

## Overview

### Useful For

Evaluation of pediatric blood specimens for chromosomal abnormalities associated with hematologic malignancies for diagnostic and prognostic purposes in patients being considered for enrollment in Children's Oncology Group clinical trials and research protocols

This test is **not useful for** congenital disorders.

### Reflex Tests

| Test Id | Reporting Name        | Available Separately | Always Performed |
|---------|-----------------------|----------------------|------------------|
| ML20C   | COG Metaphases, 1-19  | No, (Bill Only)      | No               |
| M25C    | COG Metaphases, 20-25 | No, (Bill Only)      | No               |
| MG25C   | COG Metaphases, >25   | No, (Bill Only)      | No               |
| _STAC   | Ag-Nor/CBL Stain      | No, (Bill Only)      | No               |

### Testing Algorithm

**This test is only performed on specimens from pediatric patients who are candidates for enrollment in Children's Oncology Group (COG) clinical trials and research protocols.**

This test includes a charge for cell culture of fresh specimens and professional interpretation of results. Analysis charges will be incurred for total work performed, and generally include 2 banded karyograms and the analysis of 20 metaphase cells. If no metaphase cells are available for analysis, no analysis charges will be incurred. If additional analysis work is required, additional charges may be incurred.

If this test is ordered and the laboratory is informed that the patient is not on a COG protocol, this test will be canceled and automatically reordered as CHRHB / Chromosome Analysis, Hematologic Disorders, Blood.

### Highlights

Cytogenetics testing is important for the diagnostic and prognostic classification of pediatric neoplasia, and it is a critical element for enrollment of children into clinical trials affiliated with the Children's Oncology Group (COG). For over 25 years the Mayo Clinic Genomics Laboratory has served as one of a select number of laboratories in the United States approved by the COG for the conventional chromosome analysis and fluorescence in situ hybridization analysis of pediatric bone marrow, peripheral blood, and tissue specimens.

All enrollment-required elements of cytogenetics testing will be electronically submitted by the Mayo Clinic Genomics laboratory within the guidelines of COG.

### Method Name

Cell Culture without Mitogens followed by Chromosome Analysis

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**NY State Available**

Yes

**Specimen****Specimen Type**

Whole blood

**Ordering Guidance**

**This test is only performed on specimens from pediatric patients being considered for enrollment in a Children's Oncology Group (COG) protocol.** For all other patients, order CHRHB / Chromosome Analysis, Hematologic Disorders, Blood.

For children in whom disease relapse or a secondary myeloid neoplasm is a concern and enrollment in a new COG protocol is being considered; order COGBM / Chromosome Analysis, Hematologic Disorders, Children's Oncology Group Enrollment Testing, Bone Marrow.

Consultation with personnel from the Genomics Laboratory is recommended when considering blood studies for hematologic disorders. Call 800-533-1710 and ask for the Cytogenetics Genetic Counselor on call.

**Shipping Instructions**

Advise Express Mail or equivalent if not on courier service.

**Necessary Information**

1. A reason for testing, a flow cytometry and/or a bone marrow pathology report, and a Children's Oncology Group (COG) registration number and protocol number should be submitted with each specimen. The laboratory will not reject testing if this information is not provided, but appropriate testing and interpretation may be compromised or delayed.
2. If a child has received an opposite sex bone marrow transplant prior to specimen collection for this protocol, note this information on the request.

**Specimen Required****Specimen Type:** Blood**Container/Tube:****Preferred:** Yellow top (ACD)**Acceptable:** Green top (sodium heparin) or lavender top (EDTA)**Specimen Volume:** 6 mL**Collection Instructions:** Invert several times to mix blood.**Forms**

If not ordering electronically, complete, print, and send a [Children's Oncology Group Test Request \(T829\)](#) with the

specimen.

**Specimen Minimum Volume**

3 mL

**Reject Due To**

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

**Specimen Stability Information**

| Specimen Type | Temperature         | Time | Special Container |
|---------------|---------------------|------|-------------------|
| Whole blood   | Ambient (preferred) |      |                   |
|               | Refrigerated        |      |                   |

**Clinical & Interpretive**

**Clinical Information**

Clonal chromosomal abnormalities play a central role in the pathogenesis, diagnosis, and treatment monitoring of pediatric hematologic malignancies. Whenever possible, it is best to do chromosome studies for neoplastic hematologic disorders on bone marrow. Bone marrow studies are more sensitive and the chances of finding metaphases are about 95%, compared with only a 60% chance for blood studies. When it is not possible to collect bone marrow, chromosome studies on blood may be useful.

When blood cells are cultured in a medium without mitogens, the observation of any chromosomally abnormal clone may be consistent with a neoplastic process.

Characteristic chromosome rearrangements and copy number patterns may help classify a pediatric hematologic malignancy. For example, t(1;19)(q23;p13.3) is typically observed in B-cell acute lymphoblastic leukemia/lymphoma and t(8;21)(q22;q22) defines a specific subset of patients with acute myeloid leukemia; while t(7;14)(q35;q11.2) is associated with T-lymphoblastic leukemia/lymphoma. Confirmation of classic gene fusions associated with the above translocations together with evaluation for other recurrent abnormalities are available within the appropriate Children's Oncology Group (COG) fluorescence in situ hybridization (FISH) panels; COGBF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Children's Oncology Group Enrollment Testing, FISH, Varies; COGTF / T-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Children's Oncology Group Enrollment Testing, FISH, Varies; and COGMF / Acute Myeloid Leukemia (AML), Children's Oncology Group Enrollment Testing, FISH, Varies. Some rearrangements identified by chromosomal analysis may be extremely rare but are known, recurrent entities for which the Mayo Clinic Genomics Laboratory has the most extensive catalogue of FISH testing to confirm the corollary gene fusions.

Metaphase FISH confirmation of classic translocations which are cryptic and not visually detectable by chromosome analysis [ie, t(12;21)] associated with ETV6/RUNX1 fusion) is performed as required by COG and is included as part of the electronic case submission by the Mayo Clinic Genomics Laboratory to COG for central review.

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Additional cytogenetic techniques such as chromosomal microarray (CMAH / Chromosomal Microarray, Hematologic Disorders, Varies) may be helpful to resolve questions related to ploidy (hyperdiploid clone vs doubled hypodiploid clone) or to resolve certain clonal structural rearrangements such as the presence or absence of intrachromosomal amplification of chromosome 21 (iAMP21).

**Reference Values**

An interpretative report will be provided.

**Interpretation**

The presence of an abnormal clone usually indicates a malignant neoplastic process.

The absence of an apparent abnormal clone in blood may result from a lack of circulating abnormal cells and not from an absence of disease.

On rare occasions, the presence of an abnormality may be associated with a congenital abnormality and, thus, not related to a malignant process. When this situation is suspected, follow-up with a medical genetics consultation is recommended.

**Cautions**

Interfering factors:

Technical:

- Cell lysis caused by forcing blood quickly through the needle at collection
- Use of an improper anticoagulant or improperly mixing the blood with the anticoagulant
- Clotted blood specimen
- Excessive transport time
- Exposure of the specimen to extreme temperature

Biological:

- Abnormalities missed due to sampling error
- Subtle structural chromosome abnormalities may not be detected by conventional chromosome analysis
- Neoplastic cells not dividing or not circulating in the bloodstream

**Clinical Reference**

1. Dewald GW, Ketterling RP, Wyatt WA, Stupca PJ. Cytogenetic studies in neoplastic hematologic disorders. In: McClatchey KD, ed. *Clinical Laboratory Medicine*. 2nd ed. Williams and Wilkins; 2002: 658-685
2. Rigolin GM, Cibien F, Martinelli S, et al. Chromosome aberrations detected by conventional karyotyping using novel mitogens in chronic lymphocytic leukemia with "normal" FISH: correlations with clinicobiological parameters. *Blood*. 2012;119(10):2310-2313
3. Swerdlow SH, Campo E, Harris NL, et al, eds. *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. IARC Press; 2017
4. Arber DA, Borowitz MJ, Cessna M, et al. Initial Diagnostic Workup of Acute Leukemia: Guideline from the College of American Pathologists and the American Society of Hematology. *Arch Pathol Lab Med*. 2017;141(10):1342-1393

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**Performance****Method Description**

A cell count is performed to establish a plating volume. Based on the cell count, a corresponding volume of blood is added to 2 culture flasks containing culture medium and incubated for 24 to 48 hours at 37 degrees C. In the harvest process, the cells are exposed to Colcemid and hypotonic solution, and are fixed with glacial acetic acid and methanol. Metaphase cells are dropped onto microscope slides and are stained by G-banding. Other staining methods are employed as needed. Twenty metaphases are usually examined. If a clone is suspected, but not confirmed within 20 metaphases, 30 metaphases will be analyzed. Minimal evidence for the presence of an abnormal clone is defined as 2 or more metaphases with the same structural abnormality or chromosome gain (trisomy), or 3 or more metaphases lacking the same chromosome. All cells analyzed are captured using a computerized imaging system, and 1 or more karyograms from each clone are prepared to document the abnormality and to permit systematic interpretation of the abnormalities. (Arsham, Marilyn S., et al. eds. The AGT Cytogenetics Laboratory Manual. 4<sup>th</sup> ed. Wiley-Blackwell, 2017)

**PDF Report**

No

**Day(s) Performed**

Monday through Friday

**Report Available**

9 to 11 days

**Specimen Retention Time**

4 weeks

**Performing Laboratory Location**

Rochester

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**Fees & Codes****Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

**Test Classification**

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

**CPT Code Information**

88237, 88291-Tissue culture for neoplastic disorders; bone marrow, blood, Interpretation and report  
 88264 w/ modifier 52-Chromosome analysis with less than 20 cells (if appropriate)  
 88264-Chromosome analysis with 20 to 25 cells (if appropriate)  
 88264, 88285-Chromosome analysis with greater than 25 cells (if appropriate)  
 88283-Additional specialized banding technique (if appropriate)

### LOINC® Information

| Test ID | Test Order Name                     | Order LOINC® Value |
|---------|-------------------------------------|--------------------|
| COGBL   | COG-Chromosomes, Hematologic, Blood | 62386-8            |

| Result ID | Test Result Name       | Result LOINC® Value |
|-----------|------------------------|---------------------|
| 602315    | Result Summary         | 50397-9             |
| 602316    | Interpretation         | 69965-2             |
| 602317    | Result                 | 62356-1             |
| GC024     | Reason for Referral    | 42349-1             |
| 602318    | Specimen               | 31208-2             |
| 602319    | Source                 | 31208-2             |
| 602320    | Method                 | 85069-3             |
| 602321    | Banding Method         | 62359-5             |
| 602322    | Additional Information | 48767-8             |
| 602323    | Released By            | 18771-6             |