Chimerism by STR Genotyping

Indications for Ordering

- Routine posttransplant monitoring of donor/recipient origin of white blood cells in peripheral blood and/or bone marrow
  - Assessment may include lineage-specific cell subsets
- Prognostic testing for risks of graft rejection and recurrence of disease
- Document presence of donor cells in posttransplant patient 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 or new occurrence from donor cells
- Differentiate donor cell populations in recipients who have received multiple transplants

Test Description

PCR followed by capillary electrophoresis for the following markers

- D8S1179, D21S11, D7S820, D3S1358, D13S317, D16S539, D2S1338, D19S433, D13S317, D16S539, D2S1338, 19S433, D18S51, D5S818, CSF1PO, THO1 vWa, TPOX, FGA, and one gender marker (amelogenin)

Tests to Consider

Primary tests

Chimerism, Donor 2002067
- Assesses donor genotype

Chimerism, Recipient Pre-Transplant 2002065
- Assesses recipient genotype before transplant

Chimerism, Post-Transplant 2002066
- Monitors engraftment of donor cells after transplant
- Pretransplant genotype of recipient and donor required for comparison
- If pretransplant genotype of recipient is unavailable, buccal brush or hair root samples may suffice

Chimerism, Post-Transplant, Sorted Cells 2002064
- Monitors engraftment of donor cells after transplant
- Pretransplant genotype of recipient and donor required for comparison
- Include "Cell Isolation Request for Chimerism, Post-Transplant, Sorted Cells" form with order
- Each cell sort must have a unique ARUP accession number

Disease Overview

Definitions

- Chimerism – ratio of recipient to donor cells
- Full chimerism – recipient with exclusively donor hematopoietic cells present posttransplant
- Mixed chimerism – both recipient and donor hematopoietic cells present posttransplant
  - Can be classified as transient, stable, or progressive
- Conventional stem cell transplant (SCT) – causes eradication of recipient's immune system
  - Used to treat malignant hematological disorders, genetic defects in metabolism
  - Leads to full chimeric state
- Reduced-intensity SCT (minitransplantation)
  - Used in treatment of chronic myeloid leukemia
  - Leads to mixed chimeric state

Treatment issues

- Assessing chimerism is essential for monitoring of donor cells after allogeneic SCT to determine
  - Successful engraftment
  - Relapse of disease
  - Evaluation of graft rejection
- PCR is more sensitive than FISH
  - FISH requires sex-mismatched donor-recipient pairs
- Short tandem repeat (STR) genotyping is more sensitive than HLA markers for monitoring engraftment because recipient and donor are HLA matched
- Serial analysis allows for continual monitoring
  - Development of mixed chimerism in posttransplant leukemic states is associated with relapse
- Chimerism (lineage-specific) may be important if DLI use is considered after reduced-intensity SCT
  - Presence of donor cells is required to ensure recipient is tolerant to the graft
- Use of cell sorting after reduced-intensity SCT may help in mixed chimerism states to differentiate between recurrence and normal hematopoiesis

Genetics

- Testing consists of a panel of STR markers with allele sizes that differ among individuals
- STR marker must have allele sizes that differ between the donor and recipient
  - Minimum of 1 informative locus for each donor/recipient pair is required for chimerism analysis
- Gender marker (amelogenin) is informative for sex-mismatched donor/recipients

Test Interpretation

Analytical sensitivity – 98%

Results

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

Limitations

- Cannot be used if donor and recipient are identical twins
- Posttransplant testing requires pretransplant sample for comparison
- Minor cell populations consisting of <2% of total population may not be detected