

Hematopathology Services

Bringing It All Together

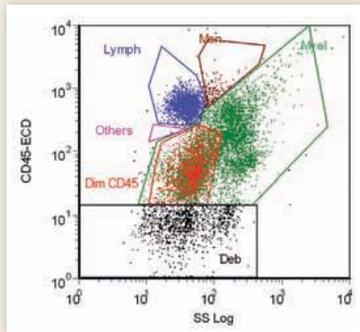
We understand that a multi-disciplinary approach is required to evaluate specific types of cancers. Through our collaboration with Clariant, we can provide extensive capabilities to ensure that the most appropriate and clinically relevant technologies are employed to provide the answers you need.

Using our combined experience, we customize our approach based upon your need for:

- Rapid turnaround time
- Maximum use of the submitted specimen, however small
- High sensitivity and specificity
- Application of all available integrated technologies



Flexibility and Expertise in Hematopathology Flow Cytometry



Flow Cytometry Offering

The utility of flow cytometric immunophenotyping is well-established in a number of hematologic disorders, including leukemia and lymphoma.¹ The primary benefit of flow analysis – quantitation of small cell subpopulations coupled with simultaneous multiple antigen expression at the individual cell level – has pushed its application into broader areas of hematopathology.

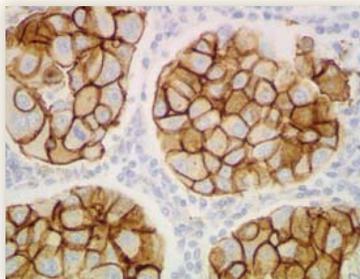
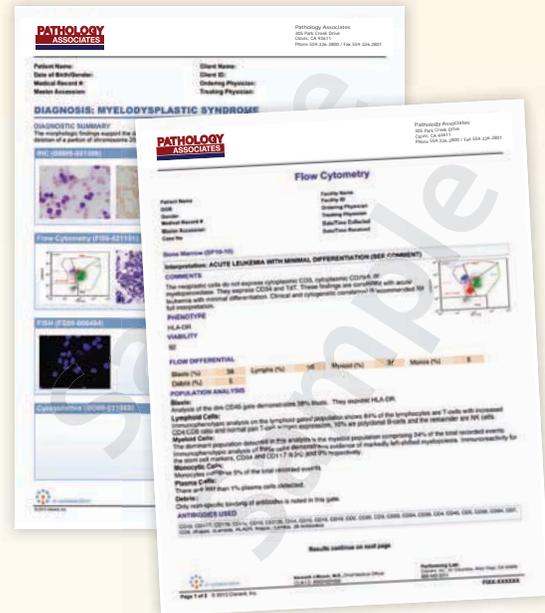
Rapid Turn Around Time – 24 hours

Expert Interpretive Value – Years of experience backed by the additional expertise of world-renowned advisors and consultants

High Quality Reporting – Clear, concise and comprehensive reports with color histograms and supporting images

Access To All Supporting Data – Ability to view flow cytometry “workbooks”

24/7 Assistance – Call-in assistance and call-backs on emergency or critical diagnostic cases



IMMUNOHISTOCHEMISTRY

Each IHC assay goes through a well-documented validation process that is shared with our clients. The extensive IHC menu allows you to bring up novel markers for complex tumor workups without having to add these markers to your laboratory's test menu.

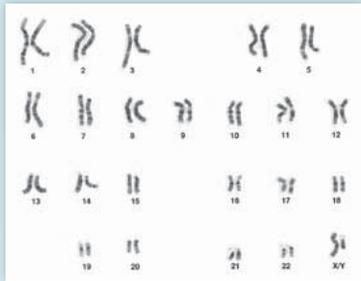
Through Clariant, we offer:

- 24-hour turnaround time
- Strict adherence to CLIA and CAP validation protocols to ensure stain quality
- An extensive menu of over 300 assays (including drug and cancer-specific markers)
- Quality control review of every slide
- All IHC slides viewable online
- Ability to order additional IHC markers online

