




PROVIDENCE HEALTH & SERVICES
CATHOLIC HEALTH INITIATIVES



CLINICAL CYTOGENETIC SERVICES

A cluster of several chromosomes, shown in a light grey, textured style, positioned in the upper right quadrant of the page.

Constitutional Diagnostic Services
Neoplastic Diagnostic Services
FISH (Fluorescence In Situ Hybridization)

Cytogenetics Laboratory

Phone: 509.434.1050

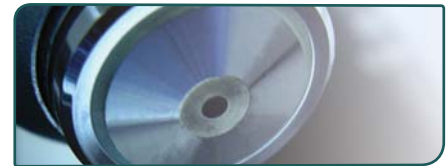
Toll Free: 800.541.7891 (Ext 1050)

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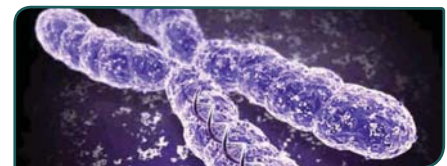
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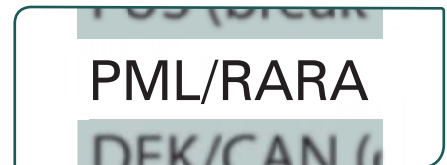
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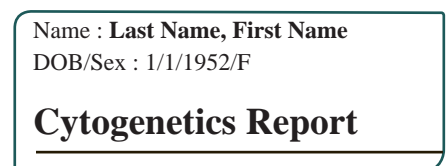
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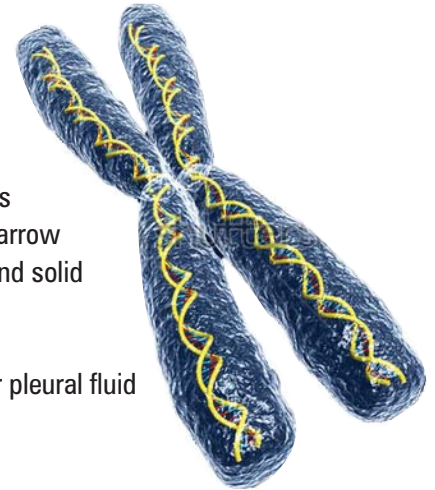
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Cytogenetics

Cytogenetics is a branch of genetics that studies the number and structure of human chromosomes, searching for balanced or unbalanced chromosomal rearrangements. These rearrangements may be present as translocations between two or more chromosomes; inversion within one chromosome; insertion, deletion or duplication of one segment of a chromosome; or gain or loss of a whole chromosome (aneuploidy). Some chromosomal rearrangements are present from birth and in every cell of the body: these are called constitutional abnormalities. Another group of chromosomal abnormalities, which are common in neoplastic and cancerous cells, are acquired chromosomal aberrations.

The PAML Cytogenetics Laboratory provides comprehensive Cytogenetic (karyotyping) and FISH (Fluorescence In Situ Hybridization) diagnostic services for prenatal and postnatal congenital disorders and neoplastic/oncologic disorders. Cytogenetic and FISH studies are performed on amniotic fluid, whole peripheral blood, tissue biopsy or products of conception for prenatal and pediatric or adult constitutional studies as well as bone marrow aspirate, bone core/biopsy, leukemic blood, lymph node biopsies and other solid tissue and solid tumors for hematologic/oncologic disorders.

In addition, FISH assay is performed on fresh and paraffin-embedded tissues and urine or pleural fluid as appropriate for the clinical indication provided for a given patient.



Contact Information

PAML Cytogenetics Department

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www.paml.com/Pages/Cytogenetics.aspx

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PAML Supply

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Billing

All billing questions should be directed to Client Services.

