



Cleveland Clinic Laboratories

Hematology Diagnostic Services

Trust in us for everything you need in a reference lab.

OUR MISSION

The Pathology and Laboratory Medicine Institute contributes to excellent patient care by providing comprehensive, high quality laboratory testing and patient-focused expert consultation. This mission is supported by innovative research and new test development, exceptional customer service, continuous quality improvement and leadership in education.

OUR VISION

We will provide the highest quality laboratory testing and expert pathology diagnosis to patients institutionally, regionally and nationally.

OUR VALUES

Clinical Excellence – We provide comprehensive and high quality laboratory testing in a patient-responsive manner.

Expert Diagnosis – Diagnoses are provided by subspecialty experts, and consultation with physicians is important for patient care.

Continuous Quality Improvement – We are continuously evaluating and implementing the best practices in laboratory testing across the testing spectrum.

Dedication to Our Staff – Our staff are our most valuable resource and are supported and recognized for their accomplishments.

Innovative Test Development – A continual focus on new test development is important to provide the best capabilities for patient diagnosis.

Research and Education – Research is crucial for leadership in laboratory medicine; education and development are important at all levels.

INTEGRITY
EXPERTISE
REPUTATION
FOCUS
INNOVATION

Trust in us for everything you need in a reference lab.



Hematology Diagnostic Services

Cleveland Clinic Laboratories offers a full range of pathology expertise and advanced laboratory diagnostics for hematology. Our subspecialty services provide accurate and timely diagnosis, aid in prognostic stratification, and guide therapeutic selection and monitoring for a range of benign and malignant hematolymphoid disorders affecting pediatric and adult patients.

Our menu combines the state-of-the art laboratory diagnostics required in modern hematology practice with a foundation of expert consultation for bone marrow biopsies and lymphoid tissues. Our robust offerings in flow cytometry, molecular hematology, immunohistochemistry and cytogenetic karyotyping supply the data needed to answer today's complex hematology questions, while interpretation by our subspecialty trained hematopathologists complements this data with meaningful clinical context.

Our spectrum of services is designed to be flexible, from performing a single test to full-service consultation depending on the needs of each client and each case.

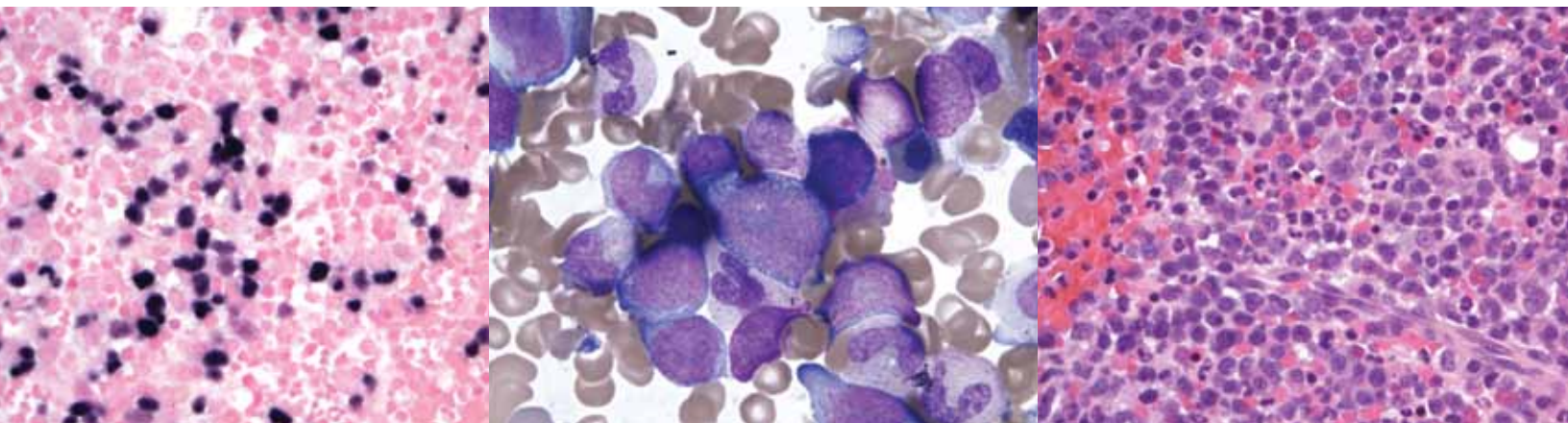




Expert Consultation Services

Hematology Diagnostic Services of Cleveland Clinic Laboratories offers prompt consultative services from pathologists with national and international reputations for diagnostic and academic excellence. Our experienced faculty is supported by technologically advanced hematology, immunophenotyping and molecular diagnostics laboratories.

- Consultations led by nationally recognized faculty and exclusively read by board-certified hematopathologists.
- Staff members publish extensively in leading medical journals, and serve on editorial boards of several journals.
- Our hematopathologists routinely collaborate with clinicians in the Cleveland Clinic Taussig Cancer Institute, named one of top 12 cancer hospitals in the country and No. 1 in Ohio by *US News & World Report*.