HEMATOPATHOLOGY IHC PANELS

- Lymphoma vs. Reactive Hyperplasia
- NHL vs. Hodgkin Lymphoma
- Plasma Cell Dyscrasia (PCD)/Multiple Myeloma (MM)
- Acute Leukemia
- Lymphoma vs. Other Malignancy
- Low Grade Lymphoma Classification
- Aggressive Lymphoma Classification
- MDS/MPD
- Mast Cell Disease
- Langerhans Cell Histiocytosis/Dendritic Cell Proliferation

State-of-the-Art Molecular Genetics



CYTOGENETICS

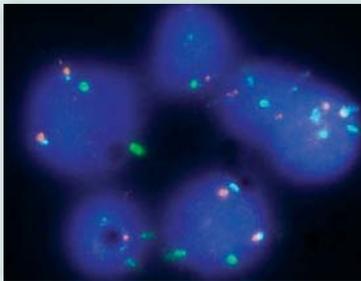
Cytogenetic analysis is an important tool in the investigation of hematological malignancies and is used to detect changes in the chromosomes of genetically altered cells.²

- Chromosomal analysis may be performed on peripheral blood, bone marrow and lymph nodes to provide diagnostic, prognostic and evaluation of patients after chemotherapy or radiotherapy treatment.
- Multiple culture systems are employed to optimize the ability to detect cytogenetic abnormalities.

FLUORESCENCE IN SITU HYBRIDIZATION (FISH)

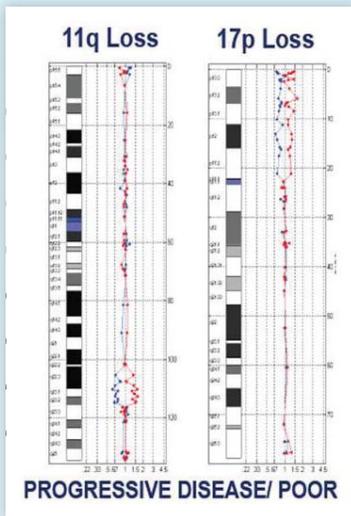
FISH analysis provides additional information not available using classic cytogenetic analysis.³

- A powerful tool for rapid testing
- Viable and dividing cells not required
- Complements classic cytogenetics
- Useful in exclusion of masked translocations such as BCR/ABL and PML/RARA
- Involves analysis of many cells
- Diagnostically useful when a specific disorder is suspected
- May be performed on peripheral blood, bone marrow and lymph nodes to provide diagnostic and prognostic information



Common Indications for FISH Analysis

Disease State	Assay
Acute Promyelocytic Leukemia (APL)	PML/RARA
Acute Lymphocytic Leukemia (ALL)	MLL, BCR/ABL
Acute Myeloid Leukemia (AML)	AML1/ETO, inv(16), MLL
Chronic Lymphocytic Leukemia (CLL)	+12, ATM, p53, 13q
Chronic Myelogenous Leukemia (CML)	BCR/ABL
Mantle Cell Lymphoma (MCL)	IGH/CCND1
Follicular Lymphoma (FL)	IGH/BCL2
Myelodysplastic Syndromes (MDS)	+8, 5q31, 7q31, 20q-
Burkitt Lymphoma (BK)	MYC, IGH/MYC
MALT Lymphoma	IGH/MALT1, AP12/MALT1
Multiple Myeloma (MM)	IGH/CCND1, p53, 13q, IGH/FGFR3
Myelodysplastic Syndromes (MDS)	5q31, 7q31, +8, 20q12, p53



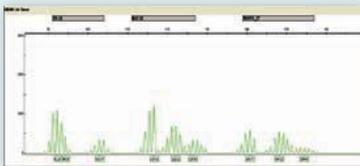
Molecular Cytogenetics-Array-Based Comparative Genomic Hybridization (A-CGH)

