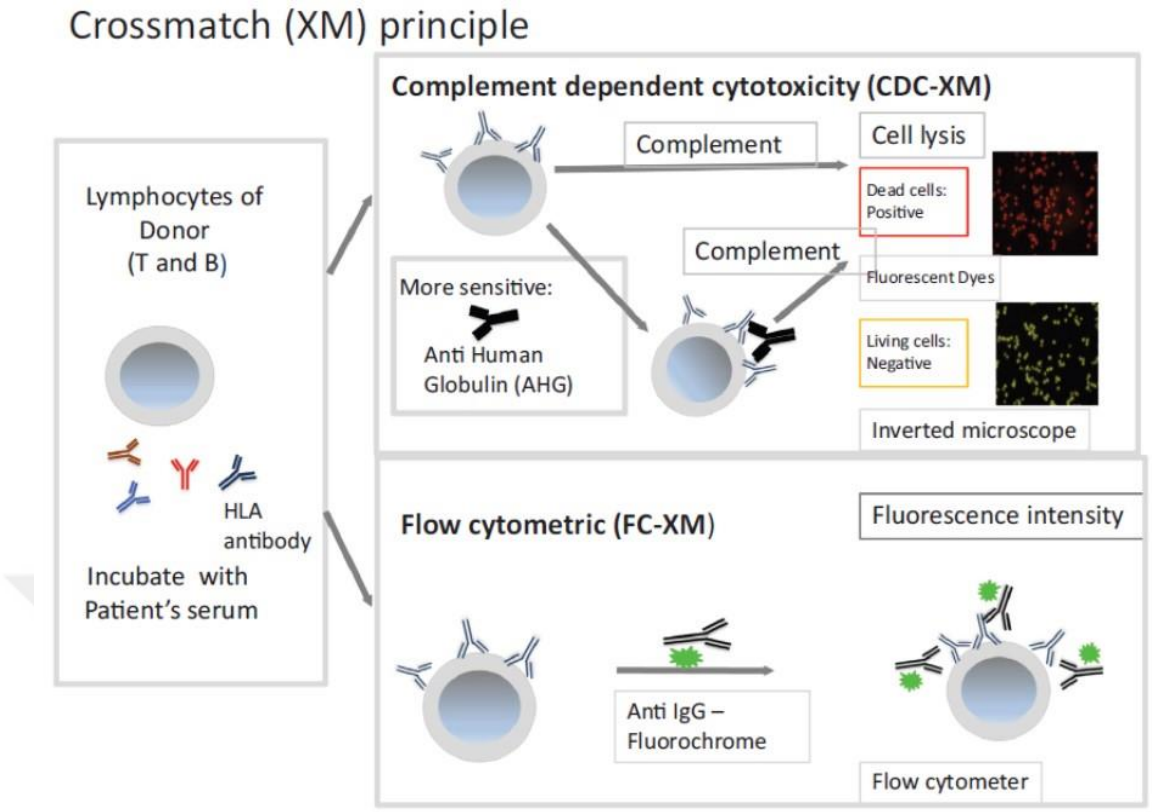

Figure 1.4 Crossmatch (XM) principle

After a few decades of routine clinical use, it became clear that CDC-XM testing lacks sensitivity and specificity. Not all clinically relevant circulating anti-HLA antibodies are detected by this method. Also, anti-HLA antibodies against the graft can develop after transplantation, as de novo DSA. Recipients developing de novo DSA are at the highest risk for graft rejection and failure. These findings strongly supported the need for more systematic and routine monitoring of anti-HLA antibodies after transplantation. The inability to identify all pretransplant immunized recipients by the lack of sensitivity and specificity of the CDC-XM test and the need for systematical post-transplant monitoring for de novo DSA led to the development of sensitive solid-phase methods. The development of specific and sensitive recombinant single (HLA) antigen bead (SAB) assays read by Luminex technology has likely been the most crucial breakthrough in transplantation in the last decades (Figure 1.5). The Luminex SAB assays for HLA antibody evaluation can detect and identify a broad range of circulating anti-HLA antibodies, even when the CDC-XM or other tests are negative. These assays were introduced in the transplant field fifteen years ago and rapidly adopted worldwide clinical routines (Figure 1.6).

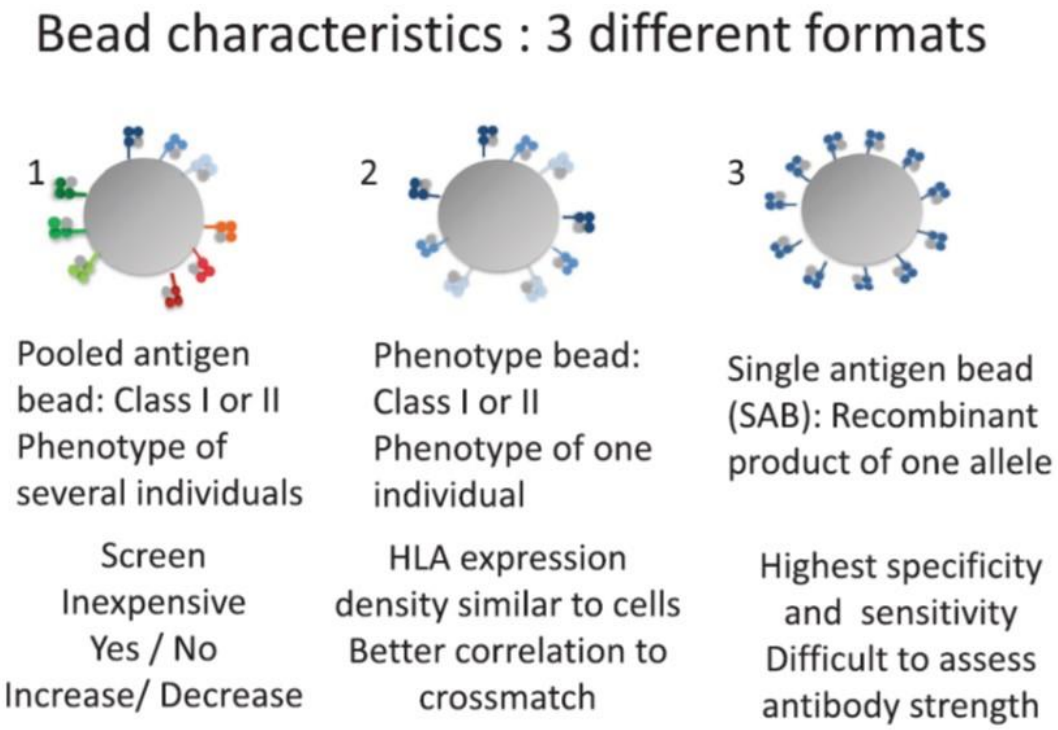

Figure 1.5 Luminex Bead characteristics

Analyzing the specificities of anti-HLA antibodies detected by Luminex SAB assays has added a new dimension of complexity and broadness in assessing HLA histocompatibility. Luminex SAB assays revealed the extensive heterogeneity of the pathogenic potential of DSA. They provided evidence that antibodies against the traditional HLA-A, -B, and -DR loci can cause graft rejection and failure, also antibodies against HLA-C, -DQ, and -DP.

The Luminex SAB assay panels often have two or more 2nd field HLA variants corresponding to the same (1st field) HLA antigen. When not all 2nd field HLA variants of a particular antigen share the same antibody reactivity, this creates a dilemma in interpreting HLA compatibility at the antigen level. Indeed, despite the worldwide use of the Luminex SAB assays and their specificity for 2nd field HLA antibody discrimination, the HLA genotyping requirements for deceased donor allocation algorithms remain at the antigen (1st field) level. This leads to imbalances between the higher HLA resolution of the sensitive Luminex SAB assays and the low HLA typing level. This imbalance often results in complex clinical cases where determining the HLA compatibility in sensitized recipients is quite challenging. This can even lead to cases with apparent antibodies

towards the own HLA antigen type, for instance, an HLA-DQ6 typed recipient who develops HLA antibodies against the same DQ6 antigen or an HLA-B44 recipient with anti-HLA-B44 antibodies. Deeper genotyping of these recipients showed that these antibodies were specific to the 2nd field HLA variants of the same antigen group and, therefore, not autoreactive. These and many other cases illustrate the inconsistencies of current allocation strategies, where allocation is based on data from low-resolution 1st field HLA typing and higher-resolution antibody identification assays. To overcome this inconsistency in current clinical practice, the 2nd field HLA antibodies detected by Luminex are often converted into their corresponding low-resolution antigens and recorded in allocation registries as unacceptable HLA antigens. This conversion (i.e., broadening the unacceptable HLA molecule repertoire) potentially negatively impacts finding a suitable, well-matched donor. Increasing the broadness of unacceptable antigens can restrict access to organ transplantation by reducing the available donor pool and increasing the waiting times in dialysis. It remains unstudied mainly whether matching the 2nd field HLA antibody profiling with 2nd field HLA typing, instead of translating the HLA antibody profiling to the antigen level, would improve risk stratification.

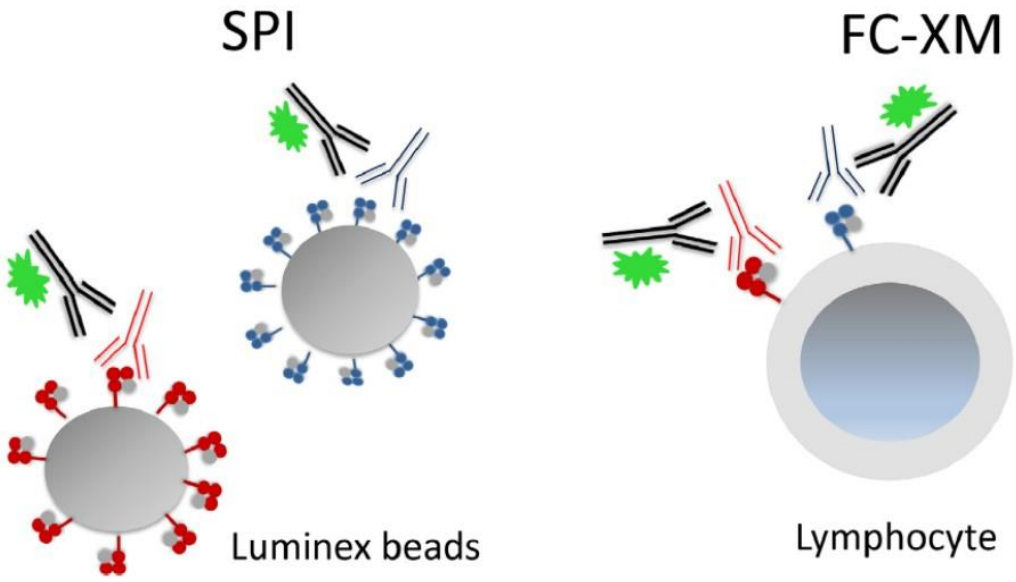

Figure 1.6 Luminex Beads and Flow Cytometer Beads

1.2.4. Molecular HLA Genotyping

The HLA match determinants used for matching and allocation in clinical kidney transplantation are currently defined at the 1st field resolution (e.g., HLA-A*02 or A2). To determine the 1st field HLA genotype, serological typing was initially used. However, with the development of molecular genotyping typing methods, it was found that the 1st field molecular typing results are more accurate than serology results and that matching by molecular HLA typing provides better graft survival than serological typing. Therefore, HLA laboratories use low- to intermediate-resolution DNA genotyping methods to map the HLA genome. In clinical kidney transplantation, PCR-sequence-specific oligonucleotides (SSO) hybridization methods (for routine testing) or a PCR with sequence-specific priming (SSP) (for urgent deceased donor typing) are the currently used methods. These techniques analyze several single nucleotide polymorphisms (SNPs) or oligonucleotide stretches present at the polymorphic antigen-presenting sites of the HLA molecules, representing the peptide-binding groove or antigen-recognition domain. These approaches primarily identify the key polymorphisms in HLA Class I exons 2-3 and HLA Class II exon 2 of the β chain, also called the critical exons, and provide an ambiguous allele typing result. Although the intermediate ambiguous typing result can be used to predict the high-resolution HLA result (based on allele frequencies), HLA laboratories apply subsequent high-resolution typing methods when a high-resolution confirmation is needed. After this initial HLA typing for clinical purposes, this is mainly done by Sanger sequencing methods. This high-resolution HLA typing level defines a set of alleles encoding the same protein sequence for the region of the antigen-recognition domain, identifying the whole exons 2-3 HLA Class I and exon 2, the β chain for HLA Class II. However, focusing on the most relevant part of the HLA molecule by including only a limited number of exons, these high-resolution tests still give little information about the complete HLA antigen on the cell membrane. This evaluation does not include differences in other parts of the HLA molecule coded by different exons. Moreover, as the whole HLA molecule is not defined, the allele typing remains ambiguous, even with HR typing. The entire surface of the HLA molecules can be a target for anti-HLA antibody formation. Restricting the genotyping to the antigen-recognition domain does not allow the revelation of the complete HLA antigen repertoire. To define the entire HLA

surface exposed to the immune system, the typing method needs to reveal the HLA genome at the 2nd field HR level by genotyping exons 2, 3, 4 for Class I and exons 2 and 3 of the α and the β chain for Class II. Alternatively, even better at the whole 2nd field level, revealing all exon information, since alterations in the amino-acid properties or size in non-key exons can affect the conformation, presentation, and accessibility of the HLA molecule on the cell membrane. For some HLA alleles, the 2nd field level is the highest reported HLA typing resolution level; therefore, it defines a unique allele. For other HLA alleles, the 2nd field level establishes a group that encodes the same HLA protein. Differences in the nucleotide sequence in the coding regions that do not change the HLA protein are defined by the 3rd field HLA resolution. These differences could affect translation efficiency but are, besides this, generally considered clinically less critical. Alterations in the non-coding regions of the gene, described by the fourth field, however, can significantly affect the protein expression and final antigen presentation on the cell membrane. Regulatory sites in the UTRs (untranslated regions) attributed to the antigen density, and a single mutation of the splice sites, responsible for the correct making of the messenger RNA, can change a normal allele and functional protein into a null allele, which does not longer encode for a functional HLA protein. It is increasingly acknowledged that HLA genotyping up to the 4th field, or complete allelic resolution, is needed to correctly investigate and identify the full HLA complexity. In recent years, powerful, innovative technologies, such as next-generation (short-read) sequencing (NGS) and third-generation real-time (long-read) sequencing (TGS), have been developed, allowing to increase the of gene sequencing targets by multiplexing. Short-read NGS resolves (near to) the complete HLA gene complexity, identifying all coding and most of the non-coding HLA molecule variants of the same antigen group up to the 3rd field resolution (for example, HLA-A*02:01:01). TGS has, due to the principle of long-read sequencing, the potential to resolve up to the 4th field allelic resolution (for example, HLA-A*02:01:01:01). Notably, these techniques also increase the number of studied HLA loci next to allowing higher field resolution. Besides HLA-A, -B, and -DRB1, other clinically relevant HLA loci such as C, DRB345, DQA1, DQB1, DPA1, and DPB1 can be included in the NGS and TGS genotyping pipelines. NGS or TGS can be introduced for prospective testing of organ recipients or living donors. Deceased donor testing requires a fast turnaround time, making these techniques unsuitable. However,

new real-time qPCR genotyping technologies offer the possibility to increase HLA typing resolution and include more loci (DRB345, DPA1, DPB1, and DQA1), within the desirable fast turnaround time, to a resolution complementary to that of the SAB assays which are helpful in the short turnaround time setting. NGS or TGS could subsequently be used post-transplantation to verify the matching level in detail and add to the knowledge of allele compatibility and antibody formation, further improving SAB assays. Today different NGS, TGS, and real-time qPCR workflows specific to HLA genotyping are commercially available. However, the 2nd field, HLA typing resolution, is not fully implemented in the clinical routines as its clinical usefulness is a matter of heavy debate within the transplant community. Using 2nd field HR HLA genotyping with the SAB assays might detect a higher number of clinically irrelevant anti-HLA antibodies, decreasing the transplant chances of sensitized recipients. In addition, 2nd field HR HLA results can be inferred from low-resolution HLA data using dedicated algorithms on large registries. This inference of the 2nd field from low-resolution data is considered a cheap alternative approach to resolve complex clinical cases, which require 2nd field HLA typing results to map with the 2nd field resolution of the SAB assays.

1.2.5. New HLA Matching Algorithms

The HLA disparity between donors and recipients is the primary driver of DSA formation and graft rejection after kidney transplantation. However, this disparity cannot be assessed correctly with the current antigen-matching approach for HLA-A, -B, and -DR loci. First, the clinically used HLA antigen level mismatch is insufficient to predict the immune risk fully. Recipients can develop antibodies against the antigen-matched donors' split or subtype antigens. Second, the current antigen-matching approaches assign equal weight to all mismatched HLA antigens, despite potential differences in immunogenicity. Finally, other HLA loci, for instance, HLA-C, -DQ, and -DP, can be responsible for developing DSA that are currently not included in the allocation algorithms. With the 2nd field HR HLA genotyping methods that became available in recent years, it is possible to evaluate HLA mismatches at a higher 2nd field HLA level and include all HLA loci. Although technically feasible, genotyping and matching for allocating the 11 HLA loci at the 2nd field HLA level would need other strategies than

the current strategy for antigen matching for only three loci. Till now, more than 27.200 different alleles have been identified. Therefore, national and international organ allocation systems seek ways to assess HLA compatibility better and minimize mismatches between donor and recipient, taking into account the immense polymorphism present in the complete HLA genome. The insights and knowledge obtained from the SAB assays in kidney transplantation suggest a new concept of HLA matching. The SAB assay explains in more detail the serological pattern reactivity of HLA antibodies against mismatched HLA molecules. In contrast to the primary antigen recognition concept, SAB showed that HLA antibodies recognize short, polymorphic fragments of the HLA molecule, referred to as epitopes, rather than the complete antigen as a whole unit. Therefore, each HLA molecule or antigen can be viewed as a collection of different epitopes defined as the entire structure of the surface of the HLA molecule that binds to the paratope of a specific antibody. These HLA epitopes can be unique to one or shared by several HLA molecules with different serological specificities. Moreover, these polymorphic epitopes can be shared across different HLA loci, especially in HLA Class I. Finally, HLA epitopes can also be located on the α chain alone or the α and β chains of HLA-DQ and -DP molecules. Recent clinical research focuses on assessing HLA compatibility at the molecular level instead of the serological (antigen) level. This approach delves into amino acid sequences of the HLA molecules of donors and recipients and tries to define small amino acid residues that constitute an immunogenic epitope that can induce an antibody response in the recipient. Two different concepts of HLA molecular mismatches provide opportunities for a more analytical study of the HLA immunogenicity and have been suggested to define better HLA compatibility between kidney transplant pairs: HLAMatchmaker and PIRCHE (Predicted Indirectly ReCognizable HLA Epitopes). The first tool, HLA Matchmaker, is a computer algorithm based on the direct allorecognition pathway by defining B cell epitopes on the surface of the mismatched donor HLA molecules. This tool enables the evaluation of HLA molecular mismatches at the eplet level. An eplet is defined as a small patch within a 3-Ångstroms area of surface-exposed amino acids of the HLA molecule and is considered the key element of the B-cell epitope that elicits a specific anti-HLA antibody. The added value of eplet mismatch calculations over current antigen-mismatch evaluation has not been fully explored in kidney transplantation. A limited number of studies have

documented the association of eplet mismatches with the risk of de novo DSA formation after transplantation, antibody-mediated rejection (ABMR), and graft failure, suggesting its potential for risk stratification of kidney transplant recipients. In line with this, a recent study has suggested thresholds for eplet mismatch loads for transplant risk stratification. Although insufficiently validated, at least one center has already replaced the antigen with the eplet approach for graft allocation in pediatric transplantation. In contrast to HLA Matchmaker, which addresses the direct allorecognition pathway, the second tool, PIRCHE, focuses on the indirect allorecognition pathway and predicts T cell-related immune responses against the donor HLA-derived peptides. This concept uses the functional peptide-binding properties of HLA Class II molecules. It indicates which mismatched donor HLA peptides will be presented by the recipient HLA Class II molecules to the helper T-cells and will lead to DSA formation after transplantation (T-cell epitopes). Thus, PIRCHE-II scores estimate and quantify the number of indirectly recognizable T cell epitopes based on the mismatched donor HLA type. The PIRCHE-II score has been defined as a marker for a donor-recipient HLA mismatch. Two large kidney transplant cohorts were associated with the risk for de novo DSA occurrence and long-term kidney failure allograft survival. This indicates that the PIRCHE-II score might quantify the recipient's immune risk more precisely and could be relevant to identifying immunogenic donor-recipient HLA mismatch combinations. However, further validation and comparison to other methods remain necessary. Despite the availability of these tools to evaluate the donor-recipient molecular mismatch for a few years, the clinical value of both epitope-based approaches, eplet mismatch calculation with HLA Matchmaker and the PIRCHE algorithm, has been studied only scarcely. Almost all studies evaluated the usefulness of these tools with inferred and incomplete HLA typing data, which does not allow the analysis of these algorithms at the required genotyping level for which they are intended. Therefore, the interpretation and generalization of these findings are hampered, and related literature is to be considered with caution.

1.3. Antibody-Mediated Rejection (ABMR)

The balance between rejection and graft tolerance after transplantation is determined by the extent and the type of genetic differences between the transplant pairs and the

reactivity of the recipient's immune system against these differences. The alloimmune responses against the graft have always been the major obstacle in organ transplantation, resulting in graft injury and functional decline, eventually leading to graft failure. The difference between the donor and recipient in the genetic makeup of the polymorphic HLA complex primarily drives graft rejection. The first type of graft rejection, T-cell mediated rejection (TCMR), usually occurs early after kidney transplantation. TCMR was the primary issue and barrier to graft survival in the early years of clinical transplantation. This barrier was successfully overcome by developing immunosuppression agents targeting T-cell activation and proliferation. The excellent short-term graft outcome illustrates the efficacy of the T-cell-targeted immunosuppressive therapies. Significant improvements in graft survival were observed during the last two decades of the previous century due to the development and clinical use of immunosuppressive agents like cyclosporine, tacrolimus, and mycophenolic acid. However, a significant decline in the improvement of graft survival has been noticed from 2000 onwards. The main reason for this lack of progress, especially in the long term, is the insufficiency of the immunosuppressive agents to control the humoral (antibody-mediated) immune responses after transplantation. Although known for decades, the development of sensitive SAB assays for detecting DSA has revealed the actual size of the problem of antibody-mediated graft injury. The humoral responses of the immune system have now become central in discussions about improving long-term outcomes after transplantation, and ABMR is considered the leading cause of late allograft failure. The main issue in allograft failure is the failure to diagnose and treat allograft rejection precisely.

To facilitate the diagnosis of graft rejection and install a worldwide standard diagnostic framework, a group of pathologists, nephrologists, and transplant surgeons met for the first time in 1991 in Banff, Canada, and established the nomenclature and classification of renal allograft pathology. This Banff classification has been accepted worldwide as the standard scheme for diagnosing kidney allograft rejection phenotypes and other injury processes. Since the first report, the Banff group has met regularly every two years. It updates the nomenclature and classification of the diagnostic criteria for graft rejections and other disease conditions upon new scientific and clinical insights. Although suggested in Banff 1997, ABMR was first defined as a distinct diagnostic entity at the Banff meeting

in 2001. The initial three diagnostic features of active ABMR (aABMR) were: (1) histological evidence of acute tissue injury, (2) evidence of antibody interaction with vascular endothelium, with C4d staining in peritubular capillaries as a footprint for complement-mediated graft injury and (3) serological evidence of DSA. Over the last two decades, considerable progress has been made in the phenotypic presentation of ABMR, resulting in adjustments to the initial Banff criteria for ABMR.

