Solid Organ and Hematopoietic Stem Cell Transplantation

Laboratory testing for transplant recipients of solid organs and hematopoietic stem cells includes compatibility testing (human leukocyte antigen [HLA] typing, HLA antibody screen) and post-transplant infectious disease detection. Pre-transplant evaluation by HLA typing and antibody screen assesses the risk of transplant rejection.[1] Infectious disease testing helps address post-transplant complications related to infection, which are among the most common types of complications affecting transplant outcomes.[2]

This Test Guide discusses the use of laboratory tests that help match donors and recipients for solid organ and bone marrow transplantation, including low-, intermediate-, and high-resolution HLA typing, as well as HLA antibody screening and identification. The guide also discusses tests that identify and monitor infectious disease in post-transplant recipients, including tests for latent, opportunistic, and community-acquired infections. Test selection and interpretation, diagnosis, and patient management decisions should be based on the physician's education, clinical expertise, and assessment of the patient.

COMPATIBILITY TESTING

A person's HLA type and antibody profile are important for assessing immunological compatibility between donor and recipient, as incompatibility can result in transplant rejection. HLA typing and antibody testing can help assess donor-recipient immunological risk. Testing options vary by HLA class and resolution (**Table 1**).

HLA proteins are grouped into 2 classes: class I includes A, B, and C antigens, and class II includes DR, DQ, and DP antigens. HLA A, B, and DR antigens are considered the most important in transplant survival; however, current Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS) guidelines mandate molecular typing of all HLA loci, which may be performed at different levels of resolution depending on transplant center requirements.[3,4] DNA-based typing at low-resolution identifies the group of alleles that encode a particular HLA antigen. Intermediate-resolution typing is limited to particular allele groups expected in a population. High-resolution typing allows for a more precise determination of an allelic variant by identifying variants based on differences in antigen recognition site domains. HLA antibody tests identify preformed antibodies to donor HLA antigens in transplant recipients, which may develop from prior sensitization.[5]

Table 1. Donor–Recipient Compatibility Tests for Solid Organ and Bone Marrow Transplantation

Test code	Test name
HLA typing	
92157	HLA A, B, C, Class I Typing, Intermediate Resolution[a]
92076	HLA-A, B, C, DRB1 and DQ High Resolution
92078	HLA-A, B, C High Resolution
15484	HLA A, B, C Low Resolution[a]
92158	HLA-A, B, Intermediate Resolution[a]
15757	HLA A, B Low Resolution[a]
92044	HLA A 02:01 Determination[a]
10951	HLA A Low Resolution[a]
17397	HLA A Typing, High Resolution[a]
92746	HLA-B*15:02 Determination with Reflex to HLA-B High Resolution[a]
10950	HLA B Low Resolution[a]

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Table 1. Donor–Recipient Compatibility Tests for Solid Organ and Bone Marrow Transplantation *(Continued)*

Test Code	Test name
17395	HLA C High Resolution[a]
15463	HLA C Low Resolution[a]
95730	HLA DPB1 Typing, High Resolution[a]
19525	HLA DQA1 Low Resolution[a]
10953	HLA DQB1 Low Resolution[a]
17394	HLA DQB1 Typing, High Resolution[a]
92159	HLA DRB1, DQB1, Intermediate Resolution[a]
15485	HLA DRB1, DQB1 Low Resolution[a]
97112	HLA DRB1,3,4,5,DQB1, Low Resolution[a]
10952	HLA DRB1 Low Resolution[a]
19526	HLA DRB3,4,5 Low Resolution[a]
17393	HLA DRB1 Typing, High Resolution[a]
95732	HLA DRB3,4,5 Typing, High Resolution[a]
92160	HLA DRB1 Typing, Intermediate Resolution[a]
92161	HLA DRB3,4,5 Typing, Intermediate Resolution[a]
HLA antibody screening and identification	
95731	HLA Antibody Identification, Class I[a]
97111	HLA Antibody Identification, Class II[a]
95735	HLA Antibody Screen, Class I[a]
95736	HLA Antibody Screen, Class II[a]

[a] This test was developed and its performance characteristics determined by this laboratory. It has not been cleared or approved by the US Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) as qualified to perform high complexity clinical laboratory testing.

POST-TRANSPLANT INFECTIOUS DISEASE TESTING

The risk of post-transplant infection varies with a patient's state of immunosuppression and source of infectious exposures.[6,7] Reactivation of donor-derived latent infections commonly occur within the first 4 weeks after transplantation, followed by a 1- to 12-month period during which patients who are immunosuppressed are at risk for opportunistic bacterial, fungal, or viral infections.[7-10] After 1 year, patients are at highest risk for community-acquired infections.[7] Certain types of infectious diseases are more common depending on epidemiological exposure, which may help guide diagnostic testing (**Table 2**).