Scientific Expertise



Reza Saleki
PhD, FACMG
Technical Director
Clinical Cytogenetics

Dr. Reza Saleki received his master's and doctorate degree from Queen's University in Kingston, Canada. He pursued research in molecular genetics during his postdoctoral fellowships at the Hospital for Sick Children in Toronto, Canada and later at the Department of Molecular Genetics at MD Anderson Cancer Center in Houston, TX. He completed the American Board of Medical Genetics training program in Clinical Cytogenetics at Baylor College of Medicine in Houston, and is board certified and a diplomat of the American Board of Medical Genetics. Before joining PAML Cytogenetics laboratory in 2005, Dr. Saleki was the director of diagnostic services at Signature Genomic Laboratories where he was involved in design, development, and launch of the SignatureChip® microarray analysis for the clinical diagnosis of unbalanced chromosomal arrangements.



Karim Ouahchi
MD, FACMG
Co-Director
Clinical Cytogenetics

Dr. Karim Ouahchi received his medical degree from the Faculty of Medicine at Tunis, Tunisia, and completed his clinical pathology residency at Northwestern Memorial Hospital in Chicago, IL. Dr. Ouahchi further specialized in molecular pathology and clinical cytogenetics by joining the Harvard Medical School Genetic Training Program in Boston, MA. He is board certified in clinical pathology by the American Board of Pathology, and in clinical cytogenetics by the American Board of Medical Genetics.



Ying S. Zou
MD, PhD, FACMG
Co-Director
Clinical Cytogenetics

After receiving a BA/BS from Peking University, Dr. Ying Zou earned her M.D. degree from Peking Union Medical College and her Ph.D. in Genetics and Development from the University of Texas, Southwestern Medical Center at Dallas, TX. Dr. Zou joins PAML from the Boston University School of Medicine, where she was a Director of Cytogenetics Laboratory, Assistant Director of Clinical Molecular Genetics Laboratory and Assistant Professor in the department of Pediatrics. Dr. Zou has a strong interest in cancer cytogenetics, having conducted her PhD work under the supervision of Dr. Jerry Shay and Woodring Wright at University of Texas Southwestern Medical Center at Dallas, TX. In her research, she developed a new method called Red-FISH to study telomere replication timing. Currently her interests focus on clinical and transitional applications, such as developing and validating new FISH probes and microarray analyses, etc.

Contact Numbers:

Dr. Saleki 509.434.1051
Dr. Ouahchi 509.434.1052
Dr. Zou 509.434.1060
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“We are dedicated to service excellence with the aim of providing the best patient care.”

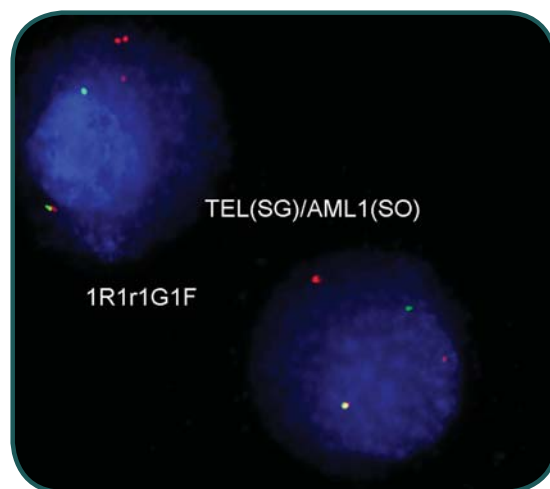
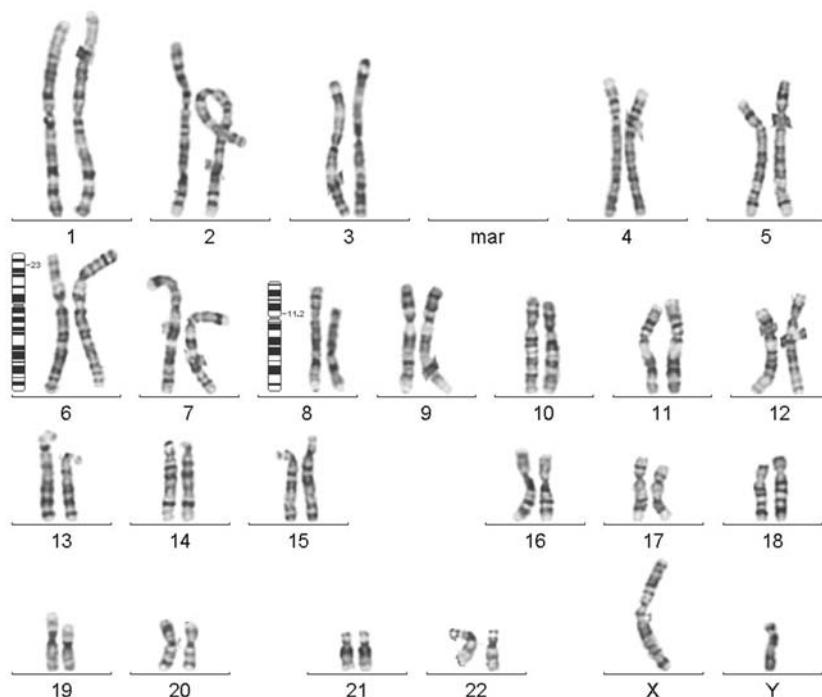
- Dr. Reza Saleki