A-CGH is a molecular cytogenetic method for the detection of chromosomal gains and losses and is not confined to the analysis of growing cells.⁴

- A-CGH assay uses a Bacterial Artificial Chromosome (BAC) chip to test for subtle unbalanced chromosomal abnormalities that may not be detected by conventional karyotyping.
- A-CGH provides a number of advantages, including:
 - Higher resolution and dynamic range
 - Simultaneous detection of multiple loci copy changes
 - Higher throughput
 - Independent of cell growth
 - Reduced costs compared to using individual FISH probes

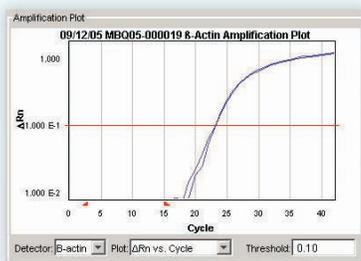
Polymerase Chain Reaction (PCR)

Using PCR technology, Clariant can readily identify unique DNA or RNA sequences in leukemias and lymphomas that are present at even a few copies per cell to assist in providing a diagnosis for your most challenging case since knowledge of these abnormalities can provide valuable prognostic information that can be used to guide treatment. PCR is a valuable technique to correlate with histologic and immunophenotypic information to arrive at a final diagnosis.⁵



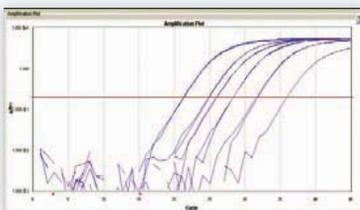
PCR with Capillary Electrophoresis

- B-Cell Clonality
- T-Cell Clonality



Qualitative Real-Time PCR (RT-PCR)

- PML/RARA
- JAK2



Quantitative Real-time PCR (RQ-PCR)

- BCR/ABL, t(9;22), Quantitative for CML, ALL

Clariant's Pathology-Oncology Collaboration

For many, geography can be isolating. Now, with our Clariant relationship, a virtual community is available to you and other physicians to help you access the expertise, tools and services you need. This is an innovative resource to elevate the critical role of the local physician in the oncology community to help your patients receive an accurate and in-depth diagnostic analysis.

You have access to a comprehensive test menu along with unique portals to obtain diagnostic answers - such as the online PATHSiTE® application for managing your cases. For those challenging cases, Clariant offers direct access to their unparalleled Medical Advisory Board and peer network. You receive unsurpassed 24/7/365 customer service. Because the timing of complex diagnostic questions is unpredictable, their customer service model is built on your schedule, not theirs. They accommodate the unpredictable, providing you with critical information when you need it.

The Clariant relationship provides education customized to the needs of the oncology community physician. You can participate in the CONTiNUUM® educational and training services in your community and webcasts with expert industry leaders.

VIRTUAL CASE REVIEW-PATHSITE®

Using Clariant's internet product, PATHSiTE, you can:

- Remotely review your cases from any location that has Internet access
- Reference any of your patient cases or cross-reference between fields

Ease-Of Use

Designed to reflect the daily physical case workflow, PATHSiTE provides a very intuitive and easy to use interface for reviewing cases and slides on the computer over the Internet.

Cases can quickly and easily be searched and sorted

Patient Name	Report	Specimen	Med. Rec. No.	Case No.	Physician	Completed
Smith, Judy	Flow Cytometry - Technical	07-6234		F1107-013909	Alan, Smith	
Rings, Alan	Flow Cytometry - Technical	SP10-10	123456789	F110-002620	<unknown>	07/02/2010
Brooks, Mike	IHC	SP10-01	235659644	AT10-009241	Demo, Pathologist	05/19/2010
Henry, David	Flow Cytometry - Technical		235-458-9684	F109-011065	<unknown>	04/29/2010
Shah, Sheila	IHC Stain Summary	SO-2611-2	073-223-603	AS10-009886	Scotto, Kelly	03/17/2010
Michael, Lori	IHC	SO-1995-2	471-247-050	AS10-009887	Scotto, Kelly	03/17/2010

Once a specific case has been chosen, it can be brought-up for viewing

Facility Location: [Dropdown]

Cases Ready for Review
Review all your pending cases. Once reviewed, you can remove the case from this list by selecting it in the pull down list, and clicking the "Remove Case from List" button. Although you are removing a case from this list, the case will still appear in your Master Worklist, now designated as COMPLETE.