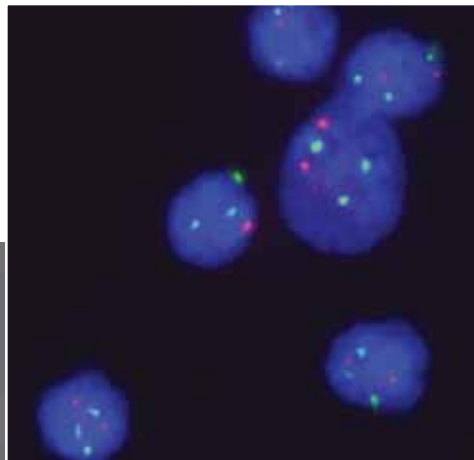
Core Diagnostic Capabilities

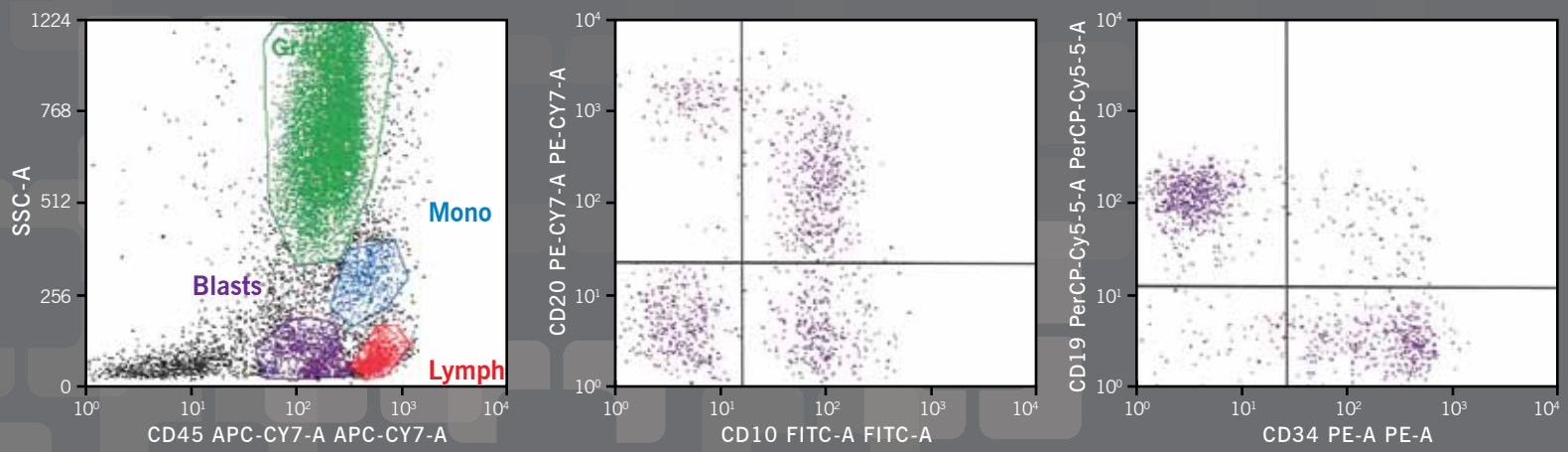
Our core diagnostic laboratories provide a wide variety of testing services to support our pathologists. Importantly, our expert faculty members gather and synthesize multiple pieces of information into one single diagnostic report.

Immunophenotyping services include automated immunohistochemical instruments that rapidly produce high quality stains with a test menu of more than 200 markers.

Multiparameter flow cytometers perform routine leukemia/lymphoma phenotyping as well as esoteric testing such as platelet flow cytometry and high sensitivity paroxysmal nocturnal hemoglobin-uria testing. Our full-service molecular diagnostics laboratory provides fluorescence *in situ* hybridization (FISH), immune receptor gene rearrangement and genetic mutational analyses required in modern hematology practice.

- Molecular diagnostics
- Flow Cytometry
- Immunohistology
- Cytogenetics Karyotyping





Research and Development

Research and development is an important activity of our laboratories. We constantly strive to develop new tests to better diagnose disease and manage patients. Translational research efforts span a wide variety of activities and include predictive and prognostic biomarker development, preclinical experimental therapeutic assessment, clinical trials correlative science, and new assay development funded through governmental and non-governmental sources. Our collaborators include local, national and international partners.

World-Class Customer Service

Cleveland Clinic Laboratories is focused in delivering world-class hematology diagnostic and laboratory medicine services to every client. Combining excellent turnaround times with a responsive Client Services department and prompt, accurate billing, the Department of Hematopathology delivers total customer satisfaction with every test result.

For more information about Hematology Diagnostic Services
at Cleveland Clinic Laboratories, please contact:

Customer Services:

216.444.5755 | 800.628.6816 (toll-free)

Submit specimens to:

Cleveland Clinic Laboratories
9500 Euclid Avenue, L15
Cleveland, OH 44195

Complete information about tests, specimen preparation
and ordering is available at clevelandcliniclabs.com