Dr. Reza Saleki, Dr. Karim Ouahchi, and Dr. Ying S. Zou are board certified by the American Board of Medical Genetics. In addition to interpreting all Cytogenetic and FISH test results and issuing final reports, the directors are available for direct consultation with physician clients to provide verbal preliminary results or assist in selection of additional or follow-up assays for management of patient care.

The laboratory is staffed by highly trained and experienced professionals and laboratory personnel. The majority of the cytogenetic technologists are certified as Clinical Laboratory Specialists in Cytogenetics by the ASCP (American Society for Clinical Pathology). “We are dedicated to service excellence with the aim of providing the best patient care,” said Dr. Reza Saleki, director of the laboratory. “We take pride in being available for physician consultation and recognize that our physician clients rely on us not only for accurate and timely results and interpretation, but also as genetic experts who can assist in choosing the appropriate primary test and/or possible additional reflex and follow-up assays based on available clinical information.”

Accuracy, Quality, Turnaround Time

- Accuracy, quality, reliable turnaround times and a highly qualified staff are all significant features of the PAML Cytogenetics Laboratory.
- PAML provides 24 to 48-hour preliminary results on newborn peripheral blood and bone marrow analysis upon request. Advanced culture methods, based on the knowledge that a small number of spontaneously mitotic (stem) cells are present in the peripheral blood of newborns, allows the laboratory to provide a 2-5 cell preliminary result at 24 to 48 hours for newborns with congenital anomalies. Turnaround time to written report is 7 days from specimen receipt date.
- Turnaround times on amniotic fluid analysis consistently average 7 days, and those of bone marrow and leukemic blood studies typically average from 5 to 8 days.
- Test results are available through an LIS interface, phoned, faxed and/or mailed upon completion of analysis.
- All abnormal prenatal results are promptly communicated by phone to the referring physician, and consultation is provided. ●



Advanced Technology

Technical advances, including improved cell culturing and harvesting methods, development of new staining techniques and the use of DNA probes for detection and characterization of subtle chromosome abnormalities, have increased the number and types of disorders in which cytogenetic analysis is clinically useful.

Our Cytogenetics Laboratory uses the newest technologies—including robotic-assisted slide scanning and computer-enhanced image capturing and analysis—to consistently produce high quality studies and increase the abnormality detection rate. Routine G-banding of metaphase chromosomes produce 550-600 band level resolution for peripheral blood specimens, 650-750 band resolution for high-resolution peripheral bloods, and 500-550 for amniotic cells. Bone marrows and other neoplastic specimens consistently yield a minimum band level resolution of 350-450.

Our high annual volume of neoplastic specimens continually reinforces our knowledge base regarding the variety of chromosomal abnormalities found in bone marrow, lymph node and other solid tumor studies. Special handling and culturing methods, developed over several years, help to yield the high quality studies that allow detection of subtle aberrations.

