Erythroid Chimerism

Versiti offers Erythroid Chimerism testing designed to monitor transplantation in sickle cell patients. Sickle cell disease (SCD) is a common and severe autosomal recessive disorder caused by a missense mutation in the hemoglobin gene (HBB) resulting in hemoglobin S (HbS). Nonmyeloablative allogeneic hematopoietic cell transplantation (HCT) is increasingly being used to treat severely affected SCD patients by engraftment of donor cells that produce normal hemoglobin (HbA).

Several studies have demonstrated that chimerism measured in the nucleated cell compartment does not always reflect the engraftment in the erythroid lineage.[1,2] Assessment of the chimerism in the erythroid lineage may be a better indicator of donor erythropoiesis. As red cells do not contain DNA, chimerism in the erythroid compartment can be monitored using quantitative measurements of HbA and HbS trancripts produced from the hemoglobin gene (HBB) expressed in red cell progenitors.

Mixed chimerism is observed in a large proportion of patients after HCT. Most patients transition to complete donor chimerism. Some patients have long-term persistent mixed chimerism without need of red cell support even with a low percentage of donor-derived nucleated cells since an adequate amount of the normal HBB transcript, HbA, is being made.[2]

Indications for testing:

- Monitor erythroid lineage chimerism in patients with sickle cell disease following allogeneic bone marrow transplantation
- Monitor effects of post-transplant therapies.

Test method:

Reverse transcription of total RNA followed by digital droplet PCR with fluorescently-labeled hydrolysis probes specific for the HBB gene HbA and HbS transcripts. The percent chimerism is calculated taking into account the genotype of the donor (AA or AS).

Assay sensitivity and limitations:

- Assay is limited to SCD patients with SS genotype transplanted with a donor whose genotype is AA or AS.
- Genotype of the donor is required to accurately quantify chimerism.
- Assay sensitivity:
  - 1% HbA and 1% HbS transcript
  - 1% Donor and 1% Recipient when the donor genotype is AA
  - 1% Donor and ~5% Recipient when the donor genotype is AS
- Specificity/sensitivity may be affected by rare polymorphisms in the PCR priming or probe binding sites.

Reporting of results:

Results are reported as 0%-100% HbA, 0-100% HbS, 0-100% Donor and 0-100% Recipient.

Specimen requirements:

3-5 ml EDTA Bone Marrow (lavender top) or 10 ml EDTA Whole Blood (lavender top)

Minimum/Pediatric volume: 1 ml

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Sample must be received within 48 hours of collection.

Indicate on specimen tube and requisition whether sample is whole blood or bone marrow.

SHIP

Shipping requirements:

Place the room temperature specimen and requisition in plastic bags, seal and insert in a Styrofoam container. Seal the Styrofoam container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Address package to:

Versiti Client Services
Molecular Oncology & Genetics Laboratory
638 N. 18th St.
Milwaukee, WI 53233-2121
800-245-3117, ext. 6250

ORDER

Required forms:

Please complete all pages of the requisition form.

CPT Codes/Billing/Turnaround time:

Test Code: 4250

CPT codes: For recommended CPT codes, visit the versiti.org/test-catalog

Turnaround time: 6 days

References:

1. Wu, Catherine, et al. Molecular assessment of erythroid lineage chimerism following nonmyeloablative allogeneic stem cell transplantation. Experimental Hematology (2003) 31: 924-933.
2. Andreanni, Marco et al. Quantitatively different red cell/ nucleated cell chimerism in patient with long-term, persistent hematopoietic mixed chimerism after bone marrow transplantation for thalassemia major or sickle cell disease. Haematologica (2011) 96:128-133.

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