Chimerism by STR Genotyping

MONITORS ENGRAFTMENT OF DONOR CELLS TO ASSESS GRAFT SUCCESS OR DISEASE RECURRENCE AFTER ALLOGENIC STEM CELL TRANSPLANTATION

Clinical Background

- Assessing chimerism, the ratio of recipient to donor cells, is essential for monitoring engraftment of donor cells to assess graft failure or relapse of disease after allogenic stem cell transplantation (SCT).
- Serial analysis of chimerism allows for continual monitoring of cellular processes.
- Full chimerism refers to a recipient with exclusively donor hematopoietic cells post- transplant. Mixed chimerism (which can be classified as transient, stable, or progressive) describes the presence of both recipient and donor hematopoietic cells.
- Conventional SCT is used to treat malignant hematological conditions by eradication of the recipient's immune system using cytostatic drugs and total-body irradiation. The goal of such treatment is full chimerism.
- Reduced-intensity SCT (or minitransplantation) may be used in the treatment of chronic myeloid leukemia (CML) and leads to a mixed chimeric state.
- The use of donor lymphocyte infusion (DLI) after reduced-intensity SCT may depend on the chimeric status of the recipient, as the presence of donor cells is required to ensure the recipient is still tolerant to the graft.
- Selection of specific cell lineages for chimerism analysis may be relevant after reduced-intensity SCT. Cell sorting selects for the cell subset matching the immunophenotype of the original leukemic clone. As mixed chimerism in a recipient may be caused by the recurrence of leukemic cells or normal recipient hematopoiesis, cell sorting may help differentiate between these possibilities.
- SCT for benign hematological disorders does not require complete donor chimerism for a successful outcome.

Genetics

- Chimerism testing commonly uses a panel of polymorphic short tandem repeat (STR) markers with allele sizes that differ among individuals.
- To be informative, an STR marker must have allele sizes that differ between the donor and recipient. The number of informative markers is greater when an unrelated donor is used. A minimum of one informative locus for each donor/recipient pair is required for chimerism analysis.
- A sex marker, amelogenin, will be informative for sex-mismatched donor/recipient pairs.
- Pre-transplant STR genotypes for the recipient and putative donor are required for post-transplant chimerism analysis.
- If a patient receives transplants from different donors, an informative locus for the patient and each donor must be identified.
- Fluorescence in situ hybridization (FISH) analysis may also be used to assess chimerism but is limited to cases with sex-mismatched donor/recipient pairs and has a lower sensitivity than STR analysis.
- STR genotyping is more sensitive than using HLA markers for monitoring engraftment, as donors are HLA-matched to recipients.

Indications for Ordering

- Routine post-transplant monitoring of donor/recipient origin of white blood cells in peripheral blood and/or marrow; assessment may include lineage-specific cell subsets (e.g., CD3-positive T cells or CD33-positive myeloid cells).
- Prognostic testing for risks of graft rejection and recurrence of disease.
- Document the presence of donor cells in post-transplant patients with residual disease or prior to donor lymphocyte infusion (DLI).
- Evaluate donor/recipient cells in patients with inadequate marrow function.
- Determine if malignancy is a recurrence from recipient cells or a new occurrence from donor cells.
- Differentiate donor cell populations in recipients who have received multiple transplants.

Additional Ordering Notes

- Post-transplantation results will be compared to pre-transplant recipient and donor genotypes; therefore, donor and recipient samples must be obtained and genotyped before the transplant.
- If a recipient pre-transplant sample is not available, buccal brushes or hair root samples may be acceptable.

Contraindication

Chimerism testing by STR analysis is not informative for donor/recipient pairs who are identical twins.

500 Chipeta Way, Salt Lake City, UT 84108 | (800) 522-2787 | (801) 583-2787 | www.aruplab.com | www.arupconsult.com
ARUP is an enterprise of the University of Utah and its Department of Pathology.

Interpretation

- Donor or recipient pre-transplant genotyping:
  - Provides the number of informative markers identified for the donor/recipient pair.
- Recipient post-transplant genotyping:
  - Provides the number of informative markers used in analysis.
  - Lists the mean percentage of recipient and donor cells present in the sample.
  - Provides the 95 percent confidence interval.
- Correlation with clinical status and consideration of the time interval between SCT and chimerism testing is necessary for proper interpretation of results.

Methodology

- Specimens are analyzed by PCR followed by capillary electrophoresis using 15 autosomal markers (D8S1179, D21S11, D7S820, CSF1PO, D3S1358, THO1, D13S317, D16S539, D2S1338, D19S433, vWa, TPOX, D18S51, D5S818, and FGA) and one gender marker (amelogenin).
- Analytical sensitivity is 98 percent.

Limitation

Minor cells populations consisting of <2 percent of the total population may not be detected.

References

1. Matsuda K, et al. Monitoring of hematopoietic chimerism by short tandem repeats and the effect of CD selection on its sensitivity. *Clin Chem* 2004;50(12):2411–4.
2. McCann SR, et al. Hematopoietic chimerism following stem cell transplantation. *Transfus Apher Sci* 2005;32(1):55–61.
3. Nollet N, et al. Standardisation of multiplex fluorescent short tandem repeat analysis for chimerism testing. Bone Marrow *Transplant* 2001;28:511–8.

Test Information

2002067 Chimerism, Donor
2002065 Chimerism, Recipient Pre-Transplant
2002066 Chimerism, Post-Transplant
2002064 Chimerism, Post-Transplant, Sorted Cells

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.