COG and SWOG

Our laboratory is one of a select group of laboratories nationwide that is approved to perform cytogenetic and FISH analysis on patients who are participating in COG (Children's Oncology Group) or SWOG (Southwest Oncology Group).

Accreditations

The laboratory is under the direction of an American Board of Medical Genetics certified clinical cytogeneticist. In addition, current staff includes thirty cytogenetic technologists, including eight who specialize in FISH techniques, and four laboratory assistants. Many of the technologists, including the division supervisor, hold current certification as clinical lab specialists in cytogenetics through the NCA. All personnel are trained in and aware of the issues regarding HIPAA and patient confidentiality and genetic laboratory testing in general.

The Cytogenetics Laboratory is CAP-accredited and takes part in proficiency testing and inspections. The staff is here to provide you and your patients the highest possible diagnostic and patient care quality. ●



Specimen Types

Amniotic Fluid

Peripheral Blood

Bone Marrow Aspirate

Leukemic Blood

Solid Tumors

Lymph Nodes

Solid Tissues

Products of Conception

Skin Biopsies

Paraffin Embedded Tissues

Constitutional Diagnostic Services

Clinical indications for prenatal cytogenetic analysis include: abnormal fetal ultrasound, advanced maternal age, parental balanced chromosome rearrangement, positive maternal serum screening indicating an increased risk of fetal chromosomal abnormality. Clinical indications for peripheral blood analysis include: dysmorphic features, congenital anomalies, developmental delay, mental retardation, infertility and multiple spontaneous abortions.

Amniotic Fluid

- Cells from amniotic fluid (AF) are cultured and analyzed using the In Situ method, a technique that provides shorter turnaround times and a more accurate interpretation in cases of mosaicism for an abnormal cell line.
- Normally, 15 cells from 15 cell colonies are analyzed. Alpha-fetoprotein and acetylcholinesterase testing are provided upon request.
- Prenatal interphase aneuploidy screening for chromosomes 13, 18, 21, X and Y (Aneuvysion™) can be performed by FISH for those specimens meeting the minimum AF volume requirement.
- If requested, additional cell cultures can be set-up and shipped to appropriate molecular diagnostic laboratories for other prenatal testing, such as fetal antigen DNA testing or other suspected genetic disorders.
- Turnaround time for aneuploidy FISH screening results is generally within 24 hours of receipt. Turnaround time for AF chromosome results averages 7 days.

Solid Tissues

Products of Conception, Skin Biopsies

- Chromosome analysis is possible on any viable solid tissue, including placental tissues such as amnion, chorion and chorionic villi, placental membranes, skin, and various organ tissues. Analysis is usually performed on In Situ cell colonies to aid in interpretation on cases with possible chromosome mosaicism.
- The laboratory has many years of experience with placental dissection and identification of chorionic villi, chorion and amnion, ensuring to the highest degree possible that fetal and not maternal cells are available for the analysis in cases of pregnancy loss.
- Turnaround time for these specimens varies based on specimen type and the percentage of viable cells present. The majority of studies are finalized within 21 days of receipt.



Peripheral Blood

Routine and High-Resolution Analysis

- Twenty cells are analyzed for either a routine or high resolution peripheral blood chromosome study. Level of resolution for a routine study averages at 550-600 band length and for a high resolution study at 650-750 band level. The latter test is more appropriate for cases where a subtle chromosome aberration is suspected, such as in individuals with developmental delay, with or without dysmorphic features.
- Turnaround time for routine and high resolution studies ranges from 8 to 15 days.

Newborn Blood

- Peripheral blood chromosome analysis requires a 48 to 72 hour culture time following mitogenic stimulation. We are usually able to analyze overnight unstimulated cultures of peripheral blood stem cell from newborns with congenital anomalies and provide a 24 to 48-hour verbal or written preliminary report upon request. This preliminary analysis is used to confirm or rule out numerical (e.g. +21, +13, +18, 45,X) or gross structural abnormalities of the chromosomes.
- Turnaround time for newborns with congenital anomalies is 7 days.