Table 2. Post-transplant Tests for Infectious Diseases

Test code	Test name
39950	Specialized Transplant Services, Post-Transplant[a]
Donor-derived latent infections (<4 weeks)	
18143	Post-Transplant, Cytomegalovirus DNA, Real-Time PCR, Blood[b]
18142	Post-Transplant, Cytomegalovirus DNA, Real-Time PCR, Plasma[b]
18144	Post-Transplant, Cytomegalovirus DNA, Real-Time PCR, Respiratory[b]
18141	Post-Transplant, Cytomegalovirus DNA, Real-Time PCR, Serum[b]
18060	Post-Transplant, Hepatitis B Virus DNA, Real-Time PCR, Plasma[b]
18059	Post-Transplant, Hepatitis B Virus DNA, Real-Time PCR, Serum[b]
18104	Post-Transplant, Hepatitis C Viral (HCV) RNA, Real-Time PCR, Plasma[b]
18103	Post-Transplant, Hepatitis C Viral (HCV) RNA, Real-Time PCR, Serum[b]
18003	Post-Transplant, HIV-1 RNA, Real-Time PCR, Plasma[b]
Opportunistic (1 month to 12 months) and community acquired infections (>12 months)	
18122	Post-Transplant, Adenovirus DNA, Real-Time PCR, Blood[b]
18120	Post-Transplant, Adenovirus DNA, Real-Time PCR, Plasma[b]
18124	Post-Transplant, Adenovirus DNA, Real-Time PCR, Respiratory[b]
18118	Post-Transplant, Adenovirus DNA, Real-Time PCR, Serum[b]
18126	Post-Transplant, Adenovirus DNA, Real-Time PCR, Urine[b]
18000	Post-Transplant, *Aspergillus* DNA, Qualitative Real-Time PCR, Blood[b]
18001	Post-Transplant, *Aspergillus* DNA, Qualitative Real-Time PCR, Respiratory[b]
18051	Post-Transplant, BK Virus DNA, Real-Time PCR, Blood[b]
18050	Post-Transplant, BK Virus DNA, Real-Time PCR, Plasma[b]
18049	Post-Transplant, BK Virus DNA, Real-Time PCR, Serum[b]
18052	Post-Transplant, BK Virus DNA, Real-Time PCR, Urine[b]
18143	Post-Transplant, Cytomegalovirus DNA, Real-Time PCR, Blood[b]
18142	Post-Transplant, Cytomegalovirus DNA, Real-Time PCR, Plasma[b]
18144	Post-Transplant, Cytomegalovirus DNA, Real-Time PCR, Respiratory[b]
18141	Post-Transplant, Cytomegalovirus DNA, Real-Time PCR, Serum[b]
18090	Post-Transplant, Epstein-Barr Virus DNA, Real-Time PCR, Blood[b]
18089	Post-Transplant, Epstein-Barr Virus DNA, Real-Time PCR, Plasma[b]
18088	Post-Transplant, Epstein-Barr Virus DNA, Real-Time PCR, Serum[b]
18060	Post-Transplant, Hepatitis B Virus DNA, Real-Time PCR, Plasma[b]
18059	Post-Transplant, Hepatitis B Virus DNA, Real-Time PCR, Serum[b]

(Continued)