1.3.1. Active Antibody-Mediated Rejection (aABMR)

Active ABMR is the first acute stage of the antibody-mediated graft injury process. The histological evidence of acute tissue injury is represented primarily by microvascular inflammation (mvi Banff score≥2) on the graft biopsy. However, the Banff histological features of glomerulitis and peritubular capillarity, which define mvi, are not specific to ABMR, which complicates the precision of the ABMR diagnosis. Therefore, several iterations of the Banff definition of active ABMR led to a diagnostic system that has become quite complicated, considering the lesions' non-specificity. In addition, as not all cases develop the complete phenotype of ABMR, the Banff scheme also defined separate categories of biopsies “suspicious for ABMR” with an incomplete phenotype and uncertain clinical outcome (meeting only 2 of the three diagnostic features for ABMR). To avoid confusion in the clinical interpretation of this phenotype, the category “suspicious for ABMR” was abandoned in the most recent Banff 2017 classification. One of the incomplete phenotypes that lead to clinical confusion and extensive discussions in the field is the recipients with the complete histological picture of ABMR (ABMRh; the presence of the first two histologic Banff criteria) in the absence of serological evidence of DSA. According to the Banff consensus, this histopathology is due to harmful antibodies that cannot be measured because of limitations of the SAB testing methods for circulating DSA or non-HLA antibodies. To remove this confusion, notable changes were made in the diagnostic criteria for ABMR at the last Banff meeting (2017), where C4d positivity was introduced as an alternative for DSA, and the category “suspicious for ABMR” was eliminated. Although these most recent changes to the Banff classification were developed in consensus, direct evaluation of how DSA-positive ABMR differs from DSA-negative ABMR cases in graft injury and clinical outcome is lacking. In addition, it

remains unclear what is the time frame to use for the DSA in the 3rd Banff criterion. Previous studies have suggested that pretransplant DSA can have a heterogeneous posttransplant evolution in specificities and strength. It remains, however, largely unknown how the heterogeneity in the development of DSA impacts the risk and outcome of ABMR.

1.3.2. Chronic Antibody-Mediated Rejection (cABMR)

The next stage of the antibody-mediated graft injury process after active ABMR is the chronic stage of ABMR (cABMR). Morphologic evidence of chronic tissue injury presents as transplant glomerulopathy (TG or Banff cg score≥0), histologically evident as duplication of the glomerular basement membrane on a graft biopsy. TG is the final pathway of chronic glomerular damage driven by DSA. In addition, severe peritubular capillary basement membrane multilayering, which requires electron microscopy, and arterial intimal fibrosis of new-onset (excluding other causes) are also morphologic evidence of chronic antibody-mediated rejection. However, electron microscopy is not routinely used in clinical practice, and excluding other causes of arterial intimal fibrosis is virtually impossible (many recipients are hypertensive, have diabetes, or are older). The morphologic criterion for chronic ABMR is therefore restricted to TG. Like the discussion on active ABMR, the final diagnosis of chronic ABMR is difficult, especially in the absence of DSA. The complete phenotype of chronic active ABMR (caABMR) is defined by the presence of all 3 Banff criteria. However, a considerable part of biopsy specimens has TG without evidence of current/recent antibody interaction with the endothelium but with a prior documented diagnosis of active or caABMR or documented proof of DSA. For these cases, the term chronic ABMR (cABMR) is applied, omitting the word "active." In addition, the most recent Banff 2017 update has also changed the diagnostic criteria for caABMR, allowing the diagnosis of caABMR in the absence of antibodies by introducing C4d positivity as an alternative for the DSA criterion, and removing the category "suspicious for chronic active ABMR." It remains unknown what represents TG in the absence of detectable DSA and which risk factors contribute to developing DSA-negative TG. Two recent reports have suggested that the number of locus-specific HLA eplet mismatches is associated with the prediction of the development of TG and graft

outcome, even in the absence of DSA, guiding the development of TG through antibody-independent processes (Senev *et al.*, 2021). Although provocative, the interpretation of these studies is hampered by the lack of information on DSA and the reliance on low-resolution HLA genotyping data. The association of HLA molecular mismatches with TG development, especially in the absence of DSA, thus remains utterly unclear.

1.3.3. Non-HLA Antibody Caused Antibody-Mediated Rejection

Finally, next to the well-known impact of the major histocompatibility anti-HLA antibodies, as described above, other antibodies against minor non-HLA antigens have been implicated in renal allograft injury processes. While the role of anti-HLA DSA in ABMR is fully validated, accepted by the field, and utilized in routine clinical practice, the role of non-HLA antibodies is less clear. The involvement of non-HLA antibodies in ABMR was first suggested in studies of HLA identical siblings with biopsy-proven ABMR in the absence of DSA. Generally, non-HLA antibodies are classified into two categories: A) alloantibodies against minor histocompatibility polymorphic antigens that differ between the donor and the recipient, and B) autoantibodies that recognize self-antigen targets. Examples of such minor histocompatibility antigens are the polymorphic Major Histocompatibility Complex Class I chain-related molecules A (MICA) and B (MICB). Alloantibodies against MICA and MICB have been associated with increased allograft rejection risk and worse graft function after kidney transplantation.

Nevertheless, not all studies have replicated these associations, and MICA and MICB antibodies or testing are not included in routine clinical practice because of the inconsistencies in the literature. The other category includes many autoantibodies directed against different self-non-HLA targets. The antibodies against the angiotensin II type 1 receptor (AT1R) are the most studied. While many studies support the association of AT1R antibodies and graft rejection, no firm conclusions about their pathogenicity in the damaging graft process can be made. However, due to the high number of recipients with rejection but without DSA, there has been an active interest in the contribution of non-HLA immunity to kidney graft outcomes in recent years. This results in an increasing number of published articles on this topic, identifying different novel non-HLA targets

with a possible impact on kidney graft outcome. These antibodies are also found in healthy individuals. The main challenge when studying these autoantibodies remains their non-pathogenic presence in these healthy controls and kidney transplant recipients with stable graft function. Finally, although non-HLA antibodies are implemented in the serological Banff criteria for ABMR, noted as antibodies against other antigens, none of the previously suggested non-HLA antibodies are currently routinely performed in clinical practice for diagnosing ABMR. This is due to the lack of direct evidence of their pathogenicity, inconsistencies in the literature, lack of validated thresholds, and lack of insight into the clinical presentation of rejection induced by these non-HLA antibodies.

1.4. Immunogenicity and Antigenicity

The immunogenicity of an eplet or functional epitope is the capacity to induce an immune response. Antigenicity is the ability of the amino acids making up the structural epitope to be bound by pre-transplantation antibodies. Therefore, whether an alloantibody binds a particular eplet-related HLA allele is not only determined by the presence of the eplet. However, it can also be influenced by amino acids surrounding the eplet or the peptide in the peptide-binding groove. Also, amino acids that cause a conformational change in the HLA molecule can influence antigenicity, even when they are located outside (but next to) the range of the structural epitope (Bezstarosti, Kramer, *et al.*, 2022). The fact that immunogenicity of mismatched HLA antigens can vary from unacceptable to acceptable mismatches has been previously recognized and demonstrated. The critical question, though, is what determines the antigenicity and immunogenicity of a certain HLA mismatch (Tambur and Claas, 2015). It is well established that recipients will develop HLA antibodies against a restricted number of mismatched epitopes. Other recipients will not develop HLA antibodies despite significant mismatching with their organ donors. One contributing factor is likely the HLA-Class II phenotype of the recipient as it will influence the interaction between CD4þ T cells and B cells, which needs indirect recognition of donor-derived peptides presented by HLA Class II on the B cells. This phenomenon was initially reported by Fuller et al, and more recently by Otten et al who demonstrated how the use of PIRCHE-II (predicted indirectly recognizable HLA epitopes, HLA Class-II presented) could explain the generation, or no generation of de

novo DSA in previously nonimmunized recipients who received and lost their grafts in the face of similar mismatches. In addition, Duquesnoy postulated that significant similarity needs to exist between the HLA antigens of the antibody producer (recipient) and those of the immunizing donor (Tambur and Claas, 2015). To account for that, the concept of HLA epitope was extended to a structural epitope rather than the mere eplet differences between certain HLA sequences, leading to a non-self/self-paradigm, requiring identity between most of the 15–25 surface amino acid residues that constitute the functional epitope, except for the implicated eplet. The functional epitope, in turn, is part of the structural epitope that meets the antibody's third complementarity-determining region (CRD). This hypothesis assumes the presence of low-affinity immunoglobulin receptors for self-HLA epitopes in the recipient's circulation. Those immunoglobulins will not elicit an immune response against self-antigens, but a strong alloantibody response will ensue once exposed to minor mismatches. Overall, B cell development and maturation rely on a similar process in which receptor editing following positive selection shapes the repertoire of alloreactive and autoreactive B cells. Indeed, many immune responses are directed at targets that deviate from self only by small modifications. Additional data to support Duquesnoy's hypothesis were recently presented by Tambur et al. The evolutionary logic to this phenomenon is that we evolved to attack self-cells, infected with intracellular parasites, based on peptides presented in the context of our antigens. The factors mentioned thus far likely explain the relative immunogenicity of a particular HLA mismatch. Additional factors may determine the strength of these responses, whether measured as Mean Fluorescence Intensity (MFI) or the actual titer of the antibody. Kosmoliaptsis et al demonstrated that the number of continuous and discontinuous eplet mismatching is associated not only with the presence of alloantibodies but also with progressively stronger alloantibody responses. However, as previously noted by other investigators, this information is insufficient to explain the heterogeneity in binding strength observed for well-recognized alloantibodies, such as antibodies to the public epitopes Bw4 and Bw6. By using comparative protein structure modeling and generation of high-resolution 3D structural and physicochemical models of common HLA Class I alleles, Kosmoliaptsis and colleagues were able to show differences in the number and distribution of polar and charged amino acid side chains outside of the conventional epitope site; changes which affected the folding and structural composition

of the different HLA antigens expression Bw4 or Bw6 that were studies. This innovative technology provided new insight into classifying and determining Class I HLA epitope antigenicity. The observation that antibody reactivity to a particular epitope can yield significantly different MFI values in a single antigen bead analysis is not unique to Class I, as has been recently shown by Tambur and colleagues. Another factor that can affect the ability of antibody binding is the peptide presented within the HLA molecule and, consequently, tissue-specific reactivity. It is pertinent to mention that the technical limitations of the current solid-phase assays, leading amongst others to a ‘‘prozone effect’’ or the detection of antibodies against denatured targets, may affect our ability to assign B cell epitopes accurately (Senev *et al.*, 2021).

1.4.1. Determinants of HLA Immunogenicity

HLA immunogenicity is principally based on mismatched amino acid residues between the donor and recipient HLA. The first studies that investigated the immunogenicity of HLA in the context of the recipient’s HLA type were able to identify specific donor-recipient HLA antigen combinations associated with an increased risk of graft loss in kidney transplantation. On the other hand, permissible HLA antigen mismatches associated with increased graft survival were also described. It was hypothesized that some HLA antigen mismatches were permissible due to polymorphic amino acid configurations on the donor HLA that were also present on the recipient and would thus not be recognized as foreign. The challenge of finding suitable donors for highly sensitized kidney transplant recipients led to the development of HLAMatchmaker by Rene Duquesnoy (Bezstarosti, Kramer, *et al.*, 2022). This program allowed for comparing amino acid sequences of donor and recipient HLA alleles to identify mismatched amino acid triplets as potentially immunogenic epitopes. Indeed, triplet mismatches were demonstrated to be associated with alloantibody formation in kidney transplant recipients and pregnancy-immunized women.

Further development of HLAMatchmaker resulted in the introduction of the term ‘‘eplet’’ to describe polymorphic amino acid residues within a 3.0–3.5 Angstrom radius, which can be discontinuous, as opposed to the linear amino acid triplets, due to the

conformational nature of epitopes recognized by the B cell receptor. Since then, many studies have demonstrated the association between high eplet mismatch load and increased risk of dnDSA formation, transplant glomerulopathy, rejection, and graft failure in kidney transplantation. Eplet mismatch load has also been shown to be an independent predictor for chronic lung allograft dysfunction, graft loss in pediatric heart transplantation, and dnDSA formation in liver transplantation (Bezstarosti, Kramer, *et al.*, 2022).

1.4.2. Differential Immunogenicity of HLA Epitopes

Several studies have defined thresholds of eplet mismatch loads above which transplant recipients are at risk for inferior outcomes. However, the fact that recipients can develop dnDSA despite an eplet mismatch load below these previously defined thresholds demonstrates the issue with this approach. Not all epitope mismatches are equally immunogenic, and the association of eplet mismatch load with dnDSA and graft survival shows that a higher number of mismatches increases the chance that immunogenic epitopes are present. Furthermore, the determination of eplet mismatch thresholds depends not only on the investigated population but also on the version of HLAMatchmaker that is used for eplet mismatch analysis since the total number and repertoire of eplets in the different versions of HLAMatchmaker varies. Therefore, although molecular mismatch loads can provide insight into the risk stratification of transplant recipients, the evaluation of differential immunogenicity of individual HLA epitopes is of critical importance before HLA epitope matching can be implemented in organ allocation algorithms (Sapir-Pichhadze *et al.*, 2015; Bezstarosti, Kramer, *et al.*, 2022).

1.5. HLA Epitopes (Epitope Mapping)

Eplets are small configurations of amino acid residues that play dominant roles in HLA epitopes reactive with antibodies. Such configurations are theoretical considerations based on residue differences in polymorphic sequence locations, but we must raise the question of how many are recognized by specific antibodies. One would expect the

clinical relevance of epitope-based matching to apply only to epitopes experimentally verified with informative antibodies. The HLA Epitope Registry has a list of antibody-verified epitopes recorded thus far for each locus, but the repertoire is still incomplete. The website recently includes a downloadable PDF file, “EpiPedia of HLA” that describes the antibody verifications of HLA epitopes in detail (Duquesnoy, 2016). With the help of participating HLA laboratories that might have interesting serum antibody reactivity patterns, we will continue our analyses to identify new epitopes. Eplets are small ligands that play dominant roles in HLA epitopes that are reactive with antibodies. These theoretical reactivity considerations are based on residue differences at polymorphic sequence positions. The question is, how many of them are recognized by specific antibodies? The clinical relevance of epitope-based matching can be expected to apply only to epitopes experimentally confirmed with informative antibodies. The HLA Epitope Registry has a list of antibody-confirmed epitopes for each locus. Recently, the website has included a downloadable “HLA EpiPedia” file detailing antibody validations of HLA epitopes. The HLAMatchmaker website www.epitopes.net (formerly www.HLAMatchmaker.net) now has a downloadable Excel document called “Five Maps of HLA Epitopia,” describing the sequence locations of antibody-confirmed eplets and polymorphic residues as potential candidates for identifying additional epitopes. These maps can navigate the HLA Epitopia continents while searching for new antibody-defined epitopes (Duquesnoy, 2016).

HLA Eplet Registry aims to serve as the main database of theoretical and confirmed HLA eplets recognizable by B-Cell receptors (*HLA Eplet Registry*, no date).

2. MATERIAL AND METHOD

We have included a total of 10 kidney transplantation recipient-donor paired data already resulting in Istanbul University, Istanbul Faculty of Medicine, Department of Medical Biology, Tissue Typing Laboratory as a retrospective study database.

In this database, we have recipient-donor paired HLA Typing data for Class I as four digits (High Resolution), recipients' pre-transplantation and post-transplantation anti-HLA antibody detection data for Class I as four digits (High Resolution with Luminex SAB method).

All eplets, eplet AA sequences, and Luminex-based anti-HLA antibodies related to the eplets are retrieved from HLA Eplet Registry (https://www.epregistry.com.br) and added as supplementary data in the ANNEX 1 section.

2.1. Bepipred-1.0 Linear Epitope Prediction Method

BepiPred predicts the location of linear B-cell epitopes using a Hidden Markov model and a propensity scale method. The residues with scores above the threshold (default value is 0.35) are predicted to be part of an epitope and colored in yellow on the graph (where y-axes depict residue scores and x-axes residue positions in the sequence). The table below shows the relationship between selected thresholds and the sensitivity/specificity of the prediction method, calculated based on the epitope/non-epitope predictions (*Antibody Epitope Prediction*, no date) (**Error! Reference source not found.**).

Table 2.1 Sensitivity/specificity of the prediction method, calculated based on the epitope/non-epitope predictions.

Threshold	Sensitivity	Specificity
-0.20	0.75	0.50
0.20	0.56	0.68
0.35	***0.49***	***0.75***
0.90	0.25	0.91

1.30	0.13	0.96

The database includes recipient-donor paired HLA Typing data for Class I as four digits (High Resolution), recipient's pre-transplantation and post-transplantation anti-HLA antibody detection data for Class I as four digits (High Resolution with Luminex SAB method) for 10 recipient-donor listed as below (Table 2.2)(Table 2.3)(Table 2.4)(Table 2.5)(Table 2.6)(Table 2.7)(Table 2.8)(Table 2.9)(Table 2.10)(Table 2.11):

Table 2.2 HLA Typing and SAB Results for Recipient-Donor pair 01.

Recipient-01	**Donor-01**	
A*02:06	A*11:01	
A*34:02	A*68:01	
B*13:01	B*44:02	
B*38:01	B*58:01	
C*03:04	C*03:02	
C*12:03	C*05:01	
SAB Pre-Transplantation Results	**MFI**	
B*81:01	1878	
B*82:02	1255	
B*45:01	1022	
B*44:02	830	
SAB Post-Transplantation Results	**Description**	**MFI**
*B*07:02*	*newly formed antibody*	*915*
*B*42:01*	*newly formed antibody*	*912*
B*81:01	pre-transplantation antibody	1937
B*82:02	pre-transplantation antibody	1007

Table 2.3 HLA Typing and SAB Results for Recipient-Donor pair 02.

Recipient-02	**Donor-02**
A*02:01	A*02:01
A*24:02	x

B*35:03	B*49:01
B*49:01	B*51:01
C*04:01	C*01:02
C*07:01	C*07:01
SAB Pre-Transplantation Results	**MFI**
A*01:01	17822
A*36:01	16003
A*11:01	11532
A*11:02	10175
A*29:02	9058
A*29:01	8672
A*80:01	8416
A*26:01	7060
A*43:01	5935
A*66:02	4919
A*25:01	4626
A*66:01	4478
A*03:01	3651
A*34:02	3254
A*30:01	1057
A*33:01	912
B*15:12	909

SAB Post-Transplantation Results	**Description**	**MFI**
A*01:01	pre-transplantation antibody	14968
A*03:01	pre-transplantation antibody	1548
A*11:01	pre-transplantation antibody	5754
A*11:02	pre-transplantation antibody	5180
A*25:01	pre-transplantation antibody	2159
A*26:01	pre-transplantation antibody	3696
A*29:01	pre-transplantation antibody	5630
A*29:02	pre-transplantation antibody	5460
*A*32:01*	*newly formed antibody*	*4351*
A*34:02	pre-transplantation antibody	1202
A*36:01	pre-transplantation antibody	11346
A*43:01	pre-transplantation antibody	3276

A*66:01	pre-transplantation antibody	1864
A*66:02	pre-transplantation antibody	1961
A*80:01	pre-transplantation antibody	4885

Table 2.4 HLA Typing and SAB Results for Recipient-Donor pair 03.

Recipient-03	**Donor-03**	
A*24:02	A*02:01	
A*31:01	A*11:01	
B*48:01	B*35:01	
B*51:01	B*49:01	
C*08:01	C*04:01	
C*14:02	C*07:01	
SAB Pre-Transplantation Results	**MFI**	
A*02:03	2015	
A*02:02	1645	
A*02:05	1605	
A*02:01	1563	
SAB Post-Transplantation Results	**Description**	**MFI**
*A*34:01*	*newly formed antibody*	*6010*

Table 2.5 HLA Typing and SAB Results for Recipient-Donor pair 04.

Recipient-04	**Donor-04**
A*02:01	A*23:01
A*24:02	A*24:02
B*18:01	B*44:03
B*51:01	B*51:01
C*07:01	C*02:02
C*14:02	C*04:01
SAB Pre-Transplantation Results	**MFI**
C*04:03	12049
C*02:02	11289
C*15:02	10117
C*17:01	9304
C*05:01	8808

C*06:02	7544	
C*18:01	6866	
A*66:02	1077	
C*08:02	961	
C*12:02	851	
B*82:02	808	
SAB Post-Transplantation Results	**Description**	**MFI**
*A*03:01*	*newly formed antibody*	*1087*

Table 2.6 HLA Typing and SAB Results for Recipient-Donor pair 05.

Recipient-05	**Donor-05**	
A*01:01	A*02:01	
A*32:01	A*25:01	
B*27:03	B*51:01	
B*52:01	x	
C*02:02	C*14:02	
C*12:02	C*15:02	
SAB Pre-Transplantation Results	**MFI**	
A*66:01	1092	
A*25:01	924	
A*26:01	878	
SAB Post-Transplantation Results	**Description**	**MFI**
*A*34:01*	*newly formed antibody*	*2064*

Table 2.7 HLA Typing and SAB Results for Recipient-Donor pair 06.

Recipient-06	**Donor-06**
A*24:02	A*02:01
x	A*26:01
B*40:06	B*07:02
B*55:01	B*35:01
C*01:02	C*04:01
C*08:01	C*07:02
SAB Pre-Transplantation Results	**MFI**

A*66:01	991	
A*25:01	907	
A*26:01	768	
SAB Post-Transplantation Results	**Description**	**MFI**
*A*43:01*	*newly formed antibody*	*4402*

Table 2.8 HLA Typing and SAB Results for Recipient-Donor pair 07.

Recipient-07	**Donor-07**	
A*24:02	A*03:01	
A*33:01	A*30:01	
B*07:02	B*13:02	
B*27:02	B*50:01	
C*02:02	C*01:02	
C*07:02	C*06:02	
SAB Pre-Transplantation Results	**MFI**	
A*11:02	2048	
A*11:01	1603	
A*36:01	1361	
A*66:01	1288	
A*01:01	1234	
A*34:02	1121	
A*80:01	1044	
SAB Post-Transplantation Results	**Description**	**MFI**
A*01:01	pre-transplantation antibody	13402
*A*03:01*	*newly formed antibody*	*1366*
*A*08:01*	*newly formed antibody*	*2045*
A*11:01	pre-transplantation antibody	15005
*A*11:02*	*newly formed antibody*	*14348*
*A*26:01*	*newly formed antibody*	*12796*
*A*29:01*	*newly formed antibody*	*2148*
*A*29:02*	*newly formed antibody*	*2731*
A*34:02	pre-transplantation antibody	14453
A*36:01	pre-transplantation antibody	14245
*A*43:01*	*newly formed antibody*	*11741*

A*66:01	pre-transplantation antibody	14296
A*80:01	pre-transplantation antibody	12660
*B*14:01*	*newly formed antibody*	*865*
*B*14:02*	*newly formed antibody*	*1252*
*B*15:01*	*newly formed antibody*	*4027*
*B*15:02*	*newly formed antibody*	*7850*
*B*15:03*	*newly formed antibody*	*1775*
*B*15:08*	*newly formed antibody*	*6806*
*B*15:12*	*newly formed antibody*	*893*
*B*15:13*	*newly formed antibody*	*4084*
*B*15:16*	*newly formed antibody*	*5381*
*B*18:01*	*newly formed antibody*	*1594*
*B*35:01*	*newly formed antibody*	*8627*
*B*35:08*	*newly formed antibody*	*6188*
*B*46:01*	*newly formed antibody*	*1700*
*B*49:01*	*newly formed antibody*	*4201*
*B*50:01*	*newly formed antibody*	*2875*
*B*51:01*	*newly formed antibody*	*7831*
*B*52:01*	*newly formed antibody*	*8192*
*B*53:01*	*newly formed antibody*	*8113*
*B*54:01*	*newly formed antibody*	*1945*
*B*56:01*	*newly formed antibody*	*2425*
*B*57:01*	*newly formed antibody*	*1986*
*B*73:01*	*newly formed antibody*	*1155*
*B*78:01*	*newly formed antibody*	*12205*
*C*03:03*	*newly formed antibody*	*1441*
*C*03:04*	*newly formed antibody*	*1991*

Table 2.9 HLA Typing and SAB Results for Recipient-Donor pair 08.