Family Studies

Family studies are offered to confirm the presence or absence of a previously identified cytogenetic abnormality within a family in additional family members. Turnaround time ranges from 8 to 10 days.

Mosaicism Analysis

- In cases of suspected chromosomal mosaicism, 10-20 cells are analyzed as for a routine or high-resolution analysis. An additional 80 cells are then examined for the anomaly in question (e.g., to rule out mosaicism for trisomy 21).
- Turnaround time ranges from 7 to 15 days. Depending on the aberration in question, FISH may be offered as an adjunct analysis. ●

Neoplastic Diagnostic Services

Many chromosome abnormalities in human cancers are non-random recurrent aberrations that provide valuable diagnostic and prognostic clinical information. Some recurring aberrations help distinguish between specific subtypes of malignancies. Others have independent prognostic significance and may be the single most important factor in determining treatment choice and predicting outcome for a given patient. Over the years, we have developed special handling and culturing methods that yield high quality metaphases; this in turn, allows detection of even subtle aberrations that may otherwise be undetected. Speed in handling and transport of specimens to the laboratory is important for cell viability and the quality of the chromosome preparations needed for analysis.

Bone Marrow Aspirate / Leukemic Blood

- A minimum of 20 metaphase cells are analyzed for all neoplastic studies, if available. Additional screening for clinically relevant cytogenetic aberrations may be performed.
- For specimens with normal cytogenetic results where diagnostic FISH probes are available (such as multiple myeloma panel, CLL panel, CML) follow-up interphase FISH testing is offered.
- Verbal preliminary results are available, usually within 24 to 48 hours upon request, and typically for new leukemia diagnoses.
- The clinical indication for the patient and current specimen is required for appropriate processing of these specimens for tissue culture.
- Turnaround time ranges from 3 to 10 days, depending on clinical indication and current laboratory specimen volumes.

Solid Tumors / Lymph Nodes

- A minimum of 20 metaphase cells are analyzed for all solid tumors and lymph nodes, if available from the submitted specimen.
- The laboratory has developed a number of culture and harvest techniques to increase the likelihood of detecting abnormal clonal cells if present.
- Follow-up interphase FISH analysis testing may be offered based on clinical information received with the specimen to look for diagnostic gene rearrangements.
- The turnaround time varies depending on tumor type and the length of time required for cell culture.

Other Services

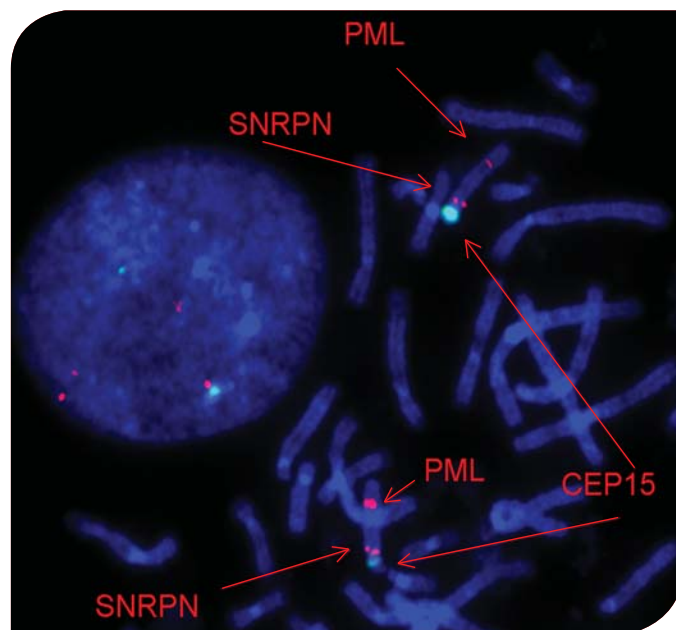
Tissue Culture and Cell Freezing

- Tissue culture and cell freezing services are available for specimens (amniotic fluid and other solid tissues) that require culture expansion and maintenance before shipping for molecular genetic or biochemical genetic testing.