Cleveland Clinic

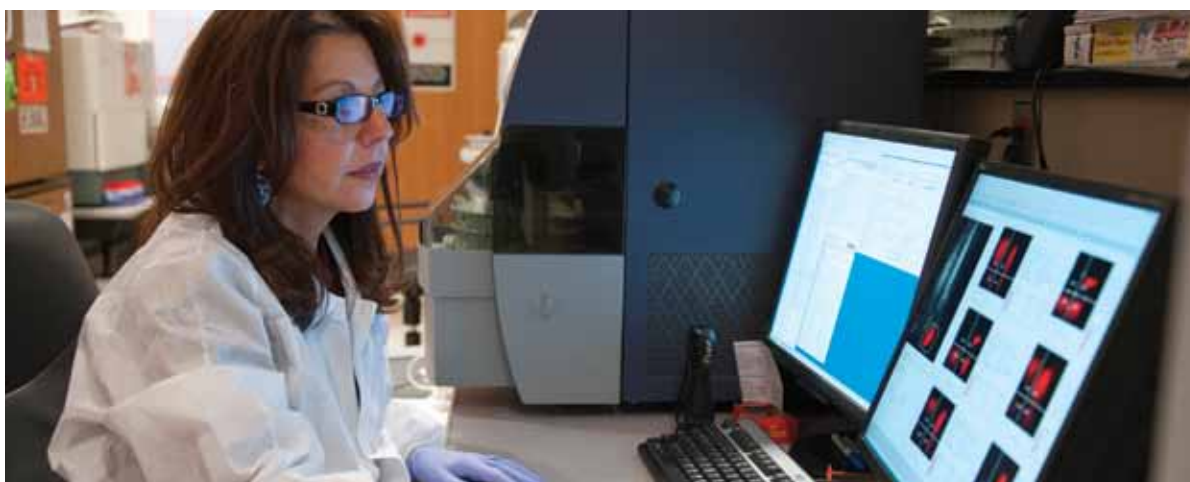
Every life deserves world class care.

9500 Euclid Avenue, Cleveland, OH 44195

Cleveland Clinic is an integrated healthcare delivery system with a main campus. 18 family health centers, eight community hospitals and locations in Ohio, Florida, Nevada, Toronto and Abu Dhabi. It is a not-for-profit group practice where nearly 3,000 staff physicians and scientists in 120 medical specialties collaborate to give every patient the best outcome and experience. Cleveland Clinic is ranked among America's top hospitals overall, and among the nation's leaders in every major medical specialty (*U.S. News & World Report*).
clevelandclinic.org

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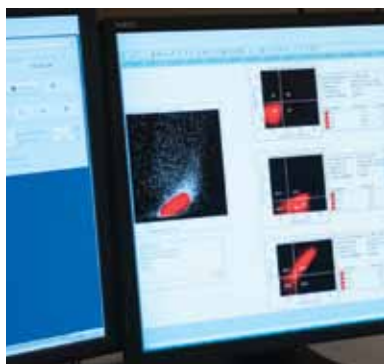
Flow Cytometry



The Flow Cytometry Laboratory provides a range of immunophenotyping services including assessment of leukemias and lymphomas, lymphocyte subsetting for immunodeficiency states and transplantation immunosuppression status, hematopoietic stem cell enumeration, and screening for paroxysmal nocturnal hemoglobinuria.

Blood samples are assessed for lymphocyte subsetting in whole blood, which may be performed as part of the initial diagnosis or in the setting of therapeutic monitoring.

Blood, bone marrow, body fluid and tissue samples suspected of being involved by leukemia or lymphoma undergo morphologic review and multiparameter flow cytometric immunopheno-



typing using antibody panels specifically designed to detect and characterize hematologic malignancies. Hematopathologists interpret the results in the context of morphologic findings, and provide information on clinical-pathologic correlations to assist clients in accurate and timely diagnosis.

Please see the Test Directory at clevelandcliniclabs.com for guidelines on specimen preparation and handling. For specific test information, please contact Client Services at 216.444.5755 or 800.628.6816 (toll-free).

Immunohistochemistry

The Immunohistochemistry Lab employs the latest technologies available to offer a wide range of stains with a rapid turnaround time.

Immunofluorescence stains are available for fresh and frozen tissue, while immunohistochemical stains and chromogenic *in situ* hybridization tests are performed on fixed, paraffin-embedded tissue. The appropriate positive controls are usually included on the same slide with the tissue to be stained. The lab also processes the paraffin blocks for the molecular tests, leading to tissue-saving practices. The immunohistochemistry lab is in close collaboration with the imaging core, allowing for a rapid scan of the stains. Stains can be employed in the work-up of a full hematopathology consult, and are also available to order as a stain only without professional interpretation. Slides from “stain only” orders may be scanned on a whole slide imager and made available for online viewing to allow for faster turnaround time.



Anatomic Pathology Special Stains

Special Stains Group II 88313	Primary Demonstration of:	Special Stains Group II 88313	Primary Demonstration of:
ASD “Leder’s modification”	Esterase, Mast cells	Giemsa (mast cell)	Eosinophilic granules and Mast cells
Colloidal iron	Mucopolysaccharides, Collagen	Iron stain	Iron
Colloidal Iron/Hyaluronidase	Differentiation of epithelial and connective tissue mucins	Reticulin	Stains for reticulum fibers
Congo Red	Amyloid	SAB	Amyloid
Crystal Violet	Amyloid	Thioflavin S	Amyloid
		Toluidine Blue	Mast cell granules

Immunohistochemistry Stains

Stain	Antibody Specificity	Stain	Antibody Specificity
ALK-1	ALK	CD1a	Cortical thymocytes-Langerhans cells
ALK(D5F3)	ALK	CD2	T-cells, NK cells
Amyloid A	Amyloidosis	CD3	T-Cells
Amyloid Kappa	Amyloidosis	CD4	T-Cells, Helper T
Amyloid Lambda	Amyloidosis	CD5	Pan T-cells, B-cell subset, Thymic carcinomas
BCL-2	Follicular lymphoma, anti-apoptotic protein	CD7	Thymocytes, Immature T-cells, NK cells,
BCL-6	Follicular and diffuse lymphomas, Burkitt lymphoma	CD8	T-Cells, Suppressor T
beta F1	T-Cells	CD10	Common acute lymphoblastic leukemia

