

17th IHI Workshop

Epitope Study

Goals:

1. To determine what HLA epitope mismatches are immunogenic
2. To determine what outcomes are related to immunogenic epitopes

Inclusion Criteria

- First kidney transplant recipients: males and females without a history of pregnancy.
- Non-sensitized at time of transplant as defined by:
 - cPRA pre-transplant 0% based on Single Antigen Bead (SAB) analysis with all bead MFI less than 1000, or lower if a clear epitope specificity is present across many beads – all sera must have been tested to exclude a prozone effect
- Molecular HLA typing of donor and recipient
 - Class I – A, B, C
 - Class II – DR β _{1/3/4/5}, DQ α/β , DP α/βNGS full length genomic sequence of donor/recipient pairs:
Required NGS HLA loci: HLA-A, B, C, DRB1, DRB3/4/5, DQB, HLA-DQA, DPA, DPB
- If unable to perform the required NGS typing, contact Tamara Vayntrub at tamara.vayntrub@stanford.edu. We will help you identify a laboratory to collaborate with for NGS HLA typing.
- Two types of patients can be considered for entry into the study:
 - Patients who develop *de novo* DSA(s) post-transplant either:
 - while on maintenance immunosuppression, or
 - have documented graft loss from chronic antibody mediated rejection, and are now off immunosuppression.
 - Patients who do not develop a *de novo* DSA post-transplant despite at least 5 years of follow up.

Exclusion Criteria

- Repeat transplant
- Pregnancy (or DNA for NGS typing if history)
- Combined renal and non-renal transplants
- Sensitized patients at the time of transplant defined by cPRA by SAB >0%
- Absence of molecular HLA typing for the donor and/or recipient unless DNA is available for molecular typing.
- Patients who have no DSA but are less than 5 years post-transplant.

Study members will be required to provide the following data/samples to be eligible to participate:

Minimal requirements:

- HLA molecular typing files for all required loci on the donor and/or recipient or DNA available.
- Pre-transplant SAB Class I and Class II antibody testing files (including lot #)
- Prevention of prozone effect (specify method)
- Induction therapy
- Baseline immunosuppression at discharge
- Baseline immunosuppression at time of *de novo* DSA detection
- Baseline immunosuppression at 5 years / last follow up in non-DSA patients
- Time post-transplant of *de novo* DSA detection
- At time of first detection of *de novo* DSA the SAB Class I and Class II antibody testing files
- For patients who are listed as non-DSA formers at 5 years / last follow up SAB Class I and Class II antibody testing files

SOPs/Methods/reagents:

Project requires participants to follow Workshop SOPs, standardized specialty reagents, defined cutoffs:

SOPs:

- Luminex single antigen beads (SAB) from One Lambda, Inc.
- IHIWS Luminex IgG Single Antigen Bead Assay
- IHIWS Luminex-BioC1q Single Antigen Bead Assay

Reagents:

- One Lambda (only) SAB (LabScreen) including expanded ethnic panel
- IgG and Bio-C1q assays for class I and II **tested neat**

Ideal requirements (in addition to minimal requirements):

- HLA NGS typing files for all required loci on the donor and recipient
 - Alternatively DNA for donor and recipient for external NGS evaluation
- Pre-transplant sera for additional local / core laboratory evaluation
- Post-transplant sera at time of *de novo* DSA detection for additional local / core laboratory evaluation
- Post-transplant sera for patients who are listed as non-DSA formers at 5 years / last follow up for local / core laboratory evaluation

Outcome Data requirements (optional, not required unless specific to the sub-project analysis)

- Recipient age at time of transplant
- Recipient sex
- Donor age

- Whether patient was classified as adherent or non-adherent
- Target trough level of CNI (if used) after 6 months post-transplant
- Acute rejection events prior to de novo DSA detection
- Serum Creatinine at 6 months, at time of de novo DSA formation, and at last follow-up
- Acute rejection after de novo DSA formation + type (ABMR_{Banff2013}, TCMR, or both)
- Graft loss + time post-transplant + cause of graft loss