Set-Up and Hold

- This service is available for neoplastic specimens for clinicians who are waiting for pathology and/or flow cytometry results before the decision to proceed with cytogenetic analysis is made.
- The specimens are minimally processed for tissue culture and harvest while still viable, but the analysis is not performed until the clinician's order to proceed with analysis is received.

For further information, please contact your marketing representative.



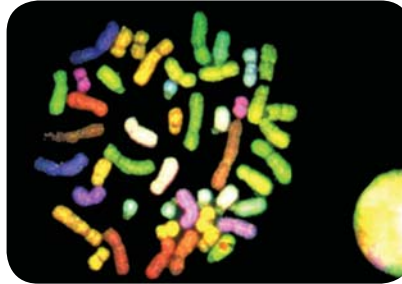
FISH (Fluorescence In Situ Hybridization)

Chromosome aberrations are variable in size. Some aberrations are detectable by studying G-banded metaphase chromosomes under light microscopes, while some other rearrangements are near or below the level of cytogenetic resolution and detection.

One approach for detection and characterization of sub-microscopic rearrangements is by hybridization of fluorescently-labeled gene or locus-specific DNA probes to metaphase spreads or interphase nuclei on a slide. FISH can be performed on any specimen type that is suitable for cytogenetic analysis or on paraffin-embedded tissue. For paraffin-embedded specimens, FISH is least likely to be successful on specimens such as bone cores or bone biopsies where decalcification has been performed using acids.

Probes for a number of constitutional and neoplastic conditions are now available and can be used for either interphase or metaphase FISH analysis.

This technique can be used as an adjunct to standard cytogenetic analysis in either constitutional or neoplastic conditions or as a stand-alone assay in certain neoplastic conditions and clinical situations. FISH can also be used to better characterize chromosomal abnormalities found during routine cytogenetic analysis.



For patients in whom a microdeletion syndrome is clinically suspected, it is recommended that a routine or high-resolution cytogenetic analysis also be performed in conjunction with FISH in the majority of cases. This is to confirm or rule out another chromosome etiology for the clinical phenotype seen.

Depending on the clinical situation, FISH probes may be used as part of the cytogenetic analysis. Please contact one of the laboratory directors for questions regarding specific requests. Information regarding the current list of clinically validated FISH probes at the Cytogenetics Laboratory is also available on the PAML website at www.paml.com.
(Go to Lab Specialties > Cytogenetics.)

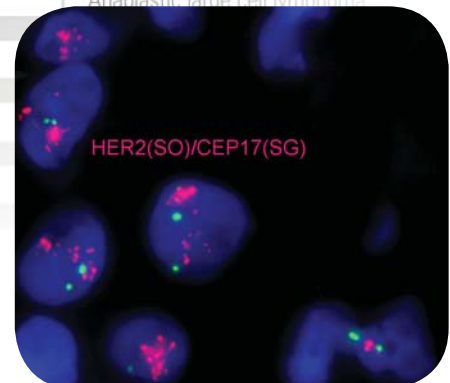
See page 14 for a list of FISH probes currently available and reflex FISH forms for constitutional, hematologic, and solid tumor testing.

Neoplastic FISH Probes

Clinically validated

Neoplastic DNA FISH Probes: Probes can be used for either interphase or metaphase analysis. Probes are clinically validated.

GENE REARRANGEMENT PROBES (alternate name)	TRANSLOCATION / LOCATION	DISEASE
258B3, MYB, 252P19	6q13, 6q23, 6q27	Lymphoma, Myeloma, Waldenstrom
ALK (break-apart)	2p23, t(2;5) or variant	Anaplastic large cell lymphoma
ETO/AML1 (RUNX1/RUNX1T1)	t(8;21)	Acute Myeloid Leukemia
ATM	11q22.3	Ataxia-telangiectasia
BCL2/IGH (dual fusion)	t(14;18)	Follicular lymphoma
BCL6 (break-apart)	3q27	Diffuse large B-cell lymphoma
BCR/ABL1 (