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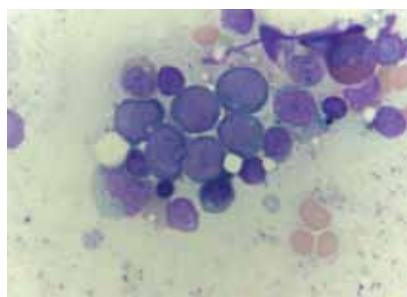
Immunohistochemistry Stains *continued*

Stain	Antibody Specificity	Stain	Antibody Specificity
CD15	Epithelial/Hodgkin/Myeloid cells	Cyclin D1	Cyclin D1/PRAD-1 oncogene product, Mantle cell lymphoma
CD20	Human B-lymphocyte antigen	EBV	Epstein-Barr virus
CD21	Dendritic cells, B-cells	Factor VIII	Von Willebrand factor, Endothelium and megakaryocytes
CD22	Mature B-cells	Fascin	Hodgkin Lymphoma, High grade breast carcinoma
CD23	Dendritic cells, Activated B-cells	Granzyme B	Serine protease
CD30	Activated T, B, RS cells	Hemoglobin-A	Hemoglobin-A
CD33	Monocytes, Myeloid cells	IgA	Immunoglobulin A
CD34	Endothelium, Stem cells, Stromal tumors	IgD	Immunoglobulin D
CD35	Dendritic cells	IgG	Immunoglobulin G
CD43	T-cells, B-cell subset, Myeloid, Histiocytes, Plasma cells (leukosialin)	IgG4	Autoimmune pancreatitis
CD44	Phagocytic glycogen-1	IgM	Immunoglobulin M
CD45	Leukocytes	Ki67	Cell proliferation marker
CD45RO	Helper, Inducer T-Cells	Kappa	Kappa light chain
CD56	Natural Killer cells	Lambda	Lambda light chain
CD57	Neural and neuroendocrine marker NK cells, Stromal tumors	Langerin	Langerhans cells
CD61	GP111A	LEF1	CLL/SLL
CD68 (KP-1)	Myelocytes/Macrophages	Mast Cell Tryptase	Human mast cells
CD68 (PG-M1)	Monocytes/Macrophages	MUM-1	Multiple myeloma oncogene-1
CD71	Erythroid progenitors	Muramidase	Muramidase/Lysozyme
CD79a	B-cells	Myeloperoxidase	Neutrophilic granulocytes and monocytes
CD117	Immature cells, GIST	OCT2	Octamer transcription factor 2
CD123	Alpha receptor for IL3	p53	Overexpression of the p53 oncogene
CD138	Plasma cell marker, Syndecan	PD1	Follicular helper T-cells
CD163	Monocytes/Macrophages	Sox11	Mantle cell lymphoma
CISH EBER	Epstein-Barr virus small RNA	TCR gamma	T-Cells
CISH Kappa	Kappa light chains mRNA	TDT	Blasts, immature lymphocytes
CISH Lambda	Lambda light chains mRNA	TIA	Cytolytic effector cells in lymphocytic infiltrates
cMYC	MYC protein	Transthyretin	Amyloidosis

Hematopathology Disease Listings

Acute Myeloid Leukemia

Diagnostic Overview



Acute myeloid leukemia (AML) is a malignant neoplasm characterized by the clonal proliferation of myeloid blasts in the peripheral blood and bone marrow. AML is clinically heterogeneous and can be further subclassified through the correlation of clinical data, morphology, phenotype and molecular cytogenetic abnormalities. Metaphase cytogenetic analysis has long been recognized as a crucial component of the diagnosis and classification of AML. In recent years, other molecular methods

have also assumed an increasingly important role in the workup, classification, prognostic assessment and monitoring of AML.

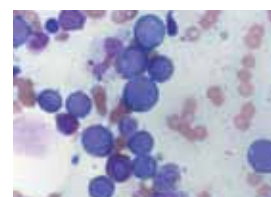
Interphase fluorescence in situ hybridization (FISH) studies offer the ability to rapidly detect cytogenetic abnormalities in nondividing cells. FISH studies are therefore an important adjunct to traditional banded karyotyping. FISH analysis can clarify suspected abnormalities identified in banded karyotypes, identify the presence of complex or cryptic cytogenetic abnormalities, or provide cytogenetic information even when banded karyotype data is not available. FISH studies for many recurrent cytogenetic abnormalities associated with AML are available through Cleveland Clinic Laboratories.

Molecular testing for specific recurrent mutations is also an important part of the workup of AML. AML with mutations in *NPM1* and *CEBPA* are now recognized as distinct clinicopathologic entities with distinct prognostic implications. Testing for mutations in the *FLT3* or *KIT* genes also provide valuable prognostic information in some patients with AML. Single nucleotide polymorphism (SNP) arrays offer the potential to identify chromosomal abnormalities, including copy neutral loss of heterozygosity (cnLOH), which are not detected by metaphase cytogenetics and may also impact the classification and prognosis of AML.

RT-PCR testing offers the ability to detect oncogenic fusion transcripts with a sensitivity much greater than that obtained with other techniques, such as metaphase cytogenetics or FISH. In acute promyelocytic leukemia, RT-PCR analysis for *PML/RARA* transcripts is utilized to monitor minimal residual disease status.

