University of Chicago Medicine
Transplant Immunology and Immunogenetics Laboratory

HLA Testing Agreement for the Liver Transplant Program

This agreement adheres to the United Network for Organ Sharing (UNOS), the American Society for Histocompatibility and Immunogenetics (ASHI), College of American Pathologists (CAP), New York State Department of Health (NYSDOH) guidelines, and the OPTN bylaws.

1. Sample requirements
   - HLA typing:
     i. 3 yellow top tubes (ACD-Solution A), from both recipients and living donors, if applicable.
     ii. Initial work-up specimens are submitted to the Transplant Immunology and Immunogenetics Laboratory (TIIL) at a time proximal to but prior to transplant and stored in case of future need.
   - Antibody testing:
     i. 2 red top tubes (serum) from recipients only.
     ii. Initial work-up specimens will be submitted to the TIIL at a time proximal to but prior to transplant.
   - Allo and auto-crossmatch will not be performed under this agreement.

2. HLA loci and level of resolution typing: HLA typing of recipient and/or donor will only be performed when necessary to help with HLA antibody interpretation. This will be determined on a case-by-case basis, and only after consensus agreement between the TIIL and the liver transplant program is reached. In these cases, HLA high- or low-resolution molecular typing for HLA-A, B, C, DRB1 DRB3/4/5 (DR52/53/51), and DQB1 is performed.
   - Additional testing for the following loci are routinely performed: HLA-DPB1, DPA1 and/or DQA1
   - If typing for HLA-DPB1, DPA1 and/or DQA1 is not obtained, these loci will not be repeated or reported, unless the recipient has antibodies to these loci and/or typing is otherwise clinically relevant
   - If STAT typing is requested, HLA-A, B, C, DRB1 DRB3/4/5 (DR52/53/51), and DQB1 will be performed at low-resolution

3. To request additional testing not included in this agreement: the transplant program should send a request to the Transplant Immunology and Immunogenetics Laboratory (TIIL) by email at #HLA-TIILLab@uchospitals.edu or by pager #8722.

4. Process for resolving HLA typing discrepancies and errors: When a typing result is found to be different from that reported by another Histocompatibility testing laboratory, the following steps are taken:
   - The TIIL reviews typing, and if necessary, typing will be repeated using re-extracted DNA. This decision will be made for each case individually by the manager or director.
   - After testing has been reviewed, the other HLA laboratory is contacted to discuss the discrepancy and compare results to resolve the discrepancy.
   - This information is documented on the Quality Assurance: Corrective Action form with the appropriate documentation by the TIIL.

5. Turnaround time from receipt of sample to reporting of results to the transplant program:
   - HLA typing
     o Routine (high resolution): 7 business days (BD)
     o STAT (low resolution): 2 BD
     o Same-day STAT (low resolution): End of day, if sample received in lab before 9am

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• Antibody testing
  o Routine: 7 BD
  o STAT: 1-2 BD
  o Same-day STAT: End of day, if sample received in lab before 11am

NOTE: for STAT testing, the transplant program should send a request to the TIIL by email at #HLA-TIILLab@uchospitals.edu or by pager #8722.

6. **Process to obtain sensitization history for each patient:** The sensitization history for each patient is to be provided by the nurse coordinator, physician, or other member of the transplant team at the time of initial work-up and/or when a known immunization event (blood transfusion, pregnancy, or transplant) has occurred by:
   • Filling out the question/comment section associated with orders transmitted through Epic
   • E-mail or phone, when applicable
   • Completing a “Information of Potential Interfering factors for HLA antibody testing” form [Appendix A]

7. **Frequency of periodic sample collection:** Antibody testing will be performed only once for each patient, at the time of initial pre-transplant workup, unless an immunizing event has occurred, or otherwise requested by the liver transplant program. If additional pre-transplant samples are received by the laboratory, they will be discarded. The liver transplant program should notify the TIIL of the day of transplant to ensure correct categorization of pre and post-transplant samples.

8. **Frequency of pre-transplant antibody screenings:**
   • See section 6.
   • The transplant program is encouraged to send new samples 14 days after any potential immunizing event (blood transfusion, pregnancy, or transplant) to document the sensitizing event as well as to re-test patient sensitization status.