Recipient-08	**Donor-08**
A*03:02	A*29:01
A*29:01	x
B*07:05	B*07:05
B*18:01	B*35:03
C*12:03	C*12:03
C*15:05	C*15:05

SAB Pre-Transplantation Results	MFI	
A*01:01	1414	
SAB Post-Transplantation Results	**Description**	**MFI**
-	-	-

Table 2.10 HLA Typing and SAB Results for Recipient-Donor pair 09.

Recipient-09	Donor-09	
A*02:05	A*26:01	
A*24:02	A*68:01	
B*27:03	B*44:02	
B*44:02	B*51:01	
C*01:02	C*02:02	
C*05:01	C*16:02	
SAB Pre-Transplantation Results	**MFI**	
B*78:01	2400	
B*35:01	1690	
B*35:08	1300	
B*51:01	1203	
B*53:01	1491	
B*15:02	1060	
B*15:18	1100	
SAB Post-Transplantation Results	**Description**	**MFI**
*A*25:01*	*newly formed antibody*	*6346*
B*35:01	pre-transplantation antibody	4696
B*35:08	pre-transplantation antibody	5636
B*51:01	pre-transplantation antibody	5498
B*53:01	pre-transplantation antibody	1683
*B*55:01*	*newly formed antibody*	*2576*

Table 2.11 HLA Typing and SAB Results for Recipient-Donor pair 10

Recipient-10	Donor-10
A*03:01	A*26:01
A*26:01	A*30:01
B*35:01	B*13:02

B*55:01	B*55:01
C*01:02	C*01:02
C*04:01	C*06:02
SAB Pre-Transplantation Results	**MFI**
A*68:01	20456
A*02:05	20453
A*02:02	20229
A*02:03	20194
A*68:02	20136
A*02:01	19914
A*69:01	16131
A*24:02	15432
A*24:03	14725
A*23:01	13027
B*57:01	6180
B*58:01	3498

SAB Post-Transplantation Results	**Description**	**MFI**
A*02:01	pre-transplantation antibody	8283
A*02:02	pre-transplantation antibody	7821
A*02:03	pre-transplantation antibody	7358
A*02:05	pre-transplantation antibody	6796
A*23:01	pre-transplantation antibody	6532
A*24:02	pre-transplantation antibody	6018
A*24:03	pre-transplantation antibody	5587
*A*29:01*	*newly formed antibody*	*4461*
*A*34:01*	*newly formed antibody*	*8825*
A*68:01	pre-transplantation antibody	4821
A*68:02	pre-transplantation antibody	5348
A*69:01	pre-transplantation antibody	3747
B*57:01	pre-transplantation antibody	2365
B*58:01	pre-transplantation antibody	1451

3. RESULTS

We have applied the calculation steps for 10 Recipient-Donor pairs, which we have as retrospective data from Istanbul University, Istanbul Faculty of Medicine, Department of Medical Biology, Tissue Typing Laboratory.

3.1. Predicting Most Likely Donor Specific Antibodies Based on Most Shared Eplets

Steps for predicting most likely antibodies based on most shared eplets.

1. Finding the mismatched donor HLA alleles by comparing HLA Typing results (Table 3.1)(Table 3.6)(Table 3.11)(Table 3.16)(Table 3.21)(Table 3.26)(Table 3.31)(Table 3.36)(Table 3.41)(Table 3.46).
2. Listing the eplets of the recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay (represented as anti-HLA antibodies) (eplets and Luminex alleles are retrieved from HLA Eplet Registry) (Table 3.2)(Table 3.7)(Table 3.12)(Table 3.17)(Table 3.22)(Table 3.27)(Table 3.32)(Table 3.37)(Table 3.42)(Table 3.47).
3. Calculating the number of shared eplets between each mismatched donor HLA allele and the recipient's Luminex alleles listed in the previous step (Table 3.3)(Table 3.8)(Table 3.13)(Table 3.18)(Table 3.23)(Table 3.28)(Table 3.33)(Table 3.38)(Table 3.43)8Table 3.48).
4. Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets (Table 3.4)(Table 3.9)(Table 3.14)(Table 3.19)(Table 3.24)(Table 3.29)(Table 3.34)(Table 3.39)(Table 3.44)(Table 3.49).
5. Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA which with the highest number of shared eplets (Table 3.5)(Table 3.10)(Table 3.15)(Table 3.20)(Table 3.25)(Table 3.30)(Table 3.35)(Table 3.40)(Table 3.45)(Table 3.50).

Sensitivity/specificity score of the prediction method calculated based on the epitope/non-epitope predictions shown as graphically for the mismatched donor HLA

allele with maximum shared eplets (Figure 3.1)(Figure 3.2)(Figure 3.3)(Figure 3.4)(Figure 3.5)(Figure 3.6)(Figure 3.7)(Figure 3.8)(Figure 3.9)(Figure 3.10).

Here are the results of the steps performed for the ten recipient-donor pairs.

Table 3.1 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 01.

Recipient	Donor	Antigen MM
A*02:06	A*11:01	yes
A*34:02	A*68:01	yes
B*13:01	B*44:02	yes
B*38:01	B*58:01	yes
C*03:04	C*03:02	yes
C*12:03	C*05:01	yes

Table 3.2 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 01.

Recipient's Luminex Alleles	Eplets Of Recipient's Pre-Transplantation Luminex Alleles
B*81:01	9Y - 24S - 45EE - 62RN - 63NI - 65QIA - 66I - 66IY - 69AA - 70IAQ - 76ES - 76ESN - 77S - 77SRN - 80N - 95L - 97S - 99Y - 113H - 113HN - 116Y - 143S - 147L - 151ARV - 152V - 156L - 163E - 163EW - 177DK - 180E - 193PI - 245TA
B*82:02	9Y - 12M - 24S - 45EE - 62RN - 63NI - 65QIA - 66I - 66IY - 69AA - 70IAQ - 76ES - 76ESN - 77S - 77SRN - 80N - 95L - 97R - 99F - 103L - 113H - 113HN - 116L - 131S - 151ARV - 152V - 156DA - 162GLS - 163L - 163LE - 163LS/G - 166ES - 193PI
B*45:01	9H - 12M - 24T - 32L - 41T - 45KE - 66I - 66IS - 69TNT - 71TTS - 74Y - 76ES - 76ESN - 77S - 77SRN - 80N - 95W - 97R - 99Y - 103L - 113YN - 116L - 131S - 151ARV - 152V - 156DA - 162GLS - 163L - 163LE - 163LS/G - 166ES - 193PI
B*44:02	9Y - 12M - 24T - 32L - 41T - 45KE - 66I - 66IS - 69TNT - 71TN - 74Y - 76EN - 76ET - 77N - 80T - 80TA - 80TLR - 81ALR - 82LR - 94I - 95I - 97R - 99Y - 113YD - 116D - 131S - 151ARV - 152V - 156DA - 162GLS - 163L - 163LE - 163LS/G - 166ES - 193PI - 199V

Table 3.3 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 01.

Donor	Number Of Shared Eplets	Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles
A*11:01	13	9Y (3) - 80T (1) - 95I (1) - 99Y (3) - 116D (1) - 193PI (4)
A*68:01	15	9Y (3) - 62RN (2) - 80T (1) - 95I (1) - 99Y (3) - 116D (1) - 152V (4)
B*44:02	77	9Y (3) - 12M (3) - 24T (2) - 32L (2) - 41T (2) - 45KE (2) - 66I (4) - 66IS (2) - 69TNT (2) - 71TN (1) - 74Y (2) - 76EN (1) - 76ET (1) - 77N (1) - 80T (1) - 80TA (1) - 80TLR (1) - 81ALR (1) - 82LR (1) - 94I (1) - 95I (1) - 97R (3) - 99Y (3) - 113YD (1) - 116D (1) - 131S (3) - 151ARV (4) - 152V (4) - 156DA (3) - 162GLS (3) - 163L (3) - 163LE (3) - 163LS/G (3) - 166ES (3) - 193PI (4) - 199V (1)
B*58:01	44	9Y (3) - 12M (3) - 69AA (2) - 71SA 74Y (2) - 76EN (1) - 77N (1) - 81ALR (1) - 82LR (1) - 94I (1) - 95I (1) - 97R (3) - 99Y (3) - 103L (2) - 113H (2) - 131S (3) - 151ARV (4) - 152V (4) - 156L (1) - 163L (3) - 163LE (3)
C*03:02	29	9Y (3) - 77S (3) - 77SRN (3) - 80N (3) - 94I (1) - 95L (2) - 97R (3) - 99Y (3) - 113YD (1) - 156L (1) - 163L (3) - 163LE (3)
C*05:01	15	1C 9Y (3) - 77N (1) - 95L (2) - 97R (3) - 99Y (3) - 103L (2) - 113YN (1)

Table 3.4 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 01.

Luminex Allele	# Shares		Luminex Allele	# Shares		Luminex Allele	# Shares
B*44:03	77		B*27:03	33		A*32:01	25
B*53:01	59		B*27:05	33		C*08:02	25
B*15:13	56		B*41:01	33		A*02:05	25
B*58:01	56		B*78:01	32		A*11:01	25
B*13:02	52		B*14:06	32		A*33:01	24
B*57:01	52		C*15:02	32		A*33:03	24
B*57:03	52		B*40:05	31		***B*07:02***	***24***
B*35:01	52		A*26:01	31		B*07:03	24
B*35:08	50		B*41:02	31		A*74:01	23
B*15:02	49		B*37:01	31		A*80:01	23
B*15:16	46		B*40:02	30		A*31:01	23
B*49:01	46		A*43:01	30		A*30:02	23
B*47:01	45		A*68:02	30		C*16:01	22
B*59:01	44		B*55:01	30		C*07:01	21

B*15:18	42		A*25:01	30		A*01:01	21
B*15:03	42		***B*42:01***	***30***		B*73:01	21
B*82:01	42		B*27:08	29		A*36:01	21
B*15:10	42		C*17:01	29		A*03:01	20
B*51:01	41		B*14:01	28		A*23:01	20
B*56:01	41		B*14:02	28		C*04:03	19
B*51:02	41		B*40:06	28		C*07:04	18
B*52:01	41		B*14:05	28		A*02:01	18
B*15:01	40		A*34:01	28		A*23:02	18
B*15:11	40		A*66:01	28		A*02:02	18
B*50:01	39		A*66:02	28		A*30:01	17
B*39:05	39		A*68:01	27		A*24:03	16
B*15:12	38		C*08:01	27		A*24:02	16
B*39:01	37		A*29:02	26		C*06:02	15
B*67:01	37		A*29:01	26		C*07:02	15
C*03:03	37		A*69:01	26		A*02:03	13
B*40:01	36		C*12:02	26		C*04:01	12
C*03:02	35		C*02:02	26		C*18:01	12
B*46:01	35		C*02:10	26		C*18:02	12
B*54:01	35		B*08:01	25		C*14:02	9
B*18:01	33		A*11:02	25		C*01:02	9
B*48:01	33		C*05:01	25			

Table 3.5 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele B*44:02 of donor 01.

No.	Start	End	Peptide	Length
1	1	1	G	1
2	13	21	SRPGRGEPR	9
3	38	75	SDATSPRKEPRAPWIEQEGPEYWDRETQISKTNTQTYR	38
4	86	91	NQSEAG	6
5	102	108	DVGPDGR	7
6	110	110	L	1
7	114	121	DQDAYDGK	8
8	131	142	SSWTAADTAAQI	12
9	144	145	QR	2
10	147	147	W	1
11	150	155	ARVAEQ	6

12	157	158	RA	2
13	173	196	ENGKETLQRADPPKTHVTHHPISD	24
14	218	241	QRDGEDQTQDTELVETRPAGDRTF	24
15	249	256	VPSGEEQR	8
16	264	268	EGLPK	5

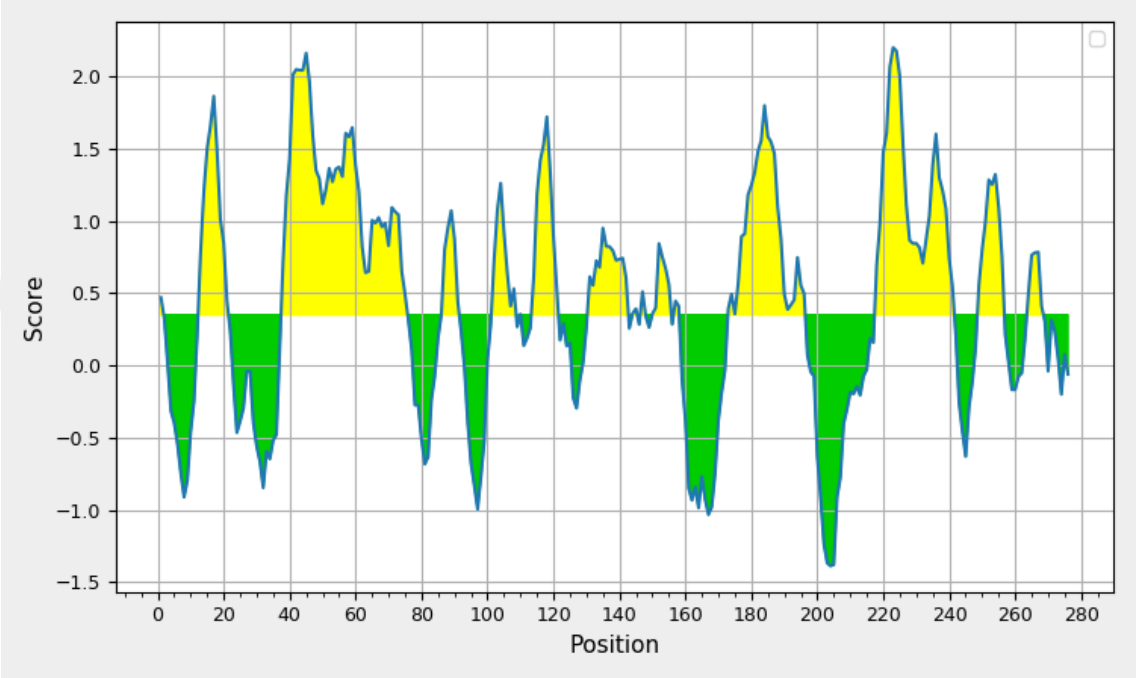

Figure 3.1 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele B*44:02 of donor 01 (Average: 0.452 Minimum: -0.012 Maximum: 2.199).

Table 3.6 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 02.

Recipient	Donor	Antigen MM
A*02:01	A*02:01	-
A*24:02	x	-
B*35:03	B*49:01	-
B*49:01	B*51:01	yes
C*04:01	C*01:02	yes
C*07:01	C*07:01	-

Table 3.7 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 02.

Recipient's Luminex Alleles	Eplets Of Recipient's Pre-Transplantation Luminex Alleles
A*01:01	9F - 44KM - 62QE - 65RA - 65RNA - 66N - 66NH - 66NM - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 151H - 152A - 152HA - 156R - 163R - 163RG - 166DG - 193PI - 275EL
A*36:01	9F - 44KM - 62QE - 65RA - 65RNA - 66N - 66NH - 66NM - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 151H - 152A - 152HA - 156R - 163T - 193PI - 275EL
A*11:01	9Y - 44RM - 44RME - 62QE - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 150AAH - 150AH - 151AHA - 151H - 152A - 152HA - 156QA - 163R - 163RW - 193PI - 275EL
A*11:02	9Y - 19K - 44RM - 44RME - 62QE - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 150AAH - 150AH - 151AHA - 151H - 152A - 152HA - 156QA - 163R - 163RW - 193PI - 275EL
A*29:02	9T - 44RM - 44RME - 62LQ - 65RA - 65RNA - 66N - 66NV - 71QS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 95I - 97M - 99Y - 105S - 109F - 114R - 116D - 138MI - 151ARV - 152V - 156L - 163T - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*29:01	9T - 44RM - 44RME - 62LQ - 65RA - 65RNA - 66N - 66NV - 71QS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 95I - 97M - 99Y - 102H - 105S - 109F - 114R - 116D - 138MI - 151ARV - 152V - 156L - 163T - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*80:01	9F - 35Q - 44RM - 44RME - 56E - 62EE - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 105S - 109F - 114R - 116D - 138MI - 144K - 144KR - 152RR - 156L - 163E - 166DG - 193PI - 207S
A*26:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*43:01	9Y - 44RM - 44RME - 62LQ - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*66:02	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT -

	149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163E - 163EW - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*25:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 76ES - 76ESI - 77S - 80I - 81ALR - 82LR - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*66:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*03:01	9F - 44RM - 44RME - 62QE - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 95I - 97I - 99Y - 105S - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 150AAH - 150AH - 151AHE - 151H - 152E - 156L - 161D - 163T - 193PI - 275EL
A*34:02	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 105S - 109F - 114R - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156L - 163T - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*30:01	9S - 17S - 44RM - 44RME - 56R - 62QE - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 95I - 97I - 99Y - 105S - 109F - 138MI - 152W - 156L - 163T - 193PI - 275EL
A*33:01	9T - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 73ID - 76VDT - 77D - 79GT - 80T - 80TL - 95I - 97M - 99Y - 105S - 109F - 114Q - 116D - 138MI - 151ARV - 152V - 156L - 163T - 170RH - 186R - 193AV - 194V - 207S - 245AS - 253Q
B*15:12	9Y - 12M - 44RM - 44RMA - 66I - 66IS - 69TNT - 71TTS - 74Y - 76ES - 76ESN - 77S - 77SRN - 80N - 95L - 97R - 99Y - 113H - 113HD - 116S - 131S - 152E - 152RE - 156WA - 163L - 163LG - 163LS/G - 166DG - 193PI

Table 3.8 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 02.

Donor	**Number Of Shared Eplets**	**Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles**
B*51:01	75	9Y (9) - 12M (1) - 62RN (6) - 66I (1) - 69TNT (1) - 74Y (1) - 77N (7) - 80I (1) - 81ALR (1) - 82LR (1) - 99Y (17) - 113H (1) - 131S (1) - 152E (8) - 152RE (1) - 156L (7) - 163L (1) - 170RH (1) - 194V (9)

C*01:02	36	9F (4) - 77S (2) - 77SRN (1) - 80N (1) - 95L (1) - 152E (8) - 152RE (1) - 156R (2) - 163T (7) - 194V (9)

Table 3.9 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 02.

Luminex Allele	#Shares		**Luminex Allele**	#Shares		**Luminex Allele**	#Shares
B*51:01	23		C*03:03	14		B*45:01	10
B*51:02	22		C*03:04	14		***A*32:01***	***10***
B*52:01	22		B*18:01	14		B*47:01	10
B*78:01	21		C*12:02	14		B*40:02	10
B*15:10	20		C*12:03	14		C*16:01	10
B*15:18	20		B*67:01	13		B*41:01	10
B*15:13	19		B*54:01	13		C*18:01	10
B*15:03	19		C*01:02	13		C*18:02	10
B*15:11	19		B*13:02	13		B*40:06	9
B*14:06	18		B*56:01	13		A*34:01	9
B*15:01	18		B*57:01	13		A*68:02	8
B*15:02	18		C*05:01	13		B*27:08	8
B*14:01	18		B*57:03	13		A*69:01	8
B*14:02	18		B*44:03	13		A*68:01	7
B*53:01	18		B*13:01	13		A*23:01	7
B*14:05	18		C*15:02	13		A*02:03	7
B*35:08	17		C*04:03	12		A*02:05	7
B*15:16	17		B*82:02	12		A*02:06	7
B*55:01	17		B*44:02	12		B*73:01	6
B*35:01	17		B*48:01	12		C*07:02	6
B*07:03	16		C*14:02	12		A*02:02	6
B*38:01	16		B*82:01	12		A*23:02	6
B*59:01	16		B*40:01	11		B*27:03	6
B*46:01	15		B*08:01	11		B*27:05	6
B*07:02	15		C*08:01	11		A*74:01	6
B*50:01	15		C*02:02	11		A*33:03	6
B*58:01	15		C*02:10	11		B*37:01	6
B*39:05	15		B*41:02	11		A*24:03	6
B*40:05	15		B*81:01	11		A*31:01	5
C*03:02	15		B*42:01	11		C*07:04	5
C*08:02	15		C*17:01	11		A*30:02	4

B*39:01	14		C*06:02	10			

Table 3.10 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele B*51:01 of donor 02.

No.	Start	End	Peptide	Length
1	1	1	G	1
2	13	20	SRPGRGEP	8
3	28	28	V	1
4	38	62	SDAASPRTEPRAPWIEQEGPEYWDR	25
5	71	75	TQTYR	5
6	87	94	QSEAGSHT	8
7	101	108	CDVGPDGR	8
8	115	121	QYAYDGK	7
9	131	142	SSWTAADTAAQI	12
10	144	145	QR	2
11	147	153	WEAAREA	7
12	173	198	ENGKETLQRADPPKTHVTHHPVSDHE	26
13	218	241	QRDGEDQTQDTELVETRPAGDRTF	24
14	249	256	VPSGEEQR	8
15	264	268	EGLPK	5

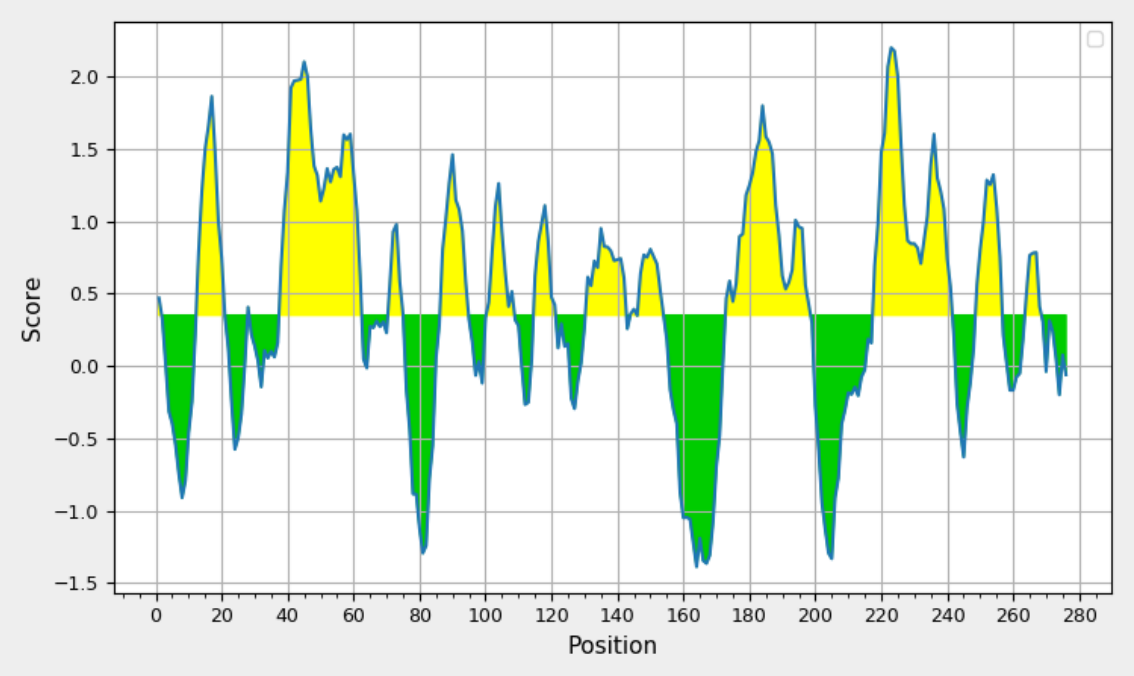

Figure 3.2 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele B*51:01 of donor 02 (Average: 0.435 Minimum: -0.008 Maximum: 2.199)

Table 3.11 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 03.