Tests Available

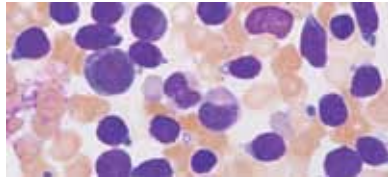
- *CEBPA* Mutation Analysis
- Chromosome Analysis, Leukemic Blood
- Chromosome Analysis, Bone Marrow
- DNA Extraction
- FISH for Acute Myeloid Leukemia Panel (t(8;21), inv(16), t(15;17), *MLL*)
- FISH for inv(16) *CBFB/MYH11*
- FISH for *MLL* (11q23) Translocation
- FISH for *RARA* (17q21) Translocation
- FISH for t(15;17) *PML/RARA*
- FISH for t(8;21) *RUNX1/RUNX1T1* (*AML1/ETO*)
- FISH for t(9;22) *BCR/ABL1*
- Flow Cytometric Immunophenotyping for Leukemia/Lymphoma
- *FLT3* ITD/D835 PCR
- *KIT* Gene Mutation AML
- Nucleophosmin Gene (*NPM1*) Mutation
- Oncologic CytoScan HDSNP Array
- *PML/RARA* RT-PCR, Qualitative



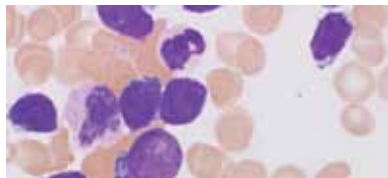
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Acute Lymphoblastic Leukemia

Diagnostic Overview



Acute lymphoblastic leukemia (ALL) is primarily a disease of childhood, with the majority of cases occurring before age 6. ALL can be further sub-classified based on the phenotypic profile and the presence of specific recurrent cytogenetic abnormalities. Approximately 80% of ALL exhibit a precursor B cell phenotype, with the remaining cases displaying a T lymphoblast phenotype.



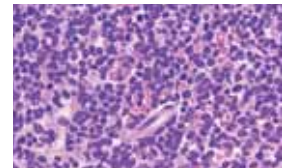
Interphase fluorescence in situ hybridization (FISH) studies offer the ability to rapidly detect cytogenetic abnormalities in nondividing cells. FISH studies are therefore an important adjunct to traditional banded karyotyping. FISH analysis can clarify suspected

abnormalities identified in banded karyotypes, identify the presence of complex or cryptic cytogenetic abnormalities, or provide cytogenetic information even when banded karyotype data is not available. FISH studies for recurrent cytogenetic abnormalities associated with B lymphoblastic leukemia are available through Cleveland Clinic Laboratories. Single nucleotide polymorphism (SNP) arrays offer the potential to identify chromosomal abnormalities, including copy neutral loss of heterozygosity (cnLOH), which are not detected by metaphase cytogenetics and may also impact the classification and prognosis of ALL.

Real time RT-PCR testing offers the ability to detect oncogenic fusion transcripts with a sensitivity much greater than that obtained with other techniques, such as metaphase cytogenetics or FISH. In Philadelphia chromosome-positive ALL, RT-PCR analysis for p190 *BCR/ABL* transcripts is utilized to monitor minimal residual disease status.

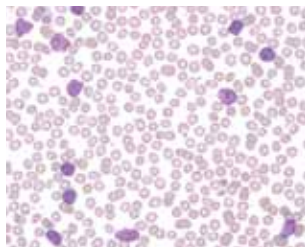
Tests Available

- *BCR/ABL* Qualitative Multiplex RT-PCR
- *BCR/ABL* p190 RT-PCR, Quantitative
- Chromosome Analysis, Leukemic Blood
- Chromosome Analysis, Bone Marrow
- FISH for *MLL* (11q23) Translocation
- FISH for t(12;21) *ETV6/RUNX1* (*TEL/AML1*)
- FISH for t(9;22) *BCR/ABL1*
- FISH for Trisomy 4, 10 and 17
- Flow Cytometric Immunophenotyping for Leukemia/Lymphoma
- Oncologic CytoScan HDSNP Array



Chronic Lymphocytic Leukemia

Diagnostic Overview



Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL) is a neoplasm of small B lymphocytes that involves the peripheral blood, bone marrow, and in some cases, the lymph nodes. Most patients with CLL are older than 50 years of age, and most cases will follow an indolent clinical course.

FISH testing for recurrent cytogenetic abnormalities (13q-, +12, 11q-, and 17p-) provides important prognostic

information in CLL. The Oncologic CytoScan HDSNP Array assay assesses for chromosomal copy number abnormalities and loss of heterozygosity across the genome, including loci not covered by FISH panels. Finally, PCR and sequencing analysis of the immunoglobulin heavy chain variable region (*IGHV*) also provides further prognostic information.

Tests Available

- Chromosome Analysis, Leukemic Blood
- Chromosome Analysis, Bone Marrow
- FISH for CLL (13q-, +12, 11q-, 17p)
- Flow Cytometric Immunophenotyping for Leukemia/Lymphoma
- *IGHV* Sequencing
- Oncologic CytoScan HDSNP Array

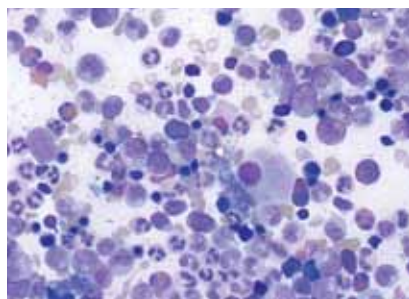


Myeloproliferative Neoplasms

Diagnostic Overview

The myeloproliferative neoplasms are clonal hematological disorders characterized by an abnormal proliferation of one or more myeloid lineages in the peripheral blood. Traditionally, four subtypes of myeloproliferative neoplasms have been recognized: chronic myeloid leukemia (CML), polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF). More recently, three additional disorders have been identified that are identified by chromosomal rearrangements involving the *PDGFRA*, *PDGFRB* or *FGFR1* genes.