9. **Assay format for antibody screening:** HLA class I and class II antibody testing is performed by solid-phase assays. Based on antibody profile, antibody titers may be performed.

10. **Criteria for determining unacceptable antigens used during organ allocation:**
    • Antibody specificities will not be reported to UNOS, nor be used for organ allocation.

11. **Duration for which specimens need to be stored for repeat or future testing:**
    • Serum specimens collected from recipients are stored frozen in the TIIL for a minimum of 6 months.
    • If possible, serum specimens collected from deceased donors are stored frozen in the TIIL for 3 to 6 months. Isolated cells collected from deceased donors are stored for a minimum of one year. Storage beyond one year may not provide viable cells for future crossmatching.
    • If possible, buffy coats and DNA specimens collected from recipient and donors (living and deceased) are stored frozen in the TIIL for a minimum of 5 years.

*Duration of deceased donor specimen storage should be established in the agreement between the Transplant Program and Gift of Hope HLA laboratory.*

12. **Virtual Crossmatch**
    • The transplant program(s) must notify the TIIL by email (#HLA-TIILLAB@uchospitals.edu) of all patients listed in UNet for liver transplants combined with kidney transplant.
    • Prospective compatibility for combined transplant patients will be determined by virtual crossmatch (vXM). Physical XM may be requested based on individual cases and per surgeon discretion. If previous transplant donor typing and/or previous HLA testing information is available to the TIIL, the presence
of repeat mismatches and/or historic donor-specific antibodies (DSA) may be noted on the vXM report.

- All patients evaluated by vXM will be followed by a physical retrospective XM performed by the TIIL, assuming sufficient donor material has been provided.
- The most recent sample (≤ 90 days) available and tested by the TIIL by either FPRA or Luminex phenotype beads and if appropriate, by single antigen beads (SAB), will be used for vXM evaluation.
- If additional allele level HLA typing is necessary and not able to be obtained from the donor OPO, testing will be performed retrospectively by the TIIL.
- Patient specific circumstances may require a physical XM. These include, but not limited to, the following: when necessary antibody testing has not been completed, when testing results are unclear, when molecular typing is incomplete, and/or when requested by the transplant physicians.
- Only test results from the TIIL will be used to perform a virtual crossmatch; the TIIL is an ASHI and CAP accredited laboratory.

13. **Protocol for monitoring antibody levels pre and post-desensitization treatment:** This is determined on a case by case basis between the Transplant Program and the TIIL.

14. **Protocol for post-transplant monitoring of antibody levels:** Post-transplant testing will be handled on a case-by-case basis.
Appendix A

Information of potential interfering factors for HLA antibody testing

Patient Name: ______________________  MRN: ______________________
Completed by: ______________________  Date: ______________________

PRE-TRANSPLANT and/or CROSSMATCH TESTING

RECIPIENT
Infections
- Human Immunodeficiency Virus (HIV) YES NO
- Hepatitis C Virus (HCV) YES NO

Autoimmune diseases
- Systemic lupus erythematosus (SLE) YES NO
- Type 1 diabetes mellitus (Type 1 DM) YES NO
- Other (Sjogren's, etc.) YES NO

Blood transfusion(s) in the last 7 days YES NO

Treatments
- RituXan (rituximab) YES NO
- Antithymocyte globulin (ATG) YES NO
- Alemtuzumab (campath) YES NO
- Intravenous immunoglobulin (IVIG) YES NO

DONOR
Blood transfusion(s) in the last 7 days YES NO

POST-TRANSPLANT SOLID-PHASE ANTIBODY TESTING

RECIPIENT
Infections
- Human Immunodeficiency Virus (HIV) YES NO
- Hepatitis C Virus (HCV) YES NO

Autoimmune diseases
- Systemic lupus erythematosus (SLE) YES NO
- Type 1 diabetes mellitus (Type 1 DM) YES NO
- Other (Sjogren's, etc.) YES NO

Blood transfusion(s) in the last 7 days YES NO

Intravenous immunoglobulin (IVIG) YES NO

Please fill out this form (pre- or post-transplant section) and return to the Transplant Immunology and Immunogenetics Laboratory (TIIL) at #HLA-TIILab@uchospitals.edu or fax: (773)-834-5573.