Recipient	Donor	Antigen MM
A*24:02	A*02:01	yes
A*31:01	A*11:01	yes
B*48:01	B*35:01	yes
B*51:01	B*49:01	yes
C*08:01	C*04:01	yes
C*14:02	C*07:01	yes

Table 3.12 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 03.

Recipient's Luminex Alleles	Eplets Of Recipient's Pre-Transplantation Luminex Alleles
A*02:03	9F - 44RM - 44RME - 62GE - 62GK - 65RA - 65RK - 66K - 66KA - 66KH - 71HS - 76VDT - 77D - 79GT - 80T - 80TL - 95V - 97R - 99Y - 105S - 107W - 109F - 114H - 116Y - 127K - 144K - 144TKH - 145HT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163T - 184A - 193AV - 194V - 207S - 253Q
A*02:02	9F - 43R - 44RM - 44RME - 62GE - 62GK - 65RA - 65RK - 66K - 66KA - 66KH - 71HS - 76VDT - 77D - 79GT - 80T - 80TL - 95L - 97R - 99Y - 105S - 107W - 109F - 114H - 116Y - 127K - 144K - 144TKH - 145KHA - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156WA - 163T - 184A - 193AV - 194V - 207S - 253Q
A*02:05	9Y - 43R - 44RM - 44RME - 62GE - 62GK - 65RA - 65RK - 66K - 66KA - 66KH - 71HS - 76VDT - 77D - 79GT - 80T - 80TL - 95L - 97R - 99Y - 105S - 107W - 109F - 114H - 116Y - 127K - 144K - 144TKH - 145KHA - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156WA - 163T - 184A - 193AV - 194V - 207S - 253Q
A*02:01	9F - 44RM - 44RME - 62GE - 62GK - 65RA - 65RK - 66K - 66KA - 66KH - 71HS - 76VDT - 77D - 79GT - 80T - 80TL - 95V - 97R - 99Y - 105S - 107W - 109F - 114H - 116Y - 127K - 144K - 144TKH - 145KHA - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156L - 163T - 184A - 193AV - 194V - 207S - 253Q

Table 3.13 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 03.

Donor	Number Of Shared Eplets	Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles

A*02:01	153	9F (3) - 44RM (4) - 44RME (4) - 62GE (4) - 62GK (4) - 65RA (4) - 65RK (4) - 66K (4) - 66KA (4) - 66KH (4) - 71HS (4) - 76VDT (4) - 77D (4) - 79GT (4) - 80T (4) - 80TL (4) - 95V (2) - 97R (4) - 99Y (4) - 105S (4) - 107W (4) - 109F (4) - 114H (4) - 116Y (4) - 127K (4) - 144K (4) - 144TKH (4) - 145KHA (3) - 149AH (3) - 150AAH (3) - 150AH (4) - 151AHV (3) - 151H (4) - 152V (3) - 156L (1) - 163T (4) - 184A (4) - 193AV (4) - 194V (4) - 207S (4) - 253Q (4)
A*11:01	59	9Y (1) - 44RM (4) - 44RME (4) - 65RA (4) - 76VDT (4) - 77D (4) - 79GT (4) - 80T (4) - 80TL (4) - 99Y (4) - 109F (4) - 144K (4) - 149AH (3) - 150AAH (3) - 150AH (4) - 151H (4)
B*35:01	17	9Y (1) - 97R (4) - 99Y (4) - 152V (3) - 156L (1) - 194V (4)
B*49:01	10	97R (4) - 99Y (4) - 152E (1) - 156L (1)
C*04:01	19	66K (4) - 95L (2) - 97R (4) - 152E (1) - 163T (4) - 194V (4)
C*07:01	19	95L (2) - 97R (4) - 99Y (4) - 156L (1) - 163T (4) - 253Q (4)

Table 3.14 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 03.

Shared Allele	# Shares		Shared Allele	# Shares		Shared Allele	# Shares
A*02:06	74		B*67:01	23		B*13:02	17
A*69:01	66		B*38:01	23		C*07:04	17
A*68:02	59		B*39:01	23		B*51:02	17
A*68:01	53		B*39:05	23		B*52:01	17
A*34:01	***51***		B*14:06	23		C*04:01	17
A*34:02	47		B*47:01	22		B*78:01	17
A*03:01	45		B*13:01	22		B*35:08	17
A*66:02	44		A*23:02	22		C*16:01	17
A*66:01	44		B*15:16	22		C*06:02	17
A*33:01	41		B*35:01	21		C*18:01	17
A*33:03	41		C*07:01	21		C*18:02	17
A*26:01	41		C*02:02	21		B*54:01	16
A*43:01	41		C*02:10	21		B*55:01	16
A*74:01	41		B*15:10	21		B*49:01	16
A*29:01	37		B*53:01	21		B*50:01	16
A*29:02	37		B*18:01	21		B*37:01	16
A*11:01	35		B*27:03	20		B*59:01	16
A*11:02	35		B*27:05	20		B*41:01	16
A*25:01	35		B*15:13	20		B*44:02	16
A*24:03	33		B*15:03	20		B*81:01	16

A*32:01	31		B*15:18	20		C*01:02	15
A*30:01	31		B*15:02	20		B*42:01	15
A*80:01	30		B*44:03	20		B*40:05	14
A*30:02	28		B*46:01	20		B*27:08	14
A*36:01	27		B*40:01	19		B*40:02	14
A*23:01	26		C*12:03	19		B*56:01	13
C*03:02	25		C*04:03	19		B*08:01	13
C*17:01	25		B*57:03	19		B*41:02	13
C*03:03	24		B*15:01	18		B*73:01	13
C*03:04	24		C*07:02	18		B*40:06	12
C*05:01	24		B*14:02	18		B*07:03	12
B*58:01	24		B*14:05	18		B*07:02	12
C*08:02	24		B*57:01	18		B*45:01	12
C*12:02	24		B*14:01	18		B*82:02	11
C*15:02	24		B*15:11	18		B*82:01	11
A*01:01	24		B*15:12	18			

Table 3.15 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele A*02:01 of donor 03:

No.	Start	End	Peptide	Length
1	1	1	G	1
2	13	20	SRPGRGEP	8
3	28	28	V	1
4	38	73	SDAASQRMEPRAPWIEQEGPEYWDGETRKVKAHSQT	36
5	84	94	YYNQSEAGSHT	11
6	102	102	D	1
7	104	104	G	1
8	116	121	YAYDGK	6
9	131	131	R	1
10	133	133	W	1
11	137	147	DMAAQTTKHKW	11
12	173	188	ENGKETLQRTDAPKTH	16
13	194	196	VSD	3
14	218	242	QRDGEDQTQDTELVETRPAGDGTFQ	25
15	249	256	VPSGQEQR	8
16	264	268	EGLPK	5

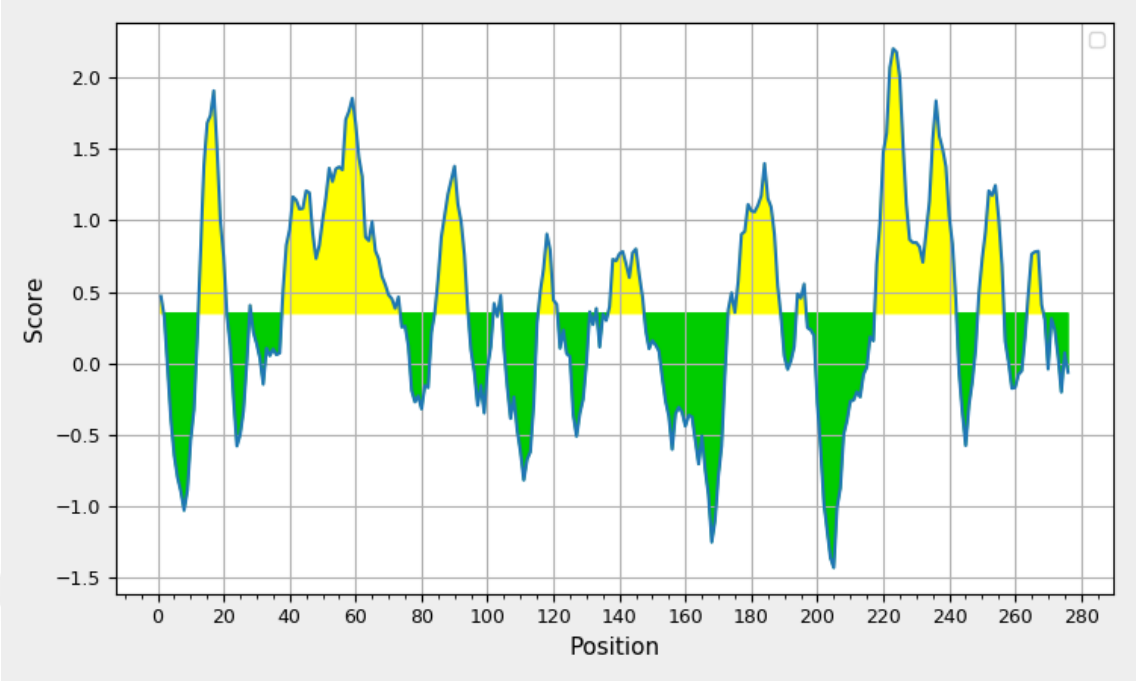

Figure 3.3 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele A*02:01 of donor 03 (Average: 0.366 Minimum: -0.027 Maximum: 2.199)

Table 3.16 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 04.

Recipient	Donor	Antigen MM
A*02:01	A*23:01	yes
A*24:02	A*24:02	-
B*18:01	B*44:03	yes
B*51:01	B*51:01	-
C*07:01	C*02:02	yes
C*14:02	C*04:01	yes

Table 3.17 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 04.

Recipient's Luminex Alleles	Eplets Of Recipient's Pre-Transplantation Luminex Alleles
A*66:02	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163E - 163EW - 184A - 193AV - 194V - 207S - 245AS - 253Q

B*82:02	9Y - 12M - 24S - 45EE - 62RN - 63NI - 65QIA - 66I - 66IY - 69AA - 70IAQ - 76ES - 76ESN - 77S - 77SRN - 80N - 95L - 97R - 99F - 103L - 113H - 113HN - 116L - 131S - 151ARV - 152V - 156DA - 162GLS - 163L - 163LE - 163LS/G - 166ES - 193PI
C*12:02	1C - 9Y - 11AV - 65QKR - 66K - 69RA - 73AS - 76VRN - 76VS - 77S - 77SRN - 80N - 95L - 97R - 99Y - 103L - 113YD - 116S - 152E - 152RE - 156WA - 163T - 184H - 193PV - 194V
C*02:02	1C - 9Y - 11AV - 16S - 21H - 65QKR - 66K - 69RT - 77N - 80K - 95L - 97R - 99Y - 103L - 113YD - 116S - 152E - 152RE - 156WA - 163E - 163EW - 184H - 193PV - 194V - 211T
C*04:03	9Y - 11AV - 16S - 21H - 65QKR - 66K - 69RA - 73AN - 77N - 80K - 90D - 95L - 97R - 99F - 103L - 113YN - 116F - 152E - 152RE - 156R - 156RA - 163T - 184H - 193PV - 194V - 219W - 275K
C*05:01	1C - 9Y - 11AV - 35Q - 65QKR - 66K - 69RT - 77N - 80K - 95L - 97R - 99Y - 103L - 113YN - 116F - 138K - 152E - 152RE - 156R - 156RA - 163T - 177KT - 184H - 193PV - 194V - 275G
C*06:02	1C - 9D - 11AV - 24S - 65QKR - 66K - 69RA - 73AN - 77N - 80K - 90D - 95L - 97W - 99Y - 103L - 113YD - 116S - 152E - 152RE - 156WA - 163T - 184H - 193PV - 194V
C*15:02	1C - 9Y - 11AV - 21H - 66N - 69RT - 77N - 80K - 94I - 95I - 97R - 99Y - 103L - 113H - 113HD - 116L - 152E - 152RE - 156L - 163T - 184H - 193PV - 194V
C*17:01	9Y - 11AV - 65QKR - 66K - 69RA - 73AN - 77N - 80K - 95I - 97R - 99Y - 103L - 113YN - 116F - 143S - 147L - 152E - 152RE - 156L - 163E - 163EW - 184R - 193PV - 194V - 253Q - 267QE - 270C - 275K
C*08:02	1C - 9Y - 11AV - 35Q - 65QKR - 66K - 69RT - 73TVS - 76VRN - 76VS - 77S - 77SRN - 80N - 95L - 97R - 99Y - 103L - 113YN - 116F - 138K - 152E - 152RE - 156R - 156RA - 163T - 177KT - 184H - 193PV - 194V - 275G

Table 3.18 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 04.

Donor	Number Of Shared Eplets	Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles
A*23:01	37	44RM (1) - 44RME (1) - 66K (7) - 77N (6) - 95L (7) - 99F (2) - 109F (1) - 138MI (1) - 151ARV (1) - 152V (1) - 156L (2) - 163T (6) - 193PI (1)
B*44:03	54	9Y (9) - 12M (1) - 66I (1) - 77N (6) - 80T (1) - 94I (1) - 95I (3) - 97R (9) - 99Y (8) - 113YD (3) - 116D (1) - 131S (1) - 151ARV (1) - 152V (1) - 156L (2) - 162GLS (1) - 163L (1) - 163LE (1) - 163LS/G (1) - 166ES (1) - 193PI (1)

C*02:02	149	1C (6) - 9Y (9) - 11AV (8) - 16S (2) - 21H (3) - 65QKR (7) - 66K (7) - 69RT (4) - 77N (6) - 80K (6) - 95L (7) - 97R (9) - 99Y (8) - 103L (9) - 113YD (3) - 116S (3) - 152E (9) - 152RE (8) - 156WA (4) - 163E (3) - 163EW (3) - 184H (7) - 193PV (8) - 194V (9) - 211T (1)
C*04:01	126	65QKR (7) - 66K (7) - 69RA (4) - 73AN (3) - 77N (6) - 80K (6) - 90D (2) - 95L (7) - 97R (9) - 99F (2) - 103L (9) - 113YN (4) - 116F (4) - 152E (9) - 152RE (8) - 156R (3) - 156RA (3) - 163T (6) - 184H (7) - 193PV (8) - 194V (9) - 219W (1) - 275K (2)

Table 3.19 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 04.

Shared Allele	# Shares		Shared Allele	# Shares		Shared Allele	# Shares
C*02:10	44		B*49:01	25		A*80:01	20
C*18:01	44		A*02:05	25		B*40:01	20
C*18:02	44		B*57:01	25		A*02:03	20
C*04:01	42		B*14:06	25		B*56:01	19
C*03:02	37		A*29:01	24		A*30:02	19
C*03:03	34		C*07:02	24		B*27:03	19
C*03:04	34		B*15:03	24		B*27:05	19
B*44:03	33		B*57:03	24		A*74:01	19
C*12:03	33		A*29:02	24		B*54:01	19
C*08:01	32		B*15:18	24		B*78:01	19
B*13:01	31		B*67:01	23		B*55:01	19
B*53:01	31		A*24:03	23		B*07:03	18
B*15:13	31		A*02:02	23		***A*03:01***	***18***
B*44:02	31		A*02:06	23		A*68:01	18
B*46:01	30		B*51:02	23		A*32:01	18
B*58:01	30		B*52:01	23		B*48:01	18
C*01:02	29		B*39:01	23		B*27:08	18
B*15:16	28		B*39:05	23		B*81:01	18
B*38:01	27		B*15:10	23		B*07:02	18
A*23:01	27		B*59:01	23		A*36:01	17
B*15:02	27		B*45:01	22		B*37:01	17
B*35:01	27		B*14:05	22		B*73:01	17
B*35:08	27		B*14:02	22		B*40:02	16
C*16:01	26		A*66:01	21		B*40:05	16
B*13:02	26		B*14:01	21		B*42:01	16

A*34:01	26		A*34:02	21		A*11:01	15
A*23:02	26		A*68:02	21		A*11:02	15
B*82:01	25		B*50:01	21		A*30:01	15
B*15:01	25		C*07:04	21		B*08:01	15
A*43:01	25		A*31:01	20		A*01:01	15
B*15:11	25		A*33:01	20		B*41:01	15
B*15:12	25		A*33:03	20		B*41:02	15
A*26:01	25		A*25:01	20		B*40:06	13
B*47:01	25		A*69:01	20			

Table 3.20 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele C*02:02 of donor 04.

No.	Start	End	Peptide	Length
1	13	20	SRPSRGEP	8
2	28	28	V	1
3	38	74	SDAASPRGEPRAPWVEQEGPEYWDRETQKYKRQAQTD	37
4	85	93	YNQSEAGSH	9
5	102	106	DLGPD	5
6	108	108	R	1
7	114	121	DQSAYDGK	8
8	131	142	RSWTAADTAAQI	12
9	144	145	QR	2
10	147	155	WEAAREAEQ	9
11	173	198	ENGKETLQRAEHPKTHVTHHPVSDHE	26
12	218	242	QRDGEDQTQDTELVETRPAGDGTFQ	25
13	249	256	VPSGEEQR	8
14	264	269	EGLPEP	6
15	271	271	T	1

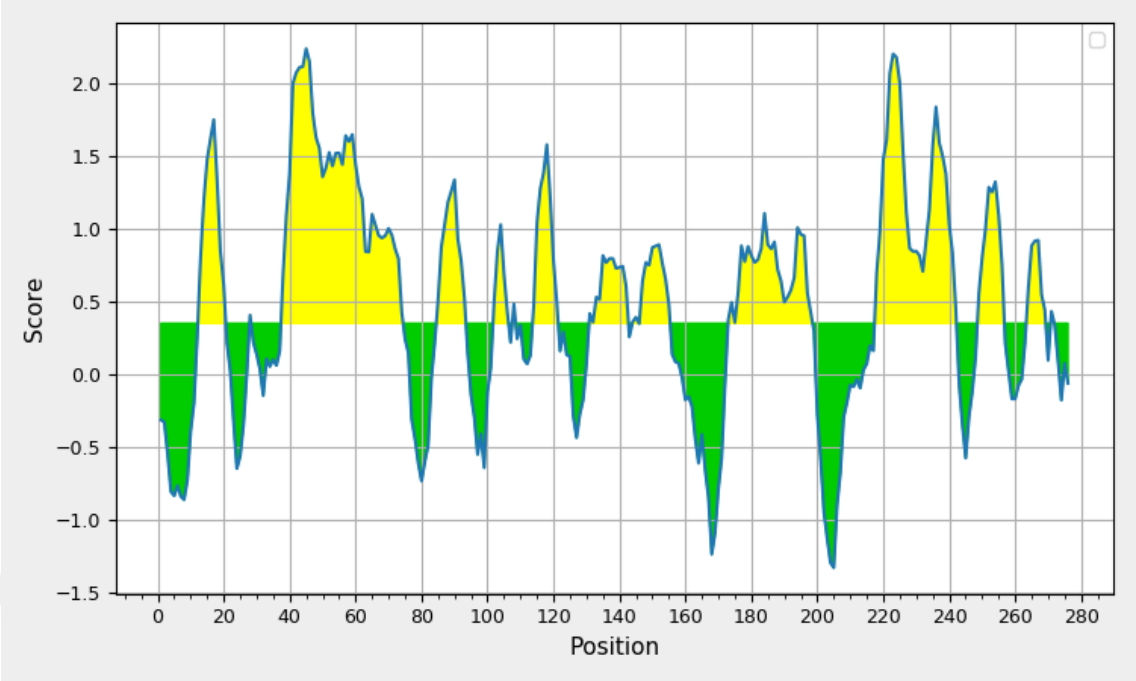

Figure 3.4 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele C*02:02 of donor 04 (Average: 0.488 Minimum: -0.004 Maximum: 2.235)

Table 3.21 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 05.

Recipient	Donor	Antigen MM
A*01:01	A*02:01	yes
A*32:01	A*25:01	yes
B*27:03	B*51:01	yes
B*52:01	x	-
C*02:02	C*14:02	yes
C*12:02	C*15:02	yes

Table 3.22 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 05.

Recipient's Luminex Alleles	Eplets Of Recipient's Pre-Transplantation Luminex Alleles
A*66:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q

A*25:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 76ES - 76ESI - 77S - 80I - 81ALR - 82LR - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*26:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q

Table 3.23 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 05.

Donor	Number Of Shared Eplets	Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles
A*02:01	49	44RM (3) - 44RME (3) - 65RA (3) - 71HS (2) - 76VDT (1) - 77D (1) - 79GT (2) - 80T (2) - 80TL (2) - 97R (3) - 99Y (3) - 109F (3) - 150AH (3) - 151H (3) - 184A (3) - 193AV (3) - 194V (3) - 207S (3) - 253Q (3)
A*25:01	106	9Y (3) - 44RM (3) - 44RME (3) - 62RN (3) - 62RR (3) - 65RA (3) - 65RNA (3) - 66N (3) - 66NH (2) - 66NV (3) - 71HS (2) - 76ES (1) - 76ESI (1) - 77S (1) - 80I (1) - 81ALR (1) - 82LR (1) - 90D (3) - 95I (3) - 97R (3) - 99Y (3) - 109F (3) - 114Q (3) - 116D (3) - 138MI (3) - 145RT (3) - 149TAH (3) - 150AH (3) - 151AHE (3) - 151H (3) - 152E (3) - 156WA (3) - 163R (3) - 163RW (3) - 184A (3) - 193AV (3) - 194V (3) - 207S (3) - 245AS (3) - 253Q (3)
B*51:01	19	9Y (3) - 62RN (3) - 77N (1) - 80I (1) - 81ALR (1) - 82LR (1) - 99Y (3) - 152E (3) - 194V (3)
C*14:02	7	77S (1) - 152E (3) - 194V (3)
C*15:02	22	9Y (3) - 66N (3) - 77N (1) - 95I (3) - 97R (3) - 99Y (3) - 152E (3) - 194V (3)

Table 3.24 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 05.

Shared Allele	# Shares		Shared Allele	# Shares		Shared Allele	# Shares
A*43:01	65		C*03:04	23		B*55:01	16
A*66:02	62		B*15:11	23		B*07:02	16
A*34:01	***59***		C*03:03	23		B*39:01	15
A*34:02	58		B*13:01	22		B*67:01	15
A*68:02	51		C*02:10	22		C*04:01	15

A*68:01	49		A*24:03	22		B*39:05	15
A*69:01	48		B*35:01	22		C*18:01	15
A*02:03	47		B*35:08	22		C*18:02	15
A*33:01	45		A*24:02	22		C*07:01	14
A*33:03	45		B*15:12	21		B*50:01	14
A*02:05	44		C*05:01	21		C*16:01	14
A*02:06	43		C*08:02	21		B*47:01	12
A*31:01	42		B*15:01	21		B*54:01	12
A*74:01	42		C*03:02	21		B*42:01	12
A*02:02	41		B*78:01	21		B*56:01	12
A*29:01	40		B*44:03	20		C*07:04	12
A*29:02	40		B*46:01	20		B*18:01	12
A*02:01	40		B*38:01	20		B*81:01	12
A*11:02	36		B*44:02	20		C*01:02	11
A*11:01	36		B*15:10	19		B*40:05	11
A*03:01	35		B*49:01	19		B*82:01	11
A*80:01	32		A*23:02	19		B*82:02	11
B*15:16	31		C*12:03	19		C*14:02	11
B*58:01	30		B*15:18	19		B*41:01	10
B*15:13	29		B*14:06	19		B*48:01	10
A*30:02	28		A*23:01	18		B*27:05	10
B*53:01	27		C*04:03	18		B*37:01	10
B*51:02	26		B*59:01	17		B*40:01	10
A*36:01	26		B*13:02	17		B*45:01	10
B*51:01	26		B*15:03	17		B*08:01	9
B*57:01	25		C*06:02	17		B*73:01	9
B*57:03	25		C*08:01	17		C*07:02	8
A*30:01	25		B*14:01	16		B*27:08	8
C*15:02	25		B*14:02	16		B*40:02	7
C*17:01	25		B*14:05	16		B*41:02	7
B*15:02	24		B*07:03	16		B*40:06	7

Table 3.25 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele A*25:01 of donor 05.