[Dropdown] [Remove Case from List](#)

Patient Information

Case No: F109-010653
Patient Name: Doc, John
DOB / Gender: 05/22/1940 / Male
Specimen ID: V901124
Other Test(s) Ordered for this Patient:

Flow Comp Panel - V901124

Reporting Options:

- Once cases have been reviewed, reports can be output directly in the digital workflow.
- Prior to the final report, comments, descriptions, values, and other text entries can be added or modified to the report.
- Specific images can be selected to be included in the final report.
- Once the report has been generated, the case can be marked as reviewed so that new pending cases can be reviewed.

IHC, Cytogenetics, PCR, FISH, and Flow Cytometry are just a few examples of how PATHSiTE® ties you into the rest of their services to help ensure that you receive the maximum resources available. Their medical staff is available to assist you review new antibodies as well as select the most appropriate antibodies for a given clinical application.

CONSULTATION

In addition to our in-house diagnostic team, Clariant has a nationally renowned network of advisors and consultants instantly available to review any case requiring another level of analysis.

Personalized Medicine

Clariant collaborates closely with their biopharmaceutical clients to help them in performing and customizing bioanalytical assays for basic research and clinical studies. They have extensive experience in developing and performing esoteric cancer assays.

Key Drug Targets and Associated Therapies

Trade Name	Generic Name	Marker	Used to Treat
Campath®	Alemtuzumab	CD52	CLL/SLL
Arzerra®	Ofatumumab	CD20	CLL/SLL
Gleevec®	Imatinib	BCR/ABL	CML
Hydrea®	Hydroxyurea	JAK2	MPN
Mylotarg®	Gemtuzumab	CD33	AML
Revlimid®	Lenolidomide	5q deletion	MDS
Rituxan®	Rituximab	CD20	NHL
Soliris®	Eculizumab	—	PNH
Sprycel®	Dasatinib	BCR/ABL	CML
Velcade®	Bortezomib	—	MM
Velcade®	Bortezomib	—	MCL
—	ATRA	PML/RARA	APL

Working Together to Bring Clarity to a Complex Disease

Together with Clariant, we can play an important role in improving the lives of those affected by cancer. The cancer diagnostics marketplace has taken on a tremendous amount of change and will continue to do so in the foreseeable future. Together, we can embrace that vital role of connecting the patient to those technologies and applications by bringing clarity to a complex disease.

To accomplish this, **Clariant is open 24/7/365 days a year** – so that you always have access to a medical professional and your results at a moment's notice.

Your Resource Portfolio

In addition to our expert staff, Clariant offers access to its board-certified hematopathology staff, advisory board members and consulting experts.

References:

- Jennings C and Foon K. Recent Advances in Flow Cytometry: Application to the Diagnosis of Hematologic Malignancy. *Blood* 1997, 90:2863-2892.
- An International System for Human Cytogenetic Nomenclature (1985), S. Karger AG, P.O. Box, CH-4009 Basel (Switzerland).
- Wolff D, Bagg A, Cooley L, et.al. Guidance for Fluorescence *in Situ* Hybridization Testing in Hematologic Disorders. *JMD* 2007, 9:134-143.
- Pinkel D and Albertson D. Array comparative genomic hybridization and its applications in cancer. *Nature Genetics (Supplement)*, 2005, 37:S11-17.
- Viljoen G, Nel C, Crowther J. Molecular Diagnostics PCR Handbook. Netherlands, *Springer Publishing Co.* 2005.

We help you find the difference that makes a difference.