In CML, molecular testing is utilized in several ways. First, CML by definition carries a BCR/ABL translocation, which can be identified through metaphase cytogenetics, FISH or RT-PCR analysis. Secondly, following initiation of therapy for CML, minimal residual disease status is monitored utilizing qualitative multiplex RT-PCR analysis for the p210 BCR/ABL fusion transcript. Finally, sequencing of the BCR/ABL kinase domain can identify mutations associated with resistance to one or more tyrosine kinase inhibitors, thereby assisting in the selection of the most appropriate therapeutic option for the patient.



rearrangements in *PDGFRA*, *PDGFRB* or *FGFR1* that define distinct myeloproliferative neoplasms.

Molecular testing also plays an important role in the non-CML myeloproliferative neoplasms. *JAK2* V617F mutations are found in >95% of PV, and in approximately 50% of ET and PMF. In the rare cases of PV lacking the V617F mutation, other mutations in exons 12-15 of *JAK2* may be identified by sequencing studies. Mutations involving the *CALR* or *MPL* genes are identified in most cases of PMF or ET lacking the *JAK2* V617F mutation. FISH testing can be utilized to detect chromosomal

Tests Available

- BCR/ABL Kinase Domain Sequencing
- BCR/ABL p210 RT-PCR, Quantitative
- BCR/ABL Qualitative Multiplex RT-PCR
- CALR Mutation Analysis
- Chromosome Analysis, Leukemic Blood
- Chromosome Analysis, Bone Marrow
- FISH for *FGFR1* (8p12) Translocation
- FISH for *PDGFRA* (4q12) Translocation
- FISH for *PDGFRB* (5q32) Translocation
- FISH for Myeloproliferative Neoplasms Panel (*BCR/ABL1*, *PDGFRA*, *PDGFRB*, *FGFR1*)
- FISH for t(9;22) *BCR/ABL1*
- Flow Cytometric Immunophenotyping for Leukemia/Lymphoma
- *JAK2* Exon 12-15 Sequencing
- *JAK2* V617F PCR
- *KIT* D816V PCR
- *MPL* Mutation Sequencing
- Oncologic CytoScan HDSNP Array

Myelodysplastic Syndromes

Diagnostic Overview

The myelodysplastic syndromes (MDS) are clonal hematologic malignancies characterized by ineffective hematopoiesis and peripheral blood cytopenias. MDS typically present in the middle age to elderly age groups. The diagnosis and subclassification of MDS is facilitated by detection of cytogenetic abnormalities. The most common recurring abnormalities in MDS include 5q-, 7q-, +8 and 20q-.

Interphase fluorescence in situ hybridization (FISH) studies offer the ability to rapidly detect cytogenetic abnormalities in nondividing cells. FISH studies are therefore an important adjunct to traditional banded karyotyping. FISH analysis can clarify suspected abnormalities identified in banded karyotypes, identify the presence of complex or cryptic cytogenetic abnormalities, or provide cytogenetic information even when banded karyotype data is not available. FISH studies for many recurrent cytogenetic abnormalities associated with MDS are available through Cleveland Clinic Laboratories. SNP array karyotyping is also useful to identify clinically significant chromosomal abnormalities which may be missed by metaphase cytogenetics and/or FISH studies alone.

Tests Available

- Chromosome Analysis, Leukemic Blood
- Chromosome Analysis, Bone Marrow FISH for Del(5q) Abnormalities
- FISH for Del(5q) Abnormalities
- Flow Cytometric Immunophenotyping for Leukemia/Lymphoma
- FISH for MDS (5q,7q,+8,20q)
- Oncologic CytoScan HDSNP Array

Non-Hodgkin Lymphoma

Diagnostic Overview

The non-Hodgkin lymphomas (NHL) are a heterogeneous group of malignancies of mature B-cells or T-cells. Approximately 90% of NHL are derived from B-cells, with the remaining 10% being of T-cell origin. On average, NHL typically presents in adults in their sixth or seventh decade, although some specific subtypes of NHL occur more commonly in children or young adults. NHL are subclassified into distinct clinicopathologic entities on the basis of clinical features, morphology, phenotype and molecular cytogenetic findings.

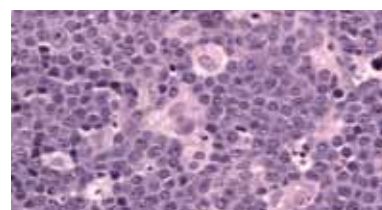
Molecular testing is useful to document the presence of a clonal B-cell or T-cell population in the workup of a suspected NHL. Historically, Southern blot studies have been considered to be the gold standard for documentation of clonal lymphoid populations. However, Southern blot studies require fresh or frozen tissue and therefore cannot be performed on formalin-fixed, paraffin embedded (FFPE) tissues. PCR studies utilizing primer sets designed by the EuroClonality (BIOMED-2) consortium offer the ability to detect clonal populations with a sensitivity approximately equal to that of Southern blot techniques, even from FFPE tissues.

Diffuse large B-cell lymphoma, which is biologically and clinically heterogeneous, can be divided into cases with gene expression profiles of activated B-cells (ABC) or germinal center B-cells (GC). Cleveland Clinic Laboratories offers a multiplex, real-time RT-PCR assay which identifies ABC vs GC gene expression profiles from FFPE tissue, providing prognostically useful information which may help guide patient management.

Several subtypes of NHL are characterized by specific recurring balanced translocations. These abnormalities may be detected by fluorescence in situ hybridization or, in some cases, by RT-PCR. In general, FISH testing is considered the gold standard for detection of these abnormalities at initial diagnosis. FISH testing for NHL-associated abnormalities can be performed on peripheral blood, bone marrow or FFPE tissues.

Tests Available

- B-cell clonality (BIOMED2 *IGH*+*IGK*)
- Chromosome Analysis, Solid Tumor
- Diffuse Large B-cell Lymphoma Molecular Subtyping
- FISH for *ALK* (2p23) Translocations
- FISH for *BCL2* (18q21.3) Translocations
- FISH for *BCL6* (3q27) Translocations
- FISH for *CCND1* (11q13) Translocation
- FISH for *IGH* (14q32) Translocations
- FISH for *MALT1* (18q21) Translocation
- FISH for *MYC* (8q24) Translocation
- FISH for t(11;14) *IGH/CCND1*
- FISH for t(11;18) *API2/MALT1*
- FISH for t(14;18) *IGH/BCL2*
- FISH for t(14;18) *IGH/MALT1*
- FISH for t(8;14) *IGH/MYC*
- Flow Cytometric Immunophenotyping for Lymphoma, Tissue
- *IGH* PCR (BIOMED2)
- *IGH/BCL2* PCR, Qualitative
- *IGK* PCR (BIOMED2)
- *MYD88* L265P PCR
- Oncologic CytoScan HDSNP Array
- T-cell clonality (BIOMED2 *TCRB*+*TGRG*)
- *TCRB* PCR (BIOMED2)
- *TCRG* PCR (BIOMED2)



Plasma Cell Neoplasms

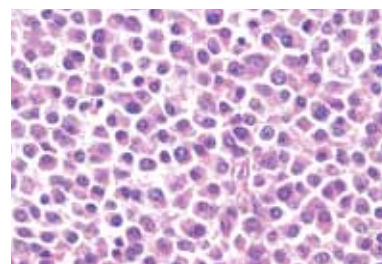
Diagnostic Overview

Plasma cell myeloma (PCM) is a malignant neoplasm of plasma cells characterized by increased plasma cells in the bone marrow and production of a monoclonal protein in the serum and/or urine. The diagnosis of PCM is based on a combination of clinical findings, bone marrow aspirate and biopsy, and radiographic studies.

The clinical course of PCM is highly variable. FISH studies for recurrent cytogenetic abnormalities, including 13q, 17p-, *IGH/CCND1*, *IGH/MMSET*, and *IGH/MAF* translocations, provide useful prognostic information in PCM. Because the malignant cells of PCM tend to grow poorly in culture, and because some clinically relevant abnormalities may be cryptic by metaphase cytogenetics, FISH analysis is generally preferred for cytogenetic evaluation of PCM.

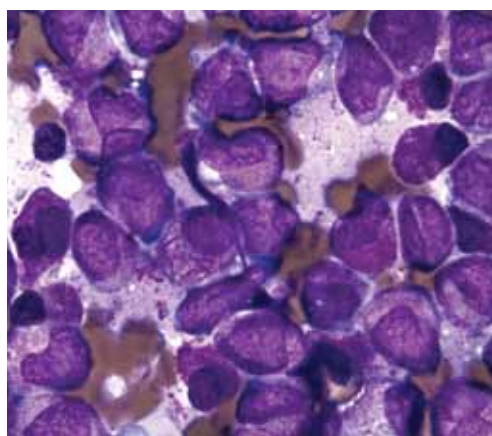
Tests Available

- Chromosome Analysis, Bone Marrow
- FISH for Myeloma
- Flow Cytometric Immunophenotyping for Leukemia/Lymphoma



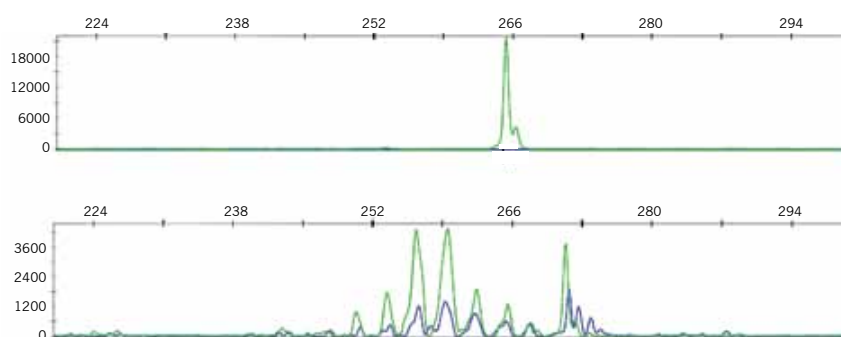
Molecular Hematopathology

Cleveland Clinic Laboratories provides comprehensive molecular testing for patients with benign and malignant disorders of the lymph nodes, peripheral blood, and bone marrow. Our state-of-the-art diagnostic techniques assist in establishing a diagnosis, predicting prognosis, and/or guiding the choice of therapy in a wide range of hematologic diseases.



Testing performed includes clonality studies for lymphoproliferative disorders, mutational analysis for acute myeloid leukemias, minimal residual disease monitoring and mutation analysis in chronic myeloid leukemia and mutation testing for myeloproliferative neoplasms. Numerous fluorescence *in situ* hybridization (FISH) assays are available to detect molecular cytogenetic abnormalities associated with myeloid and lymphoid neoplasms.

Results of molecular testing are correlated with the corresponding morphologic findings where appropriate, and an integrated interpretation is provided. Our pathologists also provide expert assistance in test selection and interpretation of unusual findings.



Molecular Hematopathology Test Menu

Acute Lymphoblastic Leukemia

BCR/ABL Qualitative Multiplex RT-PCR
BCR/ABL p190 RT-PCR, Quantitative
Chromosome Analysis, Leukemic Blood
Chromosome Analysis, Bone Marrow
Oncologic CytoScan HDSNP Array
FISH for *MLL* (11q23) Translocation
FISH for t(12;21) *ETV6/RUNX1*
(*TEL/AML1*)
FISH for t(9;22) *BCR/ABL1*
FISH for Trisomy 4, 10 and 17

Acute Myeloid Leukemia

CEBPA Mutation Analysis
Chromosome Analysis, Leukemic Blood
Chromosome Analysis, Bone Marrow
DNA Extraction
FISH for Acute Myeloid Leukemia Panel
(t(8;21), inv(16), t(15;17), *MLL*)
FISH for inv(16) *CBFB/MYH11*
FISH for *MLL* (11q23) Translocation
FISH for *RARA* (17q21) Translocation
FISH for t(15;17) *PML/RARA*
FISH for t(8;21) *RUNX1/RUNX1T1*
(*AML1/ETO*)
FISH for t(9;22) *BCR/ABL1*
FLT3 ITD/D835 PCR
KIT Gene Mutation AML
Nucleophosmin Gene (*NPM1*) Mutation
Oncologic CytoScan HDSNP Array
PML/RARA RTPCR, Qualitative

Chronic Lymphocytic Leukemia

Chromosome Analysis, Leukemic Blood
Chromosome Analysis, Bone Marrow
FISH for CLL (13q,+12,11q,17p)
IGHV Sequencing
Oncologic CytoScan HDSNP Array

Hemoglobinopathy

Alpha Thalassemia Genotyping

Myeloproliferative Neoplasms

BCR/ABL Kinase Domain Sequencing
BCR/ABL p210 RT-PCR, Quantitative
BCR/ABL Qualitative Multiplex RT-PCR
CALR Mutation Analysis
Chromosome Analysis, Leukemic Blood
Chromosome Analysis, Bone Marrow
FISH for *FGFR1* (8p12) Translocation
FISH for *PDGFRA* (4q12) Translocation
FISH for *PDGFRB* (5q32) Translocation
FISH for Myeloproliferative Neoplasms
Panel (*BCR/ABL1*, *PDGFRA*,
PDGFRB, *FGFR1*)
FISH for t(9;22) *BCR/ABL1*
JAK2 Exon 12-15 Sequencing
JAK2 V617F PCR
KIT D816V PCR
MPL Mutation Sequencing
Oncologic CytoScan HDSNP Array

Myelodysplastic Syndromes

Chromosome Analysis, Leukemic Blood
Chromosome Analysis, Bone Marrow
FISH for Del(5q) Abnormalities
FISH for MDS (5q,7q,+8,20q)
Oncologic CytoScan HDSNP Array

Non-Hodgkin Lymphoma

B-cell clonality (BIOMED2 *IGH+IGK*)
Chromosome Analysis, Solid Tumor
Diffuse Large B-cell Lymphoma
Molecular Subtyping
FISH for *ALK* (2p23) Translocations
FISH for *BCL2* (18q21.3) Translocations
FISH for *BCL6* (3q27) Translocations
FISH for *CCND1* (11q13) Translocation
FISH for *IGH* (14q32) Translocations
FISH for *MALT1* (18q21) Translocation
FISH for *MYC* (8q24) Translocation
FISH for t(11;14) *IGH/CCND1*
FISH for t(11;18) *API2/MALT1*
FISH for t(14;18) *IGH/BCL2*
FISH for t(14;18) *IGH/MALT1*
FISH for t(8;14) *IGH/MYC*
IGH PCR (BIOMED2)
IGH/BCL2 PCR, Qualitative
IGK PCR (BIOMED2)
MYD88 L265P PCR
Oncologic CytoScan HDSNP Array
T-cell clonality (BIOMED2
TCRB+TGRG)
TCRB PCR (BIOMED2)
TCRG PCR (BIOMED2)

Plasma Cell Neoplasms

Chromosome Analysis, Bone Marrow
FISH for Myeloma

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Chronic Myelogenous Leukemia

CML Diagnosis

Blood or bone marrow sample

BCR/ABL FISH

- diagnosis confirmation

Cytogenetic Karyotyping

- evaluates for additional clonal abnormalities

BCR/ABL p210 RT-PCR

- establishes baseline for subsequent monitoring (confirms that fusion is detectable, provides baseline level)

CML Disease Level Monitoring

BCR/ABL p210 RT-PCR (*blood*)

- goal of < 0.1 percent on International Scale for major molecular response

Cytogenetic Karyotyping (*marrow*)

- evaluates for clonal evolution

CML Therapy Resistance Testing

- ABL mutation analysis