No.	Start	End	Peptide	Length
1	1	1	G	1
2	12	20	VSRPGRGEP	9

3	28	28	V	1
4	38	75	SDAASQRMEPRAPWIEQEGPEYWDRNTRNVKAHSQTDR	38
5	86	94	NQSEDGSHT	9
6	102	108	DVGPDGR	7
7	114	121	QQDAYDGK	8
8	131	131	R	1
9	133	133	W	1
10	145	155	RKWETAHEAEQ	11
11	173	188	ENGKETLQRTDAPKTH	16
12	194	196	VSD	3
13	218	242	QRDGEDQTQDTELVETRPAGDGTFQ	25
14	249	256	VPSGQEQR	8
15	264	268	EGLPK	5

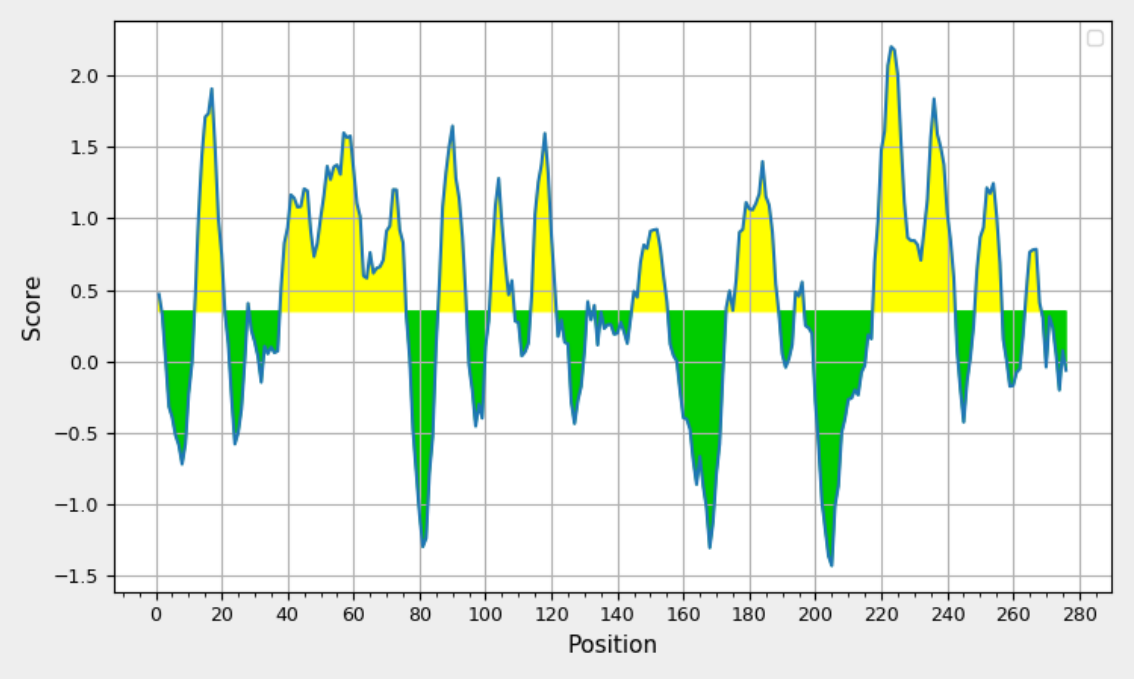

Figure 3.5 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele A*25:01 of donor 05 (Average: 0.431 Minimum: -0.013 Maximum: 2.199)

Table 3.26 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 06.

Recipient	Donor	Antigen MM
A*24:02	A*02:01	yes
x	A*26:01	yes
B*40:06	B*07:02	yes

B*55:01	B*35:01	yes
C*01:02	C*04:01	yes
C*08:01	C*07:02	yes

Table 3.27 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 06.

Recipient's Luminex Alleles	**Eplets Of Recipient's Pre-Transplantation Luminex Alleles**
A*66:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*25:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 76ES - 76ESI - 77S - 80I - 81ALR - 82LR - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*26:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q

Table 3.28 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 06.

Donor	**Number Of Shared Eplets**	**Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles**
A*02:01	49	44RM (3) - 44RME (3) - 65RA (3) - 71HS (2) - 76VDT (1) - 77D (1) - 79GT (2) - 80T (2) - 80TL (2) - 97R (3) - 99Y (3) - 109F (3) - 150AH (3) - 151H (3) - 184A (3) - 193AV (3) - 194V (3) - 207S (3) - 253Q (3)
A*26:01	109	9Y (3) - 44RM (3) - 44RME (3) - 62RN (3) - 62RR (3) - 65RA (3) - 65RNA (3) - 66N (3) - 66NH (2) - 66NV (3) - 71HS (2) - 76ANT (1) - 77N (1) - 77NGT (1) - 79GT (2) - 80T (2) - 80TL (2) - 90D (3) - 95I (3) - 97R (3) - 99Y (3) - 109F (3) - 114Q (3) - 116D (3) - 138MI (3) - 145RT (3) - 149TAH (3) - 150AH (3) - 151AHE (3) - 151H (3) - 152E (3) - 156WA (3) - 163R (3) - 163RW (3) - 184A (3) - 193AV (3) - 194V (3) - 207S (3) - 245AS (3) - 253Q (3)
B*07:02	14	9Y (3) - 62RN (3) - 76ES (1) - 77S (1) - 99Y (3) - 152E (3)

B*35:01	20	9Y (3) - 62RN (3) - 76ES (1) - 77S (1) - 95I (3) - 97R (3) - 99Y (3) - 194V (3)
C*04:01	13	77N (1) - 90D (3) - 97R (3) - 152E (3) - 194V (3)
C*07:02	10	77S (1) - 90D (3) - 97R (3) - 253Q (3)

Table 3.29 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 06.

Shared Allele	# Shares		Shared Allele	# Shares		Shared Allele	# Shares
A*43:01	***72***		C*03:04	24		B*18:01	17
A*34:01	66		C*15:02	24		C*04:01	17
A*66:02	66		B*15:01	24		B*50:01	17
A*34:02	62		B*14:06	23		C*18:01	17
A*68:02	56		B*15:10	23		C*18:02	17
A*69:01	53		C*12:02	23		B*82:02	16
A*68:01	52		B*53:01	23		B*52:01	16
A*02:03	51		B*15:18	23		A*24:03	16
A*02:05	49		B*46:01	22		B*82:01	16
A*33:03	48		B*78:01	22		B*54:01	15
A*02:06	48		C*08:02	22		B*42:01	15
A*33:01	48		C*02:02	22		B*81:01	15
A*02:02	46		C*02:10	22		B*56:01	15
A*02:01	45		C*03:02	22		B*47:01	14
A*29:02	44		B*13:01	21		B*49:01	14
A*31:01	44		C*05:01	21		B*40:01	14
A*29:01	44		B*39:05	20		B*41:01	14
A*74:01	44		B*67:01	20		C*16:01	14
A*32:01	41		B*15:03	20		C*07:02	14
A*11:02	40		B*39:01	20		B*45:01	14
A*11:01	40		C*04:03	20		B*13:02	14
A*80:01	38		C*07:01	19		B*73:01	13
A*03:01	36		B*51:02	19		A*23:02	13
A*01:01	33		B*44:03	19		B*40:05	12
A*36:01	32		B*44:02	19		A*23:01	12
A*30:02	31		B*51:01	19		B*59:01	12
B*15:02	28		B*07:03	18		B*37:01	12
A*30:01	27		B*07:02	18		B*08:01	12
B*15:11	27		B*14:01	18		B*48:01	12

B*35:01	26		C*07:04	18		B*27:05	10
B*35:08	26		B*14:02	18		B*27:03	10
C*17:01	26		B*14:05	18		B*27:08	10
B*15:16	25		C*12:03	18		C*14:02	10
B*15:13	25		B*57:01	18		B*40:02	9
B*15:12	24		B*57:03	18		B*41:02	9
B*58:01	24		B*38:01	17			
C*03:03	24		C*06:02	17			

Table 3.30 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele A*26:01 of donor 06.

No.	Start	End	Peptide	Length
1	1	1	G	1
2	12	20	VSRPGRGEP	9
3	28	28	V	1
4	38	77	SDAASQRMEPRAPWIEQEGPEYWDRNTRNVKAHSQ TDRAN	40
5	84	94	YYNQSEDGSHT	11
6	102	108	DVGPDGR	7
7	114	121	QQDAYDGK	8
8	131	131	R	1
9	133	133	W	1
10	145	155	RKWETAHEAEQ	11
11	173	188	ENGKETLQRTDAPKTH	16
12	194	196	VSD	3
13	218	242	QRDGEDQTQDTELVETRPAGDGTFQ	25
14	249	256	VPSGQEQR	8
15	264	268	EGLPK	5

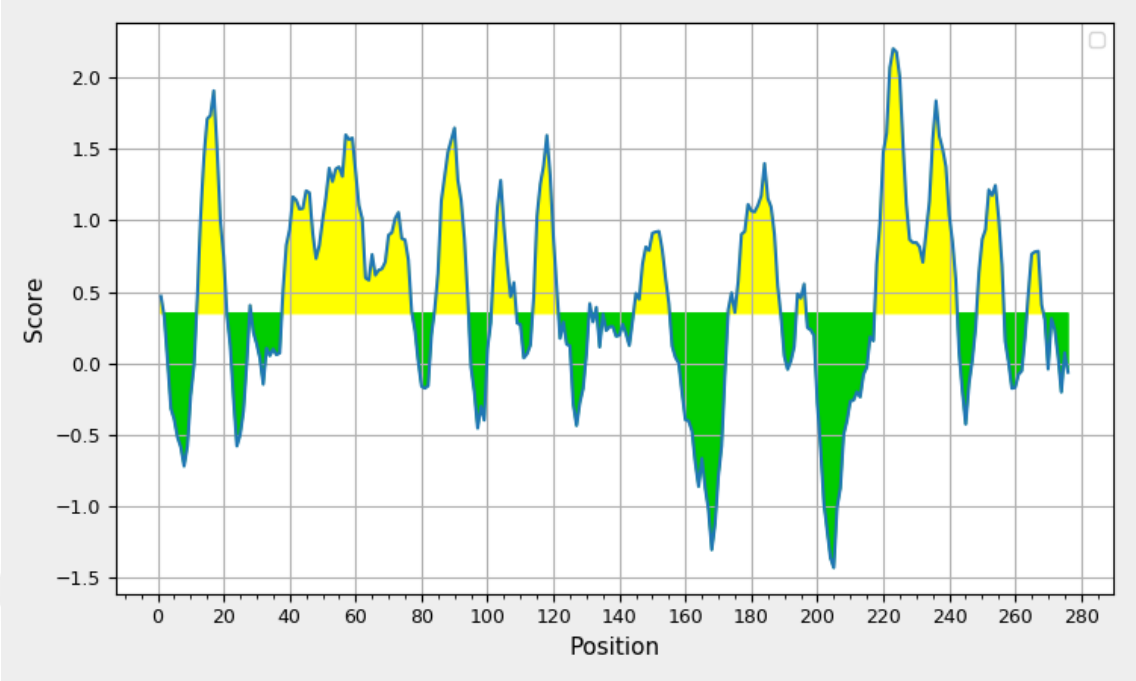

Figure 3.6 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele A*26:01 of donor 06 (Average: 0.462 Minimum: -0.013 Maximum: 2.199)

Table 3.31 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 07.

Recipient	Donor	Antigen MM
A*24:02	A*03:01	yes
A*33:01	A*30:01	yes
B*07:02	B*13:02	yes
B*27:02	B*50:01	yes
C*02:02	C*01:02	yes
C*07:02	C*06:02	yes

Table 3.32 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 07.

Recipient's Luminex Alleles	Eplets Of Recipient's Pre-Transplantation Luminex Alleles
A*11:01	9Y - 44RM - 44RME - 62QE - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 150AAH - 150AH - 151AHA - 151H - 152A - 152HA - 156QA - 163R - 163RW - 193PI - 275EL

A*11:02	9Y - 19K - 44RM - 44RME - 62QE - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 150AAH - 150AH - 151AHA - 151H - 152A - 152HA - 156QA - 163R - 163RW - 193PI - 275EL
A*36:01	9F - 44KM - 62QE - 65RA - 65RNA - 66N - 66NH - 66NM - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 151H - 152A - 152HA - 156R - 163T - 193PI - 275EL
A*66:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97R - 99Y - 109F - 114Q - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163R - 163RW - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*01:01	9F - 44KM - 62QE - 65RA - 65RNA - 66N - 66NH - 66NM - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 151H - 152A - 152HA - 156R - 163R - 163RG - 166DG - 193PI - 275EL
A*34:02	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 105S - 109F - 114R - 116D - 138MI - 145RT - 149TAH - 150AH - 151AHE - 151H - 152E - 156L - 163T - 184A - 193AV - 194V - 207S - 245AS - 253Q
A*80:01	9F - 35Q - 44RM - 44RME - 56E - 62EE - 65RA - 65RNA - 66N - 66NH - 66NV - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 105S - 109F - 114R - 116D - 138MI - 144K - 144KR - 152RR - 156L - 163E - 166DG - 193PI - 207S

Table 3.33 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 07.

Donor	Number Of Shared Eplets	Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles
A*03:01	168	9F (3) - 44RM (5) - 44RME (5) - 62QE (4) - 65RA (7) - 65RNA (7) - 66N (7) - 66NV (5) - 71QS (4) - 76VDT (4) - 77D (4) - 79GT (7) - 80T (7) - 80TL (7) - 95I (7) - 97I (6) - 99Y (7) - 105S (2) - 109F (7) - 114R (6) - 116D (7) - 138MI (7) - 144K (5) - 144KR (5) - 149AH (4) - 150AAH (2) - 150AH (4) - 151AHE (2) - 151H (6) - 152E (2) - 156L (2) - 161D 163T (2) - 193PI (5) - 275EL (4)
A*30:01	122	44RM (5) - 44RME (5) - 62QE (4) - 65RA (7) - 65RNA (7) - 66N (7) - 66NV (5) - 71QS (4) - 76VDT (4) - 77D (4) - 79GT (7) - 80T (7) - 80TL

		(7) - 95I (7) - 97I (6) - 99Y (7) - 105S (2) - 109F (7) - 138MI (7) - 156L (2) - 163T (2) - 193PI (5) - 275EL (4)
B*13:02	34	9Y (4) - 44RM (5) - 77N (3) - 80T (7) - 99Y (7) - 156L (2) - 163E (1) - 193PI (5)
B*50:01	17	97R (1) - 99Y (7) - 152E (2) - 156L (2) - 193PI (5)
C*01:02	11	9F (3) - 152E (2) - 156R (2) - 163T (2) - 194V (2)
C*06:02	24	77N (3) - 90D (7) - 99Y (7) - 152E (2) - 156WA (1) - 163T (2) - 194V (2)

Table 3.34 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 07.

Shared Allele	# Shares		Shared Allele	# Shares		Shared Allele	# Shares
A*03:01	***73***		B*27:05	22		B*51:02	18
A*30:01	57		A*23:02	22		C*02:10	17
A*30:02	53		B*55:01	22		C*07:01	17
A*69:01	52		***B*14:01***	***22***		C*08:01	17
A*68:01	52		***B*14:02***	***22***		C*03:02	17
A*66:02	51		B*14:05	22		***B*53:01***	***17***
A*31:01	50		B*27:03	22		C*12:03	17
A*29:01	***49***		C*17:01	22		B*40:05	17
A*68:02	49		B*38:01	21		B*07:03	16
A*34:01	49		C*05:01	20		C*04:03	16
A*74:01	49		***B*49:01***	20		***B*78:01***	***16***
A*29:02	***49***		B*59:01	20		B*40:01	15
A*33:03	48		***B*46:01***	***19***		***B*73:01***	***15***
A*26:01	***47***		B*47:01	19		B*27:08	15
A*43:01	***47***		***B*15:03***	***19***		C*04:01	15
A*02:01	46		B*15:18	19		B*81:01	15
A*02:03	46		B*15:10	19		***B*35:01***	***15***
A*02:06	44		B*15:11	19		B*48:01	15
A*02:02	43		***B*15:12***	***19***		C*18:01	15
A*02:05	41		B*39:01	19		C*18:02	15
A*32:01	38		B*67:01	19		B*40:02	14
A*25:01	38		***C*03:03***	***19***		***B*56:01***	***14***
B*15:16	***30***		***C*03:04***	***19***		B*40:06	14
A*24:03	27		B*39:05	19		B*41:01	14
B*57:01	***27***		C*06:02	19		B*42:01	14
B*57:03	27		B*44:02	19		C*01:02	14

C*15:02	27		***B*15:01***	***19***		B*08:01	13
B*13:01	26		***B*52:01***	***18***		B*41:02	13
B*15:13	***26***		***B*54:01***	***18***		C*16:01	12
A*23:01	25		***B*18:01***	***18***		***B*35:08***	***12***
B*15:02	24		B*37:01	18		C*14:02	11
B*14:06	23		***B*50:01***	***18***		C*07:04	11
B*13:02	23		C*08:02	18		B*45:01	10
B*58:01	23		C*12:02	18		B*82:02	6
B*44:03	23		***B*51:01***	***18***		B*82:01	6

Table 3.35 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele A*03:01 of donor 07.

No.	Start	End	Peptide	Length
1	1	1	G	1
2	13	20	SRPGRGEP	8
3	28	28	V	1
4	38	76	SDAASQRMEPRAPWIEQEGPEYWDQETRNVKAQSQTDRV	39
5	84	92	YYNQSEAGS	9
6	102	105	DVGS	4
7	115	121	QDAYDGK	7
8	131	131	R	1
9	133	133	W	1
10	147	153	WEAAHEA	7
11	173	190	ENGKETLQRTDPPKTHMT	18
12	193	197	PISDH	5
13	218	242	QRDGEDQTQDTELVETRPAGDGTFQ	25
14	249	256	VPSGEEQR	8
15	264	268	EGLPK	5

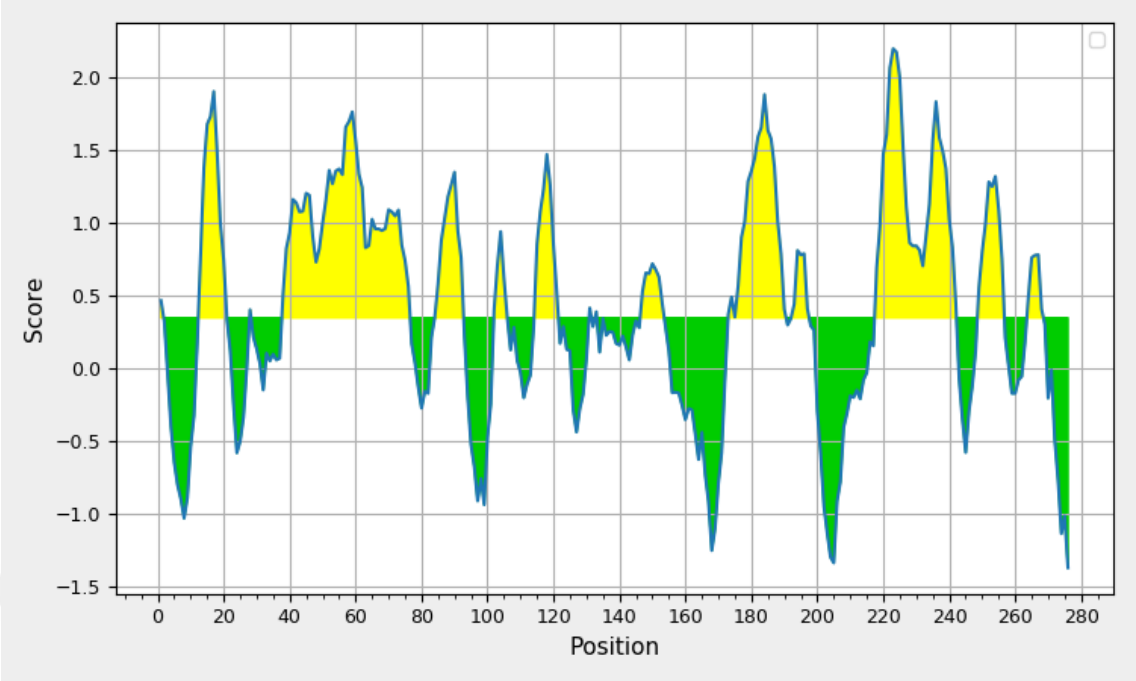

Figure 3.7 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele A*03:01 of donor 07 (Average: 0.420 Minimum: -0.008 Maximum: 2.199)

Table 3.36 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 08.

Recipient	Donor	Antigen MM
A*03:02	A*29:01	-
A*29:01	x	-
B*07:05	B*07:05	-
B*18:01	B*35:01	yes
C*12:03	C*12:03	-
C*15:05	C*15:05	-

Table 3.37 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 08.

Recipient's Luminex Alleles	Eplets Of Recipient's Pre-Transplantation Luminex Alleles
A*01:01	9F - 44KM - 62QE - 65RA - 65RNA - 66N - 66NH - 66NM - 71HS - 76ANT - 77N - 77NGT - 79GT - 80T - 80TL - 90D - 95I - 97I - 99Y - 109F - 114R - 116D - 138MI - 144K - 144KR - 149AH - 151H - 152A - 152HA - 156R - 163R - 163RG - 166DG - 193PI - 275EL

Table 3.38 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 08.

Donor	Number Of Shared Eplets	Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles
B*35:01	2	95I (1) - 97R 99Y (1)

Table 3.39 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 08.

Shared Allele	# Shares		Shared Allele	# Shares		Shared Allele	# Shares
A*03:01	3		C*03:03	3		B*48:01	1
A*11:01	3		C*03:04	3		B*49:01	1
A*11:02	3		C*15:02	3		B*50:01	1
A*25:01	3		C*17:01	3		B*51:01	1
A*26:01	3		B*37:01	2		B*51:02	1
A*29:02	3		A*02:06	1		B*52:01	1
A*30:01	3		B*15:03	1		B*08:01	1
A*30:02	3		B*15:10	1		B*54:01	1
A*31:01	3		B*15:11	1		B*55:01	1
A*32:01	3		B*15:12	1		B*56:01	1
A*33:01	3		A*02:01	1		A*02:05	1
A*33:03	3		B*15:16	1		B*13:02	1
A*34:01	3		B*15:18	1		B*14:01	1
A*34:02	3		B*27:03	1		B*59:01	1
A*36:01	3		B*27:05	1		B*67:01	1
A*43:01	3		B*27:08	1		B*73:01	1
A*66:01	3		A*69:01	1		B*78:01	1
A*66:02	3		A*02:02	1		B*81:01	1
A*68:01	3		A*02:03	1		C*02:02	1
A*68:02	3		B*38:01	1		C*02:10	1
A*74:01	3		B*39:01	1		C*03:02	1
A*80:01	3		B*39:05	1		B*14:02	1
B*13:01	3		B*40:01	1		B*14:05	1
B*15:02	3		B*40:02	1		C*05:01	1
B*15:13	3		B*40:05	1		C*06:02	1
B*35:01	3		B*40:06	1		C*07:01	1
B*35:08	3		B*41:01	1		C*07:04	1

B*44:02	3		B*41:02	1		C*08:01	1
B*44:03	3		B*42:01	1		C*08:02	1
B*53:01	3		B*07:02	1		C*12:02	1
B*57:01	3		B*07:03	1		B*14:06	1
B*57:03	3		B*45:01	1		C*16:01	1
B*58:01	3		B*46:01	1		B*15:01	1

Table 3.40 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele A*03:01 of donor 08.

No.	Start	End	Peptide	Length
1	1	1	G	1
2	13	20	SRPGRGEP	8
3	28	28	V	1
4	38	76	SDAASQRMEPRAPWIEQEGPEYWDQETRNVKAQSQ TDRV	39
5	84	92	YYNQSEAGS	9
6	102	105	DVGS	4
7	115	121	QDAYDGK	7
8	131	131	R	1
9	133	133	W	1
10	147	153	WEAAHEA	7
11	173	190	ENGKETLQRTDPPKTHMT	18
12	193	197	PISDH	5
13	218	242	QRDGEDQTQDTELVETRPAGDGTFQ	25
14	249	256	VPSGEEQR	8
15	264	268	EGLPK	5

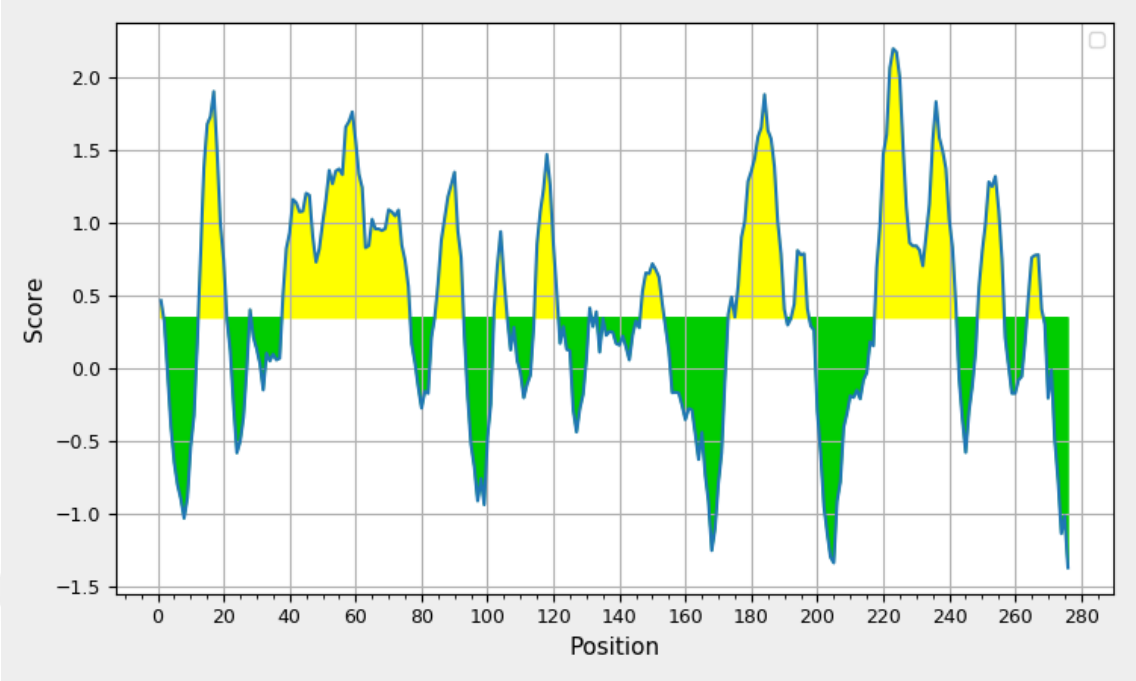

Figure 3.8 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele A*03:01 of donor 08 (Average: 0.420 Minimum: -0.008 Maximum: 2.199)

Table 3.41 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 09.

Recipient	Donor	Antigen MM
A*02:05	A*26:01	yes
A*24:02	A*68:01	yes
B*27:03	B*44:02	-
B*44:02	B*51:01	yes
C*01:02	C*02:02	yes
C*05:01	C*16:02	yes

Table 3.42 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 09.

Recipient's Luminex Alleles	Eplets Of Recipient's Pre-Transplantation Luminex Alleles
B*78:01	9Y - 12M - 44RT - 62RN - 63NI - 66I - 66IF - 69TNT - 71TTS - 76ES - 76ESN - 77S - 77SRN - 80N - 95W - 97T - 99Y - 113H - 113HN - 116Y - 131S - 152E - 152RE - 156L - 163L - 163LE - 163LW - 170RH - 193PV - 194V

B*35:01	9Y - 12M - 44RT - 62RN - 63NI - 66I - 66IF - 69TNT - 71TTS - 74Y - 76ES - 76ESN - 77S - 77SRN - 80N - 94I - 95I - 97R - 99Y - 103L - 113H - 113HD - 116S - 131S - 151ARV - 152V - 156L - 163L - 163LE - 163LW - 193PV - 194V
B*35:08	9Y - 12M - 44RT - 62RN - 63NI - 66I - 66IF - 69TNT - 71TTS - 74Y - 76ES - 76ESN - 77S - 77SRN - 80N - 94I - 95I - 97R - 99Y - 103L - 113H - 113HD - 116S - 131S - 151ARV - 152V - 156R - 156RA - 163L - 163LE - 163LW - 193PV - 194V
B*51:01	9Y - 12M - 44RT - 62RN - 63NI - 66I - 66IF - 69TNT - 71TN - 74Y - 76EN - 77N - 80I - 81ALR - 82LR - 95W - 97T - 99Y - 113H - 113HN - 116Y - 131S - 152E - 152RE - 156L - 163L - 163LE - 163LW - 170RH - 193PV - 194V
B*53:01	9Y - 12M - 44RT - 62RN - 63NI - 66I - 66IF - 69TNT - 71TN - 74Y - 76EN - 77N - 80I - 81ALR - 82LR - 94I - 95I - 97R - 99Y - 103L - 113H - 113HD - 116S - 131S - 151ARV - 152V - 156L - 163L - 163LE - 163LW - 193PV - 194V
B*15:02	9Y - 12M - 44RM - 44RMA - 62RN - 63NI - 66I - 66IS - 69TNT - 71TTS - 74Y - 76ES - 76ESN - 77S - 77SRN - 80N - 94I - 95I - 97R - 99Y - 113YD - 116S - 131S - 152E - 152RE - 156L - 163L - 163LE - 163LW - 193PI
B*15:18	9Y - 12M - 24S - 45EE - 62RN - 63NI - 66I - 66IC - 69TNT - 71TTS - 74Y - 76ES - 76ESN - 77S - 77SRN - 80N - 95L - 97R - 99Y - 113H - 113HD - 116S - 131S - 152E - 152RE - 156L - 163L - 163LE - 163LW - 193PI

Table 3.43 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 09.

Donor	Number Of Shared Eplets	Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles
A*26:01	42	9Y (7) - 44RM (1) - 62RN (7) - 77N (2) - 95I (4) - 97R (5) - 99Y (7) - 152E (4) - 194V (5)
A*68:01	34	9Y (7) - 44RM (1) - 62RN (7) - 95I (4) - 97M 99Y (7) - 152V (3) - 163T 194V (5)
B*51:01	145	9Y (7) - 12M (7) - 44RT (5) - 62RN (7) - 63NI (7) - 66I (7) - 66IF (5) - 69TNT (7) - 71TN (2) - 74Y (6) - 76EN (2) - 77N (2) - 80I (2) - 81ALR (2) - 82LR (2) - 95W (2) - 97T (2) - 99Y (7) - 113H (6) - 113HN (2) - 116Y (2) - 131S (7) - 152E (4) - 152RE (4) - 156L (6) - 163L (7) - 163LE (7) - 163LW (7) - 170RH (2) - 193PV (5) - 194V (5)
C*02:02	49	9Y (7) - 77N (2) - 95L (1) - 97R (5) - 99Y (7) - 103L (3) - 113YD (1) - 116S (5) - 152E (4) - 152RE (4) - 193PV (5) - 194V (5)
C*16:01	44	9Y (7) - 77S (5) - 77SRN (5) - 80N (5) - 95L (1) - 97W 99Y (7) - 103L (3) - 113YD (1) - 116S (5) - 194V (5)

Table 3.44 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 09.

Shared Allele	# Shares		Shared Allele	# Shares		Shared Allele	# Shares
B*51:02	51		B*39:05	30		C*18:02	21
B*52:01	47		B*14:02	30		A*32:01	20
B*15:13	47		B*14:05	30		A*33:01	20
B*58:01	43		B*39:01	29		A*29:01	19
B*15:11	40		B*07:03	29		B*41:01	19
B*15:16	40		B*54:01	29		A*29:02	19
B*15:10	38		B*07:02	28		A*33:03	19
C*03:02	38		B*67:01	28		C*07:01	19
B*59:01	37		C*06:02	28		B*41:02	18
C*03:03	37		C*08:01	28		B*47:01	18
C*03:04	37		A*34:01	28		B*40:02	18
B*15:01	36		A*43:01	28		A*02:02	18
C*02:02	36		A*66:01	28		B*40:06	18
C*02:10	36		A*66:02	28		A*02:03	18
C*12:02	36		A*68:02	28		A*02:01	17
B*13:01	35		B*18:01	27		A*31:01	16
B*38:01	35		B*82:01	27		B*73:01	16
B*15:03	35		B*82:02	27		A*74:01	16
B*15:12	34		C*04:03	27		A*11:01	15
C*12:03	34		A*34:02	27		A*11:02	15
C*15:02	34		C*16:01	27		A*23:01	14
B*57:03	33		B*50:01	27		A*30:02	14
B*44:03	33		B*81:01	26		B*27:08	14
B*46:01	33		A*69:01	26		C*07:02	14
B*13:02	33		B*40:05	25		C*07:04	14
B*55:01	***33***		B*42:01	25		A*24:03	13
B*57:01	33		A*68:01	24		A*03:01	13
C*17:01	33		B*48:01	24		A*23:02	13
B*56:01	32		C*14:02	23		A*80:01	13
C*08:02	32		A*02:06	23		B*27:05	12
A*25:01	***32***		B*08:01	22		B*37:01	11
B*14:06	32		C*04:01	21		A*01:01	10
B*49:01	32		B*40:01	21		A*36:01	10
A*26:01	31		B*45:01	21		A*30:01	10

B*14:01	30		C*18:01	21			

Table 3.45 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele A*68:01 of donor 09.

No.	Start	End	Peptide	Length
1	1	1	G	1
2	12	20	VSRPGRGEP	9
3	28	28	V	1
4	38	76	SDAASQRMEPRAPWIEQEGPEYWDRNTRNVKAQSQTDRV	39
5	84	92	YYNQSEAGS	9
6	102	105	DVGS	4
7	115	121	QDAYDGK	7
8	131	131	R	1
9	133	133	W	1
10	137	147	DMAAQTTKHKW	11
11	173	188	ENGKETLQRTDAPKTH	16
12	194	196	VSD	3
13	218	241	QRDGEDQTQDTELVETRPAGDGTF	24
14	250	256	PSGQEQR	7
15	264	268	EGLPK	5

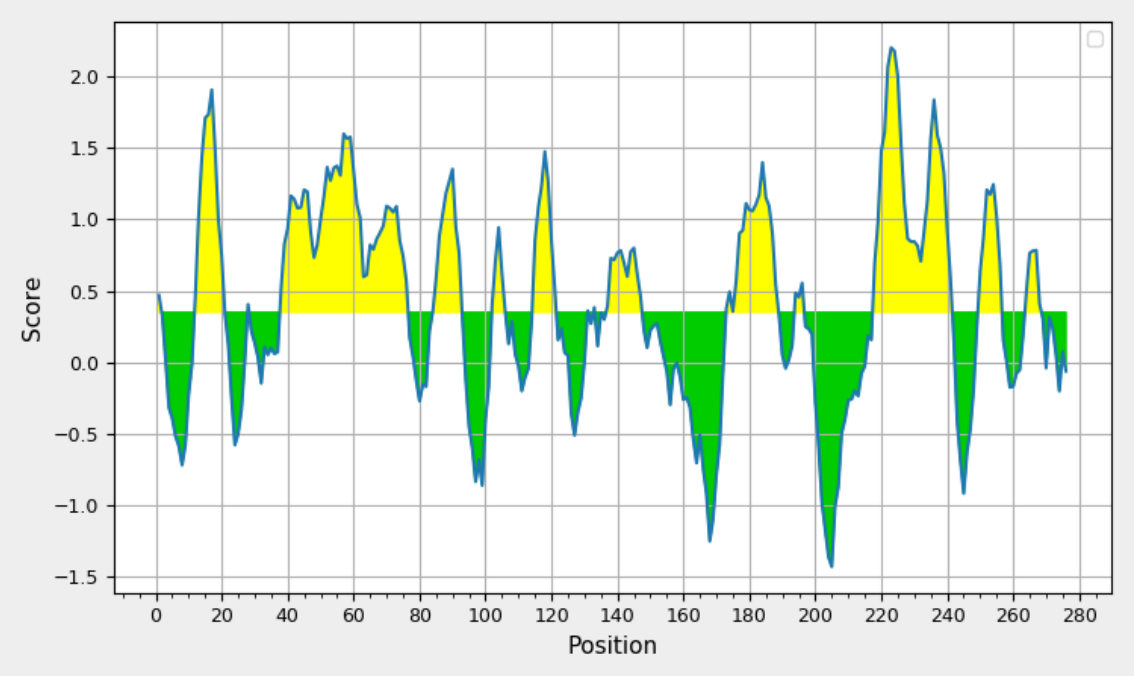

Figure 3.9 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele A*68:01 of donor 09 (Average: 0.406 Minimum: -0.002 Maximum: 2.199)

Table 3.46 Step 1: Finding the mismatched donor HLA alleles by comparing HLA Typing results for Recipient Donor pair 10.

Recipient	Donor	Antigen MM
A*03:01	A*26:01	-
A*26:01	A*30:01	yes
B*35:01	B*13:02	yes
B*55:01	B*55:01	-
C*01:02	C*01:02	-
C*04:01	C*06:02	yes

Table 3.47 Step 2: Listing the eplets of recipient's pre-transplantation Luminex alleles detected by Luminex SAB assay for Recipient 10.

Recipient's Luminex Alleles	Eplets Of Recipient's Pre-Transplantation Luminex Alleles
A*02:05	9Y - 43R - 44RM - 44RME - 62GE - 62GK - 65RA - 65RK - 66K - 66KA - 66KH - 71HS - 76VDT - 77D - 79GT - 80T - 80TL - 95L - 97R - 99Y - 105S - 107W - 109F - 114H - 116Y - 127K - 144K - 144TKH - 145KHA - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156WA - 163T - 184A - 193AV - 194V - 207S - 253Q
A*68:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 95I - 97M - 99Y - 105S - 109F - 114R - 116D - 127K - 144K - 144TKH - 145KHA - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156WA - 163T - 184A - 193AV - 194V - 207S - 245V - 253Q
A*02:02	9F - 43R - 44RM - 44RME - 62GE - 62GK - 65RA - 65RK - 66K - 66KA - 66KH - 71HS - 76VDT - 77D - 79GT - 80T - 80TL - 95L - 97R - 99Y - 105S - 107W - 109F - 114H - 116Y - 127K - 144K - 144TKH - 145KHA - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156WA - 163T - 184A - 193AV - 194V - 207S - 253Q
A*02:03	9F - 44RM - 44RME - 62GE - 62GK - 65RA - 65RK - 66K - 66KA - 66KH - 71HS - 76VDT - 77D - 79GT - 80T - 80TL - 95V - 97R - 99Y - 105S - 107W - 109F - 114H - 116Y - 127K - 144K - 144TKH - 145HT - 149TAH - 150AH - 151AHE - 151H - 152E - 156WA - 163T - 184A - 193AV - 194V - 207S - 253Q
A*68:02	9Y - 12M - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 95I - 97R - 99Y - 109F - 114H - 116Y - 127K - 144K - 144TKH - 145KHA - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156WA - 163T - 184A - 193AV - 194V - 207S - 245V - 253Q
A*02:01	9F - 44RM - 44RME - 62GE - 62GK - 65RA - 65RK - 66K - 66KA - 66KH - 71HS - 76VDT - 77D - 79GT - 80T - 80TL - 95V - 97R - 99Y - 105S - 107W - 109F - 114H -

	116Y - 127K - 144K - 144TKH - 145KHA - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156L - 163T - 184A - 193AV - 194V - 207S - 253Q
A*69:01	9Y - 44RM - 44RME - 62RN - 62RR - 65RA - 65RNA - 66N - 66NV - 71QS - 76VDT - 77D - 79GT - 80T - 80TL - 95V - 97R - 99Y - 105S - 107W - 109F - 114H - 116Y - 127K - 144K - 144TKH - 145KHA - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156L - 163T - 184A - 193AV - 194V - 207S - 253Q
A*24:02	9S - 44RM - 44RME - 62EE - 65GK - 66K - 66KA - 66KH - 71HS - 76EN - 77N - 80I - 81ALR - 82LR - 95L - 97M - 99F - 105S - 109F - 114H - 116Y - 127K - 138MI - 144K - 144KR - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156QA - 163T - 166DG - 193PI
A*24:03	9S - 44RM - 44RME - 62EE - 65GK - 66K - 66KA - 66KH - 71HS - 76EN - 77N - 80I - 81ALR - 82LR - 95L - 97M - 99F - 105S - 109F - 114H - 116Y - 127K - 138MI - 144K - 144KR - 149AH - 150AAH - 150AH - 151AHV - 151H - 152V - 156QA - 163T - 193PI
A*23:01	9S - 44RM - 44RME - 62EE - 65GK - 66K - 66KA - 66KH - 71HS - 76EN - 77N - 80I - 81ALR - 82LR - 95L - 97M - 99F - 105S - 109F - 114H - 116Y - 127K - 138MI - 151ARV - 152V - 156L - 163T - 166DG - 193PI
B*57:01	9Y - 12M - 44RM - 44RMA - 62GE - 62GRN - 65RA - 65RNA - 66N - 66NM - 69AA - 71SA - 74Y - 76EN - 77N - 80I - 81ALR - 82LR - 94I - 95I - 97V - 99Y - 113H - 113HD - 116S - 131S - 151ARV - 152V - 156L - 163L - 163LE - 163LW - 193PI
B*58:01	9Y - 12M - 44RT - 62GE - 62GRN - 65RA - 65RNA - 66N - 66NM - 69AA - 71SA - 74Y - 76EN - 77N - 80I - 81ALR - 82LR - 94I - 95I - 97R - 99Y - 103L - 113H - 113HD - 116S - 131S - 151ARV - 152V - 156L - 163L - 163LE - 163LW - 193PV - 194V

Table 3.48 Step 3: Calculating the number of shared eplets between each mismatched donor HLA allele and recipient's Luminex alleles listed in the previous step for Recipient-Donor pair 10.

Donor	Number Of Shared Eplets	Shared Eplets Between Each Mismatched Donor HLA Allele And Recipient's Luminex Alleles
A*30:01	138	9S (3) - 44RM (11) - 44RME (10) - 65RA (9) - 65RNA (5) - 66N (5) - 66NV (3) - 71QS (3) - 76VDT (7) - 77D (7) - 79GT (7) - 80T (7) - 80TL (7) - 95I (4) - 97I 99Y (9) - 105S (9) - 109F (10) - 138MI (3) - 156L (5) - 163T (10) - 193PI (4)
B*13:02	87	9Y (6) - 12M (3) - 44RM (11) - 44RMA (1) - 74Y (2) - 76EN (5) - 77N (5) - 80T (7) - 81ALR (5) - 82LR (5) - 99Y (9) - 103L (1) - 113H (2) - 131S (2) - 151ARV (3) - 152V (11) - 156L (5) - 193PI (4)
C*06:02	54	66K (7) - 77N (5) - 95L (5) - 99Y (9) - 103L (1) - 116S (2) - 152E (1) - 156WA (5) - 163T (10) - 193PV (1) - 194V (8)

Table 3.49 Step 4: Sorting and listing the Luminex alleles to predict the most likely Donor Specific Antibodies (DSA) by the number of most shared eplets for Recipient-Donor 10.

Shared Allele	# Shares		Shared Allele	# Shares		Shared Allele	# Shares
A*30:01	29		B*51:02	18		B*50:01	13
A*30:02	29		B*52:01	18		B*41:02	13
A*29:02	28		C*15:02	18		C*08:02	13
A*29:01	***28***		A*01:01	17		B*14:05	13
A*34:02	28		B*54:01	17		B*14:06	13
A*33:01	27		B*46:01	17		B*14:01	13
A*33:03	27		B*15:01	17		B*14:02	13
A*31:01	27		B*15:02	17		C*04:03	12
B*13:01	27		B*15:11	17		B*08:01	12
B*15:16	27		B*15:12	17		B*42:01	12
B*13:02	26		B*47:01	16		C*07:01	12
B*57:03	26		B*27:03	16		B*78:01	12
A*74:01	25		B*39:05	16		B*81:01	12
A*34:01	***24***		B*27:05	16		B*40:02	12
A*80:01	24		B*18:01	16		B*41:01	12
A*66:01	24		C*06:02	16		C*14:02	12
A*66:02	24		B*35:08	16		C*03:02	12
A*43:01	23		B*39:01	15		C*16:01	12
A*11:02	23		B*56:01	15		B*45:01	12
B*53:01	23		B*67:01	15		C*03:04	11
A*02:06	23		C*02:02	15		B*82:01	11
A*11:01	23		C*02:10	15		B*82:02	11
B*59:01	23		C*05:01	15		B*40:05	11
B*15:13	22		B*15:03	15		B*40:06	11
A*23:02	22		C*12:02	15		B*27:08	11
A*32:01	21		C*12:03	15		C*03:03	11
B*38:01	21		B*15:18	15		C*18:01	11
B*44:03	21		C*17:01	15		C*18:02	11
A*36:01	19		B*37:01	14		B*73:01	9
A*25:01	19		C*08:01	14		B*07:03	9
B*44:02	19		B*15:10	14		C*07:02	9
B*49:01	18		B*48:01	13		B*07:02	9
B*51:01	18		B*40:01	13		C*07:04	8

Table 3.50 Step 5: Listing the epitope's peptide AA sequences using the IEDB Bepipred-1.0 Antibody Epitope Prediction method for the donor's mismatched HLA allele A*30:01 of donor 10.

No.	Start	End	Peptide	Length
1	1	1	G	1
2	11	21	SVSRPGSGEPR	11
3	28	28	V	1
4	38	76	SDAASQRMEPRAPWIEQERPEYWDQETRNVKAQSQTDRV	39
5	84	92	YYNQSEAGS	9
6	102	105	DVGS	4
7	115	121	QHAYDGK	7
8	131	131	R	1
9	133	133	W	1
10	145	145	R	1
11	147	147	W	1
12	173	190	ENGKETLQRTDPPKTHMT	18
13	193	197	PISDH	5
14	218	242	QRDGEDQTQDTELVETRPAGDGTFQ	25
15	249	256	VPSGEEQR	8
16	264	268	EGLPK	5

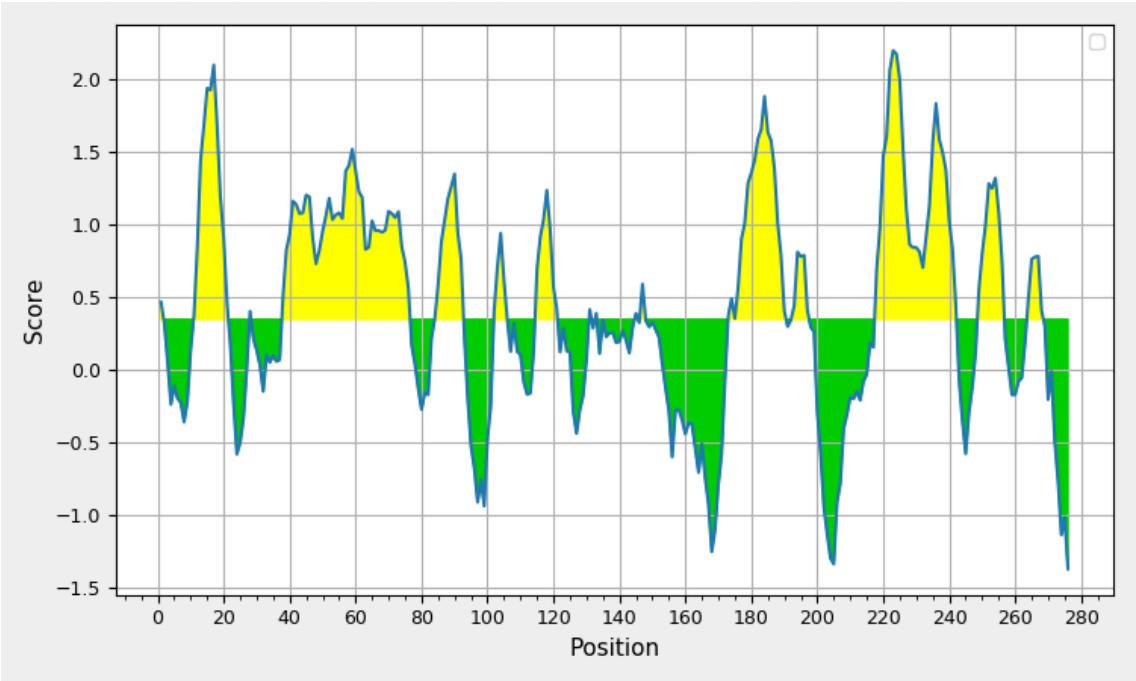

Figure 3.10 Sensitivity/Specificity score with the threshold 0.35 for the mismatched HLA allele A*30:01 of donor 10 (Average: 0.420 Minimum: -0.008 Maximum: 2.199)

4. DISCUSSION

The immunogenicity of an eplet or functional epitope is the capacity to induce an immune response. Antigenicity is the ability of the amino acids making up the structural epitope to be bound by pre-transplantation antibodies. Therefore, whether an alloantibody binds a particular HLA antigen is determined by the presence of the eplet. However, it can also be influenced by amino acids surrounding the eplet or the peptide in the peptide-binding groove. Also, amino acids that cause a conformational change in the HLA molecule can affect antigenicity, even when they are found outside (but next to) the range of the structural epitope. The immunogenicity of mismatched HLA antigens can vary from unacceptable to acceptable mismatches has been previously recognized and proved. The critical question, though, is what determines the antigenicity and immunogenicity of a particular HLA mismatch. It is well known that recipients will develop HLA antibodies against a restricted number of mismatched epitopes. Other recipients will not develop HLA antibodies despite significant mismatching with their organ donors. The factors mentioned thus far explain the relative immunogenicity of a particular HLA mismatch. Additional factors may determine the strength of these responses, whether measured as Mean Fluorescence Intensity (MFI) or the actual titer of the antibody. The observation that antibody reactivity to a particular epitope can yield significantly different MFI values in a single antigen bead analysis is not unique to Class I. Another factor that can affect the ability of antibody binding is the peptide presented within the HLA molecule and tissue-specific reactivity. It is pertinent to mention that the technical limitations of the current solid-phase assays, leading, amongst others, to a "prozone effect," or the detection of antibodies against denatured targets, may affect our ability to assign B cell epitopes accurately.

The table shows below the number of predicted antibodies according to the steps that we followed. It shows that all predicted antibodies are also experimentally detected by Luminex SAB method (Table 4.1).

This will help together to predicting of Donor Specific Antibodies using immunogenicity of an eplet or functional epitope.

Table 4.1 Demographic information together with the number of predicted antibodies.

Receiver	Age	Gender	Donor Relation	Number of Pregnancy	Number of Pre-Existed Antibody	Number of Newly Formed Antibody	Number of Predicted Antibody
01	40	F	Sibling	5	4	2	2
02	38	M	Father	-	17	1	1
03	33	F	Sibling	2	4	1	1
04	39	F	Unrelated	2	11	1	1
05	52	F	Husband	4	3	1	1
06	40	F	Husband	1	3	1	1
07	29	F	Unrelated	1	7	32	28
08	8	M	Father	-	1	0	0
09	36	F	Sibling	2	7	2	2
10	44	F	Husband	2	12	2	2

5. CONCLUSION

In this study, we have observed that not only the eplet mismatches between the donor and recipient’s HLA antigens are playing an important role but also the ability of antibody binding to epitopes together with the shared eplets between the mismatched donor HLA antigens and recipient’s pre-transplantation anti-HLA antibodies to develop DSAs after transplantation.

We believe that the 5 steps using the antigenicity which we described here will help to predict the DSA by finding the HLA antigen mismatches, searching the eplets of antigens that bind to the recipient's anti-HLA antibodies, calculating the number of shared eplets between the mismatched donor HLA antigens and the recipient's pre-transplantation anti-HLA antibody-bound antigens besides with HLAMatchmaker and PIRCHE tools.

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APPENDIX A

Table A. 1 HLA Class I Eplets and Eplet AA sequences from Eplet Registry database with Luminex Alleles.

#	Eplet	Luminex Alleles	Eplet AA
1	1C	C*01:02, C*02:02, C*02:10, C*05:01, C*06:02, C*07:01, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*15:02, C*16:01, C*18:01, C*18:02	1C
2	9D	B*08:01, C*06:02, C*07:01, C*07:02, C*07:04, C*18:01, C*18:02	9D
3	9F	A*01:01, A*02:01, A*02:02, A*02:03, A*03:01, A*32:01, A*36:01, A*74:01, A*80:01, C*01:02	9F
4	9H	B*18:01, B*27:03, B*27:05, B*27:08, B*37:01, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*45:01, B*49:01, B*50:01, B*73:01	9H
5	9S	A*23:01, A*23:02, A*24:02, A*24:03, A*30:01, A*30:02, C*04:01, C*14:02	9S
6	9T	A*29:01, A*29:02, A*31:01, A*33:01, A*33:03	9T
7	9Y	A*02:05, A*02:06, A*11:01, A*11:02, A*25:01, A*26:01, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, B*07:02, B*07:03, B*13:01, B*13:02, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:16, B*15:18, B*35:01, B*35:08, B*38:01, B*39:01, B*39:05, B*42:01, B*44:02, B*44:03, B*46:01, B*47:01, B*48:01, B*51:01, B*51:02, B*52:01, B*53:01, B*54:01, B*55:01, B*56:01, B*57:01, B*57:03, B*58:01, B*59:01, B*67:01, B*78:01, B*81:01, B*82:01, B*82:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:03, C*05:01, C*08:01, C*08:02, C*12:02, C*12:03, C*15:02, C*16:01, C*17:01	9Y
8	11AV	B*14:02, B*14:05, B*14:06, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:03, C*05:01, C*06:02, C*07:01, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*15:02, C*16:01, C*17:01, C*18:01, C*18:02	11A 12V
9	12M	A*68:02, B*08:01, B*13:01, B*13:02, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:16,	12M

		B*15:18, B*35:01, B*35:08, B*40:01, B*41:01, B*41:02, B*44:02, B*44:03, B*45:01, B*46:01, B*47:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*54:01, B*55:01, B*56:01, B*57:01, B*57:03, B*58:01, B*59:01, B*78:01, B*82:01, B*82:02	
10	14W	C*04:01	14W (49E)
11	16S	C*02:02, C*02:10, C*04:03	16S
12	17S	A*30:01, A*30:02	17S
13	19K	A*11:02	19K
14	21H	C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:03, C*15:02	21H
15	24S	B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:03, B*15:10, B*15:18, B*18:01, B*37:01, B*38:01, B*39:01, B*39:05, B*42:01, B*48:01, B*67:01, B*81:01, B*82:01, B*82:02, C*01:02, C*06:02, C*07:01, C*07:02, C*07:04, C*18:01, C*18:02	24S
16	24T	B*13:01, B*13:02, B*27:03, B*27:05, B*27:08, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*44:02, B*44:03, B*45:01, B*47:01, B*49:01, B*50:01, B*73:01	24T
17	30G	B*18:01	30G
18	32L	B*27:03, B*27:05, B*27:08, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*44:02, B*44:03, B*45:01, B*47:01, B*49:01, B*50:01	32L
19	35Q	A*80:01, C*05:01, C*08:01, C*08:02	35Q
20	41T	B*13:01, B*13:02, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*44:02, B*44:03, B*45:01, B*47:01, B*49:01, B*50:01	41T
21	43R	A*02:02, A*02:05	43R
22	44KM	A*01:01, A*36:01	44K 45M (149A 150V 151H 152A) (158V)

23	44RM	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*23:01, A*23:02, A*24:02, A*24:03, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01, B*13:01, B*13:02, B*15:01, B*15:02, B*15:11, B*15:12, B*15:13, B*15:16, B*46:01, B*57:01, B*57:03	44R 45M
24	44RMA	B*13:01, B*13:02, B*15:01, B*15:02, B*15:11, B*15:12, B*15:13, B*15:16, B*46:01, B*57:01, B*57:03	44R 45M 46A
25	44RME	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*23:01, A*23:02, A*24:02, A*24:03, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01	44R 45M 46E (67V)
26	44RT	B*18:01, B*35:01, B*35:08, B*37:01, B*51:01, B*51:02, B*52:01, B*53:01, B*58:01, B*78:01	44R 45T
27	45EE	B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:03, B*15:10, B*15:18, B*27:03, B*27:05, B*27:08, B*38:01, B*39:01, B*39:05, B*42:01, B*48:01, B*55:01, B*56:01, B*59:01, B*67:01, B*73:01, B*81:01, B*82:01, B*82:02	45E 46E
28	45KE	B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*44:02, B*44:03, B*45:01, B*47:01, B*49:01, B*50:01	45K 46E
29	56E	A*80:01	56E (74N 76A 77N 163E 166D 253K)
30	56R	A*30:01, A*30:02, A*31:01	56R
31	59H	B*27:03	59H
32	62EE	A*23:01, A*23:02, A*24:02, A*24:03, A*80:01	62E 63E
33	62GE	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, B*57:01, B*57:03, B*58:01	62G 63E
34	62GK	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06	62G 66K (74H 77D)

35	62GRN	B*57:01, B*57:03, B*58:01	62G 65R 66N
36	62LQ	A*29:01, A*29:02, A*43:01	62L 63Q
37	62QE	A*01:01, A*03:01, A*11:01, A*11:02, A*30:01, A*30:02, A*31:01, A*32:01, A*36:01, A*74:01	62Q 63E
38	62RN	A*25:01, A*26:01, A*33:01, A*33:03, A*34:01, A*34:02, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:02, B*15:10, B*15:11, B*15:13, B*15:18, B*18:01, B*35:01, B*35:08, B*38:01, B*39:01, B*39:05, B*42:01, B*51:01, B*51:02, B*53:01, B*54:01, B*55:01, B*56:01, B*59:01, B*67:01, B*73:01, B*78:01, B*81:01, B*82:01, B*82:02	62R 63N
39	62RR	A*25:01, A*26:01, A*33:01, A*33:03, A*34:01, A*34:02, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, B*15:16	62R 65R
40	63NI	B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:02, B*15:10, B*15:11, B*15:13, B*15:18, B*18:01, B*35:01, B*35:08, B*38:01, B*39:01, B*39:05, B*42:01, B*51:01, B*51:02, B*53:01, B*54:01, B*55:01, B*56:01, B*59:01, B*67:01, B*73:01, B*78:01, B*81:01, B*82:01, B*82:02	63N 66I
41	65GK	A*23:01, A*23:02, A*24:02, A*24:03	65G 66K
42	65QIA	B*07:02, B*27:03, B*27:05, B*27:08, B*42:01, B*54:01, B*55:01, B*56:01, B*67:01, B*73:01, B*81:01, B*82:01, B*82:02	65Q 66I 69A
43	65QKR	B*46:01, C*01:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:01, C*04:03, C*05:01, C*06:02, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*16:01, C*17:01, C*18:01, C*18:02	65Q 66K 69R
44	65RA	A*01:01, A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01, B*15:16, B*57:01, B*57:03, B*58:01	65R 69A
45	65RK	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*34:01	65R 66K

46	65RNA	A*01:01, A*03:01, A*11:01, A*11:02, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01, B*15:16, B*57:01, B*57:03, B*58:01	65R 66N 69A
47	66I	B*07:02, B*07:03, B*08:01, B*13:01, B*13:02, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:18, B*18:01, B*27:03, B*27:05, B*27:08, B*35:01, B*35:08, B*37:01, B*38:01, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*44:02, B*44:03, B*45:01, B*47:01, B*48:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*54:01, B*55:01, B*56:01, B*59:01, B*67:01, B*73:01, B*78:01, B*81:01, B*82:01, B*82:02	66I
48	66IC	B*14:01, B*14:02, B*14:05, B*14:06, B*15:10, B*15:18, B*27:03, B*27:05, B*27:08, B*38:01, B*39:01, B*39:05, B*73:01	66I 67C
49	66IF	B*08:01, B*35:01, B*35:08, B*51:01, B*51:02, B*53:01, B*59:01, B*78:01	66I 67F
50	66IS	B*13:01, B*13:02, B*15:01, B*15:02, B*15:03, B*15:12, B*15:13, B*18:01, B*37:01, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*44:02, B*44:03, B*45:01, B*47:01, B*48:01, B*49:01, B*50:01, B*52:01	66I 67S
51	66IY	B*07:02, B*07:03, B*15:11, B*42:01, B*54:01, B*55:01, B*56:01, B*67:01, B*81:01, B*82:01, B*82:02	66I 67Y
52	66K	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*23:01, A*23:02, A*24:02, A*24:03, A*34:01, B*46:01, C*01:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:01, C*04:03, C*05:01, C*06:02, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*16:01, C*17:01, C*18:01, C*18:02	66K
53	66KA	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*23:01, A*23:02, A*24:02, A*24:03, A*34:01	66K 69A
54	66KH	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*23:01, A*23:02, A*24:02, A*24:03	66K 70H
55	66N	A*01:01, A*03:01, A*11:01, A*11:02, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01,	66N

		A*33:01, A*33:03, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01, B*15:16, B*57:01, B*57:03, B*58:01, C*07:01, C*15:02	
56	66NH	A*01:01, A*25:01, A*26:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*36:01, A*43:01, A*74:01, A*80:01	66N 70H
57	66NM	A*01:01, A*36:01, B*15:16, B*57:01, B*57:03, B*58:01	66N 67M
58	66NV	A*03:01, A*11:01, A*11:02, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01	66N 67V
59	69AA	B*07:02, B*15:16, B*27:03, B*27:05, B*27:08, B*42:01, B*54:01, B*55:01, B*56:01, B*57:01, B*57:03, B*58:01, B*67:01, B*73:01, B*81:01, B*82:01, B*82:02	69A 71A
60	69RA	C*04:01, C*04:03, C*06:02, C*07:01, C*07:02, C*07:04, C*12:02, C*12:03, C*17:01, C*18:01, C*18:02	69R 73A
61	69RT	B*46:01, C*01:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*05:01, C*08:01, C*08:02, C*14:02, C*15:02, C*16:01	69R 73T
62	69TNT	B*07:03, B*08:01, B*13:01, B*13:02, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:18, B*18:01, B*35:01, B*35:08, B*37:01, B*38:01, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*44:02, B*44:03, B*45:01, B*47:01, B*48:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*59:01, B*78:01	69T 70N 71T
63	70IAQ	B*07:02, B*42:01, B*54:01, B*55:01, B*56:01, B*67:01, B*81:01, B*82:01, B*82:02	66I 69A 70Q
64	71ATD	B*27:03, B*27:05	71A 73T 77D
65	71HS	A*01:01, A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*23:01, A*23:02, A*24:02, A*24:03, A*25:01, A*26:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*36:01, A*43:01, A*74:01, A*80:01	70H 71S
66	71KA	B*27:03, B*27:05, B*27:08, B*73:01	70K 71A
67	71QS	A*03:01, A*11:01, A*11:02, A*29:01, A*29:02, A*30:01, A*34:01, A*34:02, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01	70Q 71S

68	71SA	B*15:16, B*57:01, B*57:03, B*58:01	70S 71A
69	71TD	B*37:01, B*47:01	71T 77D
70	71TN	B*13:01, B*13:02, B*15:13, B*38:01, B*44:02, B*44:03, B*49:01, B*51:01, B*51:02, B*52:01, B*53:01, B*59:01	71T 77N
71	71TTS	B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:18, B*18:01, B*35:01, B*35:08, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*45:01, B*48:01, B*50:01, B*78:01	71T 73T 77S
72	73AN	C*04:01, C*04:03, C*06:02, C*17:01, C*18:01, C*18:02	73A 77N
73	73AS	C*07:01, C*07:02, C*07:04, C*12:02, C*12:03	73A 77S
74	73ID	A*31:01, A*33:01, A*33:03	73I 77D
75	73TVS	B*46:01, C*01:02, C*03:02, C*03:03, C*03:04, C*08:01, C*08:02, C*14:02, C*16:01	73T 76V 77S
76	74Y	B*13:01, B*13:02, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:16, B*15:18, B*18:01, B*35:01, B*35:08, B*37:01, B*38:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*44:02, B*44:03, B*45:01, B*47:01, B*48:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*57:01, B*57:03, B*58:01, B*59:01	74Y
77	76ANT	A*01:01, A*26:01, A*29:01, A*29:02, A*36:01, A*43:01, A*80:01	76A 77N 80T
78	76ED	B*27:03, B*27:05, B*37:01, B*47:01	76E 77D
79	76EG	A*30:02	76E 79G
80	76EN	A*23:01, A*23:02, A*24:02, A*24:03, A*30:02, B*13:01, B*13:02, B*15:13, B*15:16, B*38:01, B*44:02, B*44:03, B*49:01, B*51:01, B*51:02, B*52:01, B*53:01, B*57:01, B*57:03, B*58:01, B*59:01	76E 77N
81	76ES	A*25:01, A*32:01, B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:18, B*18:01, B*27:08, B*35:01, B*35:08, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*45:01,	76E 77S

		B*48:01, B*50:01, B*54:01, B*55:01, B*56:01, B*67:01, B*78:01, B*81:01, B*82:01, B*82:02	
82	76ESI	A*25:01, A*32:01	76E 77S 80I
83	76ESN	B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:18, B*18:01, B*27:08, B*35:01, B*35:08, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*45:01, B*48:01, B*50:01, B*54:01, B*55:01, B*56:01, B*67:01, B*78:01, B*81:01, B*82:01, B*82:02	76E 77S 80N
84	76ET	A*30:02, B*13:01, B*13:02, B*27:03, B*27:05, B*37:01, B*44:02, B*44:03, B*47:01	76E 80T
85	76VDT	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*30:01, A*31:01, A*33:01, A*33:03, A*34:01, A*34:02, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01	76V 77D 80T
86	76VRN	B*46:01, B*73:01, C*01:02, C*03:02, C*03:03, C*03:04, C*07:01, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*16:01	76V 79R 80N
87	76VS	B*46:01, C*01:02, C*03:02, C*03:03, C*03:04, C*07:01, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*16:01	76V 77S
88	77D	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*30:01, A*31:01, A*33:01, A*33:03, A*34:01, A*34:02, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, B*27:03, B*27:05, B*37:01, B*47:01	77D
89	77N	A*01:01, A*23:01, A*23:02, A*24:02, A*24:03, A*26:01, A*29:01, A*29:02, A*30:02, A*36:01, A*43:01, A*80:01, B*13:01, B*13:02, B*15:13, B*15:16, B*38:01, B*44:02, B*44:03, B*49:01, B*51:01, B*51:02, B*52:01, B*53:01, B*57:01, B*57:03, B*58:01, B*59:01, C*02:02, C*02:10, C*04:01, C*04:03, C*05:01, C*06:02, C*15:02, C*17:01, C*18:01, C*18:02	77N
90	77NGT	A*01:01, A*26:01, A*29:01, A*29:02, A*30:02, A*36:01, A*43:01, A*80:01	77N 79G 80T
91	77S	A*25:01, A*32:01, B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03,	77S

		B*15:10, B*15:11, B*15:12, B*15:18, B*18:01, B*27:08, B*35:01, B*35:08, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*45:01, B*46:01, B*48:01, B*50:01, B*54:01, B*55:01, B*56:01, B*67:01, B*78:01, B*81:01, B*82:01, B*82:02, C*01:02, C*03:02, C*03:03, C*03:04, C*07:01, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*16:01	
92	77SRN	B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:18, B*18:01, B*27:08, B*35:01, B*35:08, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*45:01, B*46:01, B*48:01, B*50:01, B*54:01, B*55:01, B*56:01, B*67:01, B*78:01, B*81:01, B*82:01, B*82:02, C*01:02, C*03:02, C*03:03, C*03:04, C*07:01, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*16:01	77S 79R 80N
93	79GT	A*01:01, A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*33:01, A*33:03, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01	79G 80T
94	80I	A*23:01, A*23:02, A*24:02, A*24:03, A*25:01, A*32:01, B*15:13, B*15:16, B*38:01, B*49:01, B*51:01, B*51:02, B*52:01, B*53:01, B*57:01, B*57:03, B*58:01, B*59:01	80I
95	80K	C*02:02, C*02:10, C*04:01, C*04:03, C*05:01, C*06:02, C*15:02, C*17:01, C*18:01, C*18:02	80K
96	80N	B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:18, B*18:01, B*27:08, B*35:01, B*35:08, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*45:01, B*46:01, B*48:01, B*50:01, B*54:01, B*55:01, B*56:01, B*67:01, B*73:01, B*78:01, B*81:01, B*82:01, B*82:02, C*01:02, C*03:02, C*03:03, C*03:04, C*07:01, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*16:01	80N
97	80T	A*01:01, A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*33:01, A*33:03, A*34:01,	80T

		A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01, B*13:01, B*13:02, B*27:03, B*27:05, B*37:01, B*44:02, B*44:03, B*47:01	
98	80TA	B*13:01, B*13:02, B*44:02, B*44:03	80T 81A
99	80TL	A*01:01, A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*33:01, A*33:03, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01, B*27:03, B*27:05, B*37:01, B*47:01	80T 81L
100	80TLR	B*13:01, B*13:02, B*27:03, B*27:05, B*37:01, B*44:02, B*44:03, B*47:01	80T 82L 83R
101	81ALR	A*23:01, A*23:02, A*24:02, A*24:03, A*25:01, A*32:01, B*13:01, B*13:02, B*15:13, B*15:16, B*38:01, B*44:02, B*44:03, B*49:01, B*51:01, B*51:02, B*52:01, B*53:01, B*57:01, B*57:03, B*58:01, B*59:01	81A 82L 83R
102	82LR	A*23:01, A*23:02, A*24:02, A*24:03, A*25:01, A*32:01, B*13:01, B*13:02, B*15:13, B*15:16, B*27:03, B*27:05, B*37:01, B*38:01, B*44:02, B*44:03, B*47:01, B*49:01, B*51:01, B*51:02, B*52:01, B*53:01, B*57:01, B*57:03, B*58:01, B*59:01	82L 83R
103	90D	A*01:01, A*11:01, A*11:02, A*25:01, A*26:01, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*80:01, B*73:01, C*04:01, C*04:03, C*06:02, C*07:01, C*07:02, C*07:04, C*18:01, C*18:02	90D
104	91R	C*03:03	91R
105	94I	B*13:01, B*15:02, B*15:13, B*35:01, B*35:08, B*44:02, B*44:03, B*53:01, B*57:01, B*57:03, B*58:01, C*03:02, C*03:03, C*03:04, C*15:02	94I
106	95F	C*07:04	95F
107	95I	A*01:01, A*03:01, A*11:01, A*11:02, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*74:01, A*80:01, B*13:01, B*15:02, B*15:13, B*35:01, B*35:08, B*37:01,	95I

		B*44:02, B*44:03, B*53:01, B*57:01, B*57:03, B*58:01, C*03:03, C*03:04, C*15:02, C*17:01	
108	95L	A*02:02, A*02:05, A*23:01, A*23:02, A*24:02, A*24:03, B*07:02, B*07:03, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:03, B*15:10, B*15:11, B*15:12, B*15:18, B*18:01, B*27:03, B*27:05, B*27:08, B*38:01, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*41:02, B*42:01, B*46:01, B*47:01, B*48:01, B*67:01, B*81:01, B*82:01, B*82:02, C*01:02, C*02:02, C*02:10, C*03:02, C*04:01, C*04:03, C*05:01, C*06:02, C*07:01, C*07:02, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*16:01, C*18:01, C*18:02	95L
109	95V	A*02:01, A*02:03, A*02:06, A*69:01	95V
110	95W	B*13:02, B*15:16, B*40:06, B*41:01, B*45:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*54:01, B*55:01, B*56:01, B*59:01, B*73:01, B*78:01	95W
111	97I	A*01:01, A*03:01, A*11:01, A*11:02, A*30:01, A*30:02, A*34:02, A*36:01, A*80:01	97I
112	97M	A*23:01, A*23:02, A*24:02, A*24:03, A*29:01, A*29:02, A*31:01, A*32:01, A*33:01, A*33:03, A*68:01, A*74:01	97M
113	97N	B*27:03, B*27:05, B*27:08	97N
114	97R	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*25:01, A*26:01, A*34:01, A*43:01, A*66:01, A*66:02, A*68:02, A*69:01, B*13:01, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:16, B*15:18, B*18:01, B*35:01, B*35:08, B*37:01, B*38:01, B*39:01, B*39:05, B*40:01, B*41:01, B*44:02, B*44:03, B*45:01, B*46:01, B*47:01, B*49:01, B*50:01, B*53:01, B*58:01, B*67:01, B*82:01, B*82:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:01, C*04:03, C*05:01, C*07:01, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*15:02, C*17:01, C*18:01, C*18:02	97R
115	97S	B*07:02, B*07:03, B*08:01, B*14:05, B*40:02, B*40:05, B*41:02, B*42:01, B*48:01, B*81:01	97S
116	97T	B*13:02, B*40:06, B*51:01, B*51:02, B*52:01, B*54:01, B*55:01, B*56:01, B*59:01, B*73:01, B*78:01	97T

117	97V	B*57:01, B*57:03	97V
118	97W	B*14:01, B*14:02, C*01:02, C*06:02, C*12:03, C*14:02, C*16:01	97W
119	99F	A*23:01, A*23:02, A*24:02, A*24:03, B*47:01, B*82:01, B*82:02, C*04:01, C*04:03, C*14:02, C*18:01, C*18:02	99F
120	99S	B*37:01, C*07:02	99S
121	99Y	A*01:01, A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01, B*07:02, B*07:03, B*08:01, B*13:01, B*13:02, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:16, B*15:18, B*18:01, B*27:03, B*27:05, B*27:08, B*35:01, B*35:08, B*38:01, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*44:02, B*44:03, B*45:01, B*46:01, B*48:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*54:01, B*55:01, B*56:01, B*57:01, B*57:03, B*58:01, B*59:01, B*67:01, B*73:01, B*78:01, B*81:01, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*05:01, C*06:02, C*07:01, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*15:02, C*16:01, C*17:01	99Y
122	102H	A*29:01	102H
123	103L	B*13:01, B*13:02, B*15:16, B*35:01, B*35:08, B*45:01, B*49:01, B*50:01, B*53:01, B*54:01, B*55:01, B*56:01, B*58:01, B*59:01, B*82:01, B*82:02, C*01:02, C*02:02, C*02:10, C*04:01, C*04:03, C*05:01, C*06:02, C*07:01, C*07:02, C*07:04, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*15:02, C*16:01, C*17:01, C*18:01, C*18:02	103L
124	103M	B*73:01	103M
125	105S	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*23:01, A*23:02, A*24:02, A*24:03, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*33:01, A*33:03, A*34:02, A*68:01, A*69:01, A*80:01	105S

126	107W	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*69:01	107W
127	109F	A*01:01, A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*23:01, A*23:02, A*24:02, A*24:03, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*33:01, A*33:03, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*80:01	109F
128	113H	B*07:02, B*07:03, B*08:01, B*13:01, B*13:02, B*15:01, B*15:03, B*15:10, B*15:11, B*15:12, B*15:16, B*15:18, B*18:01, B*35:01, B*35:08, B*38:01, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*46:01, B*48:01, B*51:01, B*51:02, B*52:01, B*53:01, B*54:01, B*55:01, B*56:01, B*57:01, B*57:03, B*58:01, B*59:01, B*67:01, B*78:01, B*81:01, B*82:01, B*82:02, C*15:02	113H
129	113HD	B*07:02, B*07:03, B*15:01, B*15:03, B*15:10, B*15:11, B*15:12, B*15:16, B*15:18, B*18:01, B*35:01, B*35:08, B*46:01, B*53:01, B*57:01, B*58:01, C*15:02	113H 114D
130	113HN	B*08:01, B*13:01, B*13:02, B*38:01, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*48:01, B*51:01, B*51:02, B*52:01, B*54:01, B*55:01, B*56:01, B*57:03, B*59:01, B*67:01, B*78:01, B*81:01, B*82:01, B*82:02	113H 114N
131	113YD	B*15:02, B*15:13, B*44:02, B*44:03, C*01:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*06:02, C*07:01, C*07:02, C*07:04, C*12:02, C*12:03, C*14:02, C*16:01	113Y 114D
132	113YN	B*14:01, B*14:02, B*14:05, B*14:06, B*37:01, B*45:01, B*49:01, B*50:01, B*73:01, C*04:01, C*04:03, C*05:01, C*08:01, C*08:02, C*17:01, C*18:01, C*18:02	113Y 114N
133	114H	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*23:01, A*23:02, A*24:02, A*24:03, A*68:02, A*69:01, B*27:03, B*27:05, B*27:08, B*47:01	114H
134	114Q	A*25:01, A*26:01, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*43:01, A*66:01, A*66:02, A*74:01	114Q
135	114R	A*01:01, A*03:01, A*11:01, A*11:02, A*29:01, A*29:02, A*34:02, A*36:01, A*68:01, A*80:01	114R

136	116D	A*01:01, A*03:01, A*11:01, A*11:02, A*25:01, A*26:01, A*29:01, A*29:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*74:01, A*80:01, B*27:03, B*27:05, B*27:08, B*44:02, B*44:03, B*47:01	116D
137	116F	B*14:01, B*14:02, B*14:05, B*14:06, B*37:01, B*38:01, B*39:01, B*39:05, B*67:01, B*73:01, C*04:01, C*04:03, C*05:01, C*07:04, C*08:01, C*08:02, C*17:01, C*18:01, C*18:02	116F
138	116L	B*13:01, B*13:02, B*45:01, B*49:01, B*50:01, B*54:01, B*55:01, B*56:01, B*59:01, B*82:01, B*82:02, C*15:02	116L
139	116S	B*15:01, B*15:02, B*15:03, B*15:11, B*15:12, B*15:13, B*15:16, B*15:18, B*18:01, B*35:01, B*35:08, B*46:01, B*53:01, B*57:01, B*58:01, C*02:02, C*02:10, C*03:02, C*06:02, C*07:01, C*07:02, C*12:02, C*12:03, C*14:02, C*16:01	116S
140	116Y	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*23:01, A*23:02, A*24:02, A*24:03, A*68:02, A*69:01, B*07:02, B*07:03, B*08:01, B*15:10, B*40:01, B*40:02, B*40:05, B*40:06, B*41:01, B*41:02, B*42:01, B*48:01, B*51:01, B*51:02, B*52:01, B*57:03, B*78:01, B*81:01, C*01:02, C*03:03, C*03:04	116Y
141	127K	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*23:01, A*23:02, A*24:02, A*24:03, A*68:01, A*68:02, A*69:01	127K
142	131S	B*13:01, B*13:02, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:16, B*15:18, B*18:01, B*27:03, B*27:05, B*27:08, B*35:01, B*35:08, B*37:01, B*38:01, B*39:01, B*39:05, B*44:02, B*44:03, B*45:01, B*46:01, B*47:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*54:01, B*55:01, B*56:01, B*57:01, B*57:03, B*58:01, B*59:01, B*67:01, B*78:01, B*82:01, B*82:02	131S
143	138K	C*05:01, C*08:02	138K
144	138MI	A*01:01, A*03:01, A*11:01, A*11:02, A*23:01, A*23:02, A*24:02, A*24:03, A*25:01, A*26:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*74:01, A*80:01	138M 142I

145	143S	B*40:01, B*48:01, B*81:01, C*17:01	143S
146	144K	A*01:01, A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*24:02, A*24:03, A*36:01, A*68:01, A*68:02, A*69:01, A*80:01	144K
147	144KR	A*01:01, A*03:01, A*11:01, A*11:02, A*24:02, A*24:03, A*36:01, A*80:01	144K 145R
148	144QL	B*13:01, B*13:02	144Q 145L
149	144TKH	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*68:01, A*68:02, A*69:01	142T 144K 145H
150	145HT	A*02:03	144K 145H 149T
151	145KHA	A*02:01, A*02:02, A*02:05, A*02:06, A*68:01, A*68:02, A*69:01	144K 145H 149A
152	145RT	A*25:01, A*26:01, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02	145R 149T
153	147L	B*40:01, B*48:01, B*81:01, C*07:01, C*07:02, C*07:04, C*17:01	147L
154	149AH	A*01:01, A*02:01, A*02:02, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*24:02, A*24:03, A*36:01, A*68:01, A*68:02, A*69:01	149A 151H
155	149TAH	A*02:03, A*25:01, A*26:01, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02	149T 150A 151H
156	150AAH	A*02:01, A*02:02, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*24:02, A*24:03, A*68:01, A*68:02, A*69:01	149A 150A 151H
157	150AH	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*24:02, A*24:03, A*25:01, A*26:01, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01	150A 151H
158	151AHA	A*11:01, A*11:02	150A 151H 152A
159	151AHE	A*02:03, A*03:01, A*25:01, A*26:01, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02	150A 151H 152E
160	151AHV	A*02:01, A*02:02, A*02:05, A*02:06, A*24:02, A*24:03, A*68:01, A*68:02, A*69:01	150A 151H 152V
161	151ARV	A*23:01, A*23:02, A*29:01, A*29:02, A*31:01, A*32:01, A*33:01, A*33:03, A*74:01, B*08:01, B*13:01, B*13:02, B*18:01, B*27:03, B*27:05, B*27:08, B*35:01, B*35:08,	150A 151R 152V

		B*37:01, B*38:01, B*39:01, B*39:05, B*40:01, B*40:02, B*40:06, B*41:01, B*41:02, B*42:01, B*44:02, B*44:03, B*45:01, B*47:01, B*48:01, B*53:01, B*54:01, B*56:01, B*57:01, B*57:03, B*58:01, B*59:01, B*67:01, B*73:01, B*81:01, B*82:01, B*82:02	
162	151H	A*01:01, A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*11:01, A*11:02, A*24:02, A*24:03, A*25:01, A*26:01, A*34:01, A*34:02, A*36:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01	151H
163	152A	A*01:01, A*11:01, A*11:02, A*36:01, C*07:01, C*07:02, C*07:04, C*16:01	152A
164	152E	A*02:03, A*03:01, A*25:01, A*26:01, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, B*07:02, B*07:03, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:16, B*15:18, B*40:05, B*46:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*55:01, B*78:01, C*01:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:01, C*04:03, C*05:01, C*06:02, C*08:02, C*12:02, C*12:03, C*14:02, C*15:02, C*17:01, C*18:01, C*18:02	152E
165	152HA	A*01:01, A*11:01, A*11:02, A*36:01	151H 152A
166	152RA	C*07:01, C*07:02, C*07:04, C*16:01	151R 152A
167	152RE	B*07:02, B*07:03, B*14:01, B*14:02, B*14:05, B*14:06, B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:16, B*15:18, B*40:05, B*46:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*55:01, B*78:01, C*01:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:01, C*04:03, C*05:01, C*06:02, C*08:02, C*12:02, C*12:03, C*14:02, C*15:02, C*17:01, C*18:01, C*18:02	151R 152E
168	152RR	A*30:02, A*80:01	151R 152R
169	152T	C*08:01	152T
170	152V	A*02:01, A*02:02, A*02:05, A*02:06, A*23:01, A*23:02, A*24:02, A*24:03, A*29:01, A*29:02, A*31:01, A*32:01, A*33:01, A*33:03, A*68:01, A*68:02, A*69:01, A*74:01, B*08:01, B*13:01, B*13:02, B*18:01, B*27:03, B*27:05, B*27:08, B*35:01, B*35:08, B*37:01, B*38:01, B*39:01,	152V

		B*39:05, B*40:01, B*40:02, B*40:06, B*41:01, B*41:02, B*42:01, B*44:02, B*44:03, B*45:01, B*47:01, B*48:01, B*53:01, B*54:01, B*56:01, B*57:01, B*57:03, B*58:01, B*59:01, B*67:01, B*73:01, B*81:01, B*82:01, B*82:02	
171	152W	A*30:01	152W
172	156DA	B*08:01, B*37:01, B*41:01, B*41:02, B*42:01, B*44:02, B*45:01, B*82:01, B*82:02, C*07:04	156D 158A
173	156L	A*02:01, A*02:06, A*03:01, A*23:01, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:02, A*69:01, A*74:01, A*80:01, B*13:01, B*13:02, B*14:01, B*14:02, B*14:05, B*14:06, B*15:02, B*15:03, B*15:10, B*15:13, B*15:16, B*15:18, B*18:01, B*27:03, B*27:05, B*27:08, B*35:01, B*38:01, B*39:01, B*39:05, B*40:01, B*40:02, B*40:05, B*40:06, B*44:03, B*47:01, B*48:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*54:01, B*55:01, B*56:01, B*57:01, B*57:03, B*58:01, B*59:01, B*67:01, B*73:01, B*78:01, B*81:01, C*03:02, C*03:03, C*03:04, C*07:01, C*07:02, C*08:01, C*15:02, C*17:01	156L
174	156QA	A*11:01, A*11:02, A*24:02, A*24:03, C*16:01	156Q 158A
175	156R	A*01:01, A*36:01, B*07:02, B*07:03, B*35:08, C*01:02, C*04:01, C*04:03, C*05:01, C*08:02, C*14:02, C*18:01, C*18:02	156R
176	156RA	B*07:02, B*07:03, B*35:08, C*01:02, C*04:01, C*04:03, C*05:01, C*08:02, C*14:02, C*18:01, C*18:02	156R 158A
177	156WA	A*02:02, A*02:03, A*02:05, A*23:02, A*25:01, A*26:01, A*34:01, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, B*15:01, B*15:11, B*15:12, B*46:01, C*02:02, C*02:10, C*06:02, C*12:02, C*12:03	156W 158A
178	158T	B*38:01, B*39:01, B*39:05, B*67:01	158T
179	161D	A*03:01	161D
180	162DLS	B*82:01	162D 163L 167S
181	162GLS	B*44:02, B*44:03, B*45:01, B*82:02	162G 163L 167S

182	163E	A*66:02, A*80:01, B*07:02, B*07:03, B*13:01, B*13:02, B*27:03, B*27:05, B*27:08, B*40:01, B*40:02, B*40:06, B*47:01, B*48:01, B*73:01, B*81:01, C*02:02, C*02:10, C*17:01	163E
183	163EW	A*66:02, B*07:02, B*07:03, B*13:01, B*13:02, B*27:03, B*27:05, B*27:08, B*40:01, B*40:02, B*40:06, B*47:01, B*48:01, B*73:01, B*81:01, C*02:02, C*02:10, C*17:01	163E 167W
184	163L	B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:12, B*15:13, B*15:16, B*15:18, B*35:01, B*35:08, B*40:05, B*44:02, B*44:03, B*45:01, B*46:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*56:01, B*57:01, B*57:03, B*58:01, B*78:01, B*82:01, B*82:02, C*03:02, C*03:03, C*03:04	163L
185	163LE	B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:13, B*15:16, B*15:18, B*35:01, B*35:08, B*40:05, B*44:02, B*44:03, B*45:01, B*46:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*56:01, B*57:01, B*57:03, B*58:01, B*78:01, B*82:01, B*82:02, C*03:02, C*03:03, C*03:04	163L 166E
186	163LG	B*15:12	163L 167G
187	163LS/G	B*15:12, B*44:02, B*44:03, B*45:01, B*82:01, B*82:02	163L - 167G / S
188	163LW	B*15:01, B*15:02, B*15:03, B*15:10, B*15:11, B*15:13, B*15:16, B*15:18, B*35:01, B*35:08, B*40:05, B*46:01, B*49:01, B*50:01, B*51:01, B*51:02, B*52:01, B*53:01, B*56:01, B*57:01, B*57:03, B*58:01, B*78:01, C*03:02, C*03:03, C*03:04	163L 167W
189	163R	A*01:01, A*11:01, A*11:02, A*25:01, A*26:01, A*43:01, A*66:01	163R
190	163RG	A*01:01	163R 167G
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192	163T	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*03:01, A*23:01, A*23:02, A*24:02, A*24:03, A*29:01, A*29:02, A*30:01, A*30:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*36:01, A*68:01, A*68:02, A*69:01, A*74:01, B*08:01, B*14:01, B*14:02, B*14:05, B*14:06,	163T

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193	166DG	A*01:01, A*23:01, A*23:02, A*24:02, A*80:01, B*15:12	166D 167G
194	166ES	B*44:02, B*44:03, B*45:01, B*82:01, B*82:02	166E 167S
195	170RH	A*33:01, B*14:01, B*14:02, B*14:05, B*14:06, B*18:01, B*51:01, B*52:01, B*73:01, B*78:01	170R 171H
196	173K	C*03:02, C*03:03, C*03:04	173K
197	177DK	B*07:02, B*07:03, B*40:01, B*48:01, B*81:01	177D 178K
198	177DT	B*08:01, B*41:01, B*41:02, B*42:01	177D 178T
199	177KT	C*05:01, C*07:04, C*08:01, C*08:02	177K 178T
200	180E	B*07:02, B*07:03, B*08:01, B*40:01, B*41:01, B*41:02, B*42:01, B*48:01, B*81:01	180E
201	184A	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*25:01, A*26:01, A*29:01, A*29:02, A*32:01, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01	184A
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203	184R	C*17:01	184R (170G 171Y)
204	186R	A*33:01	186R
205	193AV	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*25:01, A*26:01, A*29:01, A*29:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01	193A 194V
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207	193PI	A*01:01, A*03:01, A*11:01, A*11:02, A*23:01, A*23:02, A*24:02, A*24:03, A*30:01, A*30:02, A*36:01, A*80:01,	193P 194I

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208	193PL	C*07:01, C*07:02, C*07:04	193P 194L (273S)
209	193PV	B*35:01, B*35:08, B*51:01, B*51:02, B*52:01, B*53:01, B*58:01, B*78:01, C*01:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:01, C*04:03, C*05:01, C*06:02, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*15:02, C*17:01, C*18:01, C*18:02	193P 194V
210	194V	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*25:01, A*26:01, A*29:01, A*29:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, B*35:01, B*35:08, B*51:01, B*51:02, B*52:01, B*53:01, B*58:01, B*78:01, C*01:02, C*02:02, C*02:10, C*03:02, C*03:03, C*03:04, C*04:01, C*04:03, C*05:01, C*06:02, C*08:01, C*08:02, C*12:02, C*12:03, C*14:02, C*15:02, C*16:01, C*17:01, C*18:01, C*18:02	194V
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212	207S	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*25:01, A*26:01, A*29:01, A*29:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, A*80:01	207S
213	211T	C*02:02	211T
214	219W	C*01:02, C*03:02, C*03:03, C*03:04, C*04:01, C*04:03, C*14:02, C*18:01, C*18:02	219W
215	245AS	A*25:01, A*26:01, A*29:01, A*29:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*74:01	245A 246S

216	245TA	B*48:01, B*81:01	245T 246A
217	245V	A*68:01, A*68:02	245V
218	248M	C*01:02	248M (6K) (99C)
219	253Q	A*02:01, A*02:02, A*02:03, A*02:05, A*02:06, A*25:01, A*26:01, A*29:01, A*29:02, A*31:01, A*32:01, A*33:01, A*33:03, A*34:01, A*34:02, A*43:01, A*66:01, A*66:02, A*68:01, A*68:02, A*69:01, A*74:01, B*73:01, C*07:01, C*07:02, C*07:04, C*17:01	253Q
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224	275K	B*73:01, C*04:01, C*04:03, C*17:01, C*18:01, C*18:02	275K

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Publications:

1) Itır Erkan, Kadir Dastan, Sedat Karadeniz, Yemliha Yıldız, Dilek Alpsar, Hülya Yükseloğlu, "Mitochondrial DNA analysis of the domestic dogs in Turkey", January 2017, European Journal of Forensic Sciences 4(3):1, DOI: 10.5455/ejfs.230996

2) Sedat Karadeniz, Sebahat Usta AkgulY, eliz Ogret, Kemal Yelekci, F. Aydin, "Corrected Panel-Reactive Antibody Positivity Rates for Hypersensitized Patients in Turkish Population With Calculated Panel-Reactive Antibody Software", April 2017, Transplantation Proceedings 49(3):445-447, DOI: 10.1016/j.transproceed.2017.01.032

3) Karadeniz, Sedat Tanju; Akgul, Sabahat; Ciftci, Hayriye Senturk; Ogret, Yeliz; Oguz, Fatma; Yelekci, Kemal; Aydin, Filiz, "Epitope Based Hla Matching By Using Antibody Reactivity With High Resolution Allele Typing And HLAMatchmaker Algorithm Based Software", WILEY, 2017

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2022, Türk Biyokimya Dergisi / Turkish Journal of Biochemistry 47(3), DOI: 10.1515/tjb-2021-0083

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Presentations:

1) Sedat Karadeniz, Sebahat Usta, Rustu Suleyman Oguz, Yeliz Ogret, Kemal Yelekci, Fatma Savran Oguz," Augmented Virtual-Cross-Match for Donor-Induced Antibody Prediction by Using High Resolution HLA Typing and HLA Epitope Mapping for Better Donor Match", March 2018, Conference: 12th East West Immunogenetic Conference

2) Sedat Karadeniz, Cigdem Kekik Cinar, S. Rustu Oguz, Fatma Savran Oğuz, Kemal Yelekci, "Can Predicted T-Cell/B-Cell Epitopes And Most Possible Selective Antigen Recognized By Hla Antibodies Using Immunoinformatic Methods Help For Better Donor Match?", March 2019, DOI: 10.13140/RG.2.2.26292.94084, Conference: East West Immunogenetic Conference