Table 2. Post-transplant Tests for Infectious Diseases *(Continued)*

Test code	Test name
18104	Post-Transplant, Hepatitis C Viral (HCV) RNA, Real-Time PCR, Plasma[b]
18103	Post-Transplant, Hepatitis C Viral (HCV) RNA, Real-Time PCR, Serum[b]
18022	Post-Transplant, Herpesvirus 6 DNA, Real-Time PCR, Blood[b]
18020	Post-Transplant, Herpesvirus 6 DNA, Real-Time PCR, Plasma[b]
18019	Post-Transplant, Herpesvirus 6 DNA, Real-Time PCR, Serum[b]
18078	Post-Transplant, Herpesvirus 7 DNA, Real-Time PCR, Blood[b]
18076	Post-Transplant, Herpesvirus 7 DNA, Real-Time PCR, Plasma[b]
18074	Post-Transplant, Herpesvirus 7 DNA, Real-Time PCR, Serum[b]
18132	Post-Transplant, Herpesvirus 8 DNA, Real-Time PCR, Blood[b]
18130	Post-Transplant, Herpesvirus 8 DNA, Real-Time PCR, Plasma[b]
18128	Post-Transplant, Herpesvirus 8 DNA, Real-Time PCR, Serum[b]
18003	Post-Transplant, HIV-1 RNA, Real-Time PCR, Plasma[b]
18011	Post-Transplant, JC Virus DNA, Real-Time PCR, CSF[b]
18010	Post-Transplant, JC Virus DNA, Real-Time PCR, Plasma[b]
18009	Post-Transplant, JC Virus DNA, Real-Time PCR, Serum[b]
18070	Post-Transplant, Parvovirus B19 DNA, Real-Time PCR, Blood[b]
18068	Post-Transplant, Parvovirus B19 DNA, Real-Time PCR, Plasma[b]
18066	Post-Transplant, Parvovirus B19 DNA, Real-Time PCR, Serum[b]
18110	Post-Transplant, *Toxoplasma gondii* DNA, Real-Time PCR, CSF[b]
18109	Post-Transplant, *Toxoplasma gondii* DNA, Real-Time PCR, Plasma[b]
18108	Post-Transplant, *Toxoplasma gondii* DNA, Real-Time PCR, Serum[b]
18146	Post-Transplant, Varicella-zoster Virus DNA, Real-Time PCR, Blood[b]
18148	Post-Transplant, Varicella-zoster Virus DNA, Real-Time PCR, CSF[b]
18005	Post-Transplant, *Pneumocystis jiroveci*, Real-Time PCR, Respiratory[b]

[a] Specialized transplant services include collection and shipping kits provided to the customer, direct shipping via FedEx, post-transplant-specific requisitions, and rapid turnaround (8-12 hours from laboratory receipt of sample). Test code 39950 designates special handling for these services; it is a single-use test code that may be applied to 1 or more tests in this section.

[b] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by FDA. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

OTHER TESTS

Laboratory tests can also be used during early follow-up to evaluate transplant viability, bone marrow cell engraftment, cell-mediated immune response complications, and the possibility of rejection or complications (**Table 3**).

Laboratory tests can also be used to monitor immunosuppressive and antifungal drug therapies (**Table 4**) and help optimize dose, avoid toxicity, and assure patient adherence.

Table 3. Post-transplant Testing for Early Follow-up

Test code	Test name	Primary clinical use
4944	Beta-2-Microglobulin, Random Urine	Evaluate transplant viability and anticipate rejection
38994	Beta-2-Microglobulin, Random Urine with Creatinine	
852	Beta-2-Microglobulin, Serum	
14619	FISH, X/Y, Post Bone Marrow Transplant (BMT)	Monitor progression of bone marrow cell engraftment when bone marrow is from a donor of the opposite sex
15435	Immune Cell Function	Monitor cell-mediated immune response to optimize immunosuppressant therapy
34298	Interleukin-2 Receptor Alpha Chain (IL-2Ra/CD25), Soluble[a]	Assess possibility of acute transplant rejection
34473	Interleukin-6 (IL-6), Serum[a]	Assess possibility of transplant-related complications after hematopoietic stem cell transplantation (SCT)
93917	Neopterin, Serum[b]	Monitor cell-mediated immunity

[a] This test was performed using a kit that has not been cleared or approved by the FDA. The analytical performance characteristics of this test have been determined by Quest Diagnostics. This test should not be used for diagnosis without confirmation by other medically established means.

[b] This test was performed using a kit that has not been cleared or approved by the FDA. The analytical performance characteristics of this test have been determined by Laboratory Corporation of America (LabCorp). This test should not be used for diagnosis without confirmation by other medically established means.

Table 4. Post-transplant Testing for Therapeutic Drug Monitoring

Test code	Test name	Primary clinical use
Immunosuppressive therapy		
10720	Cyclosporine A Panel (Trough, 1 Hour, 2 Hour Post)	Monitor immunosuppressive therapy to optimize dose, avoid toxicity, and help assure adherence to a treatment regimen
10719	Cyclosporine A Peak (2 Hour), Blood	
8812	Cyclosporine A, Trough, Blood	
15220	Cyclosporine A Trough, LC/MS/MS, Blood[a]	
18883	Everolimus, LC/MS/MS, Blood[a]	
10662	Mycophenolic Acid[a]	
36712	Sirolimus, LC/MS/MS[a]	
70007	Tacrolimus, Highly Sensitive, LC/MS/MS[a]	
91745	Thiopurine Metabolites[a]	
Antifungal therapy		
94092	Itraconazole[a]	Monitor drug levels when unexpected toxicity is encountered; optimize dosage when drug interactions are suspected
94010	Posaconazole[a]	
94096	Voriconazole[a]	
94692	Voriconazole, CSF[a]	

[a] This test was developed and its analytical performance characteristics have been determined by Quest Diagnostics. It has not been cleared or approved by the FDA. This assay has been validated pursuant to the CLIA regulations and is used for clinical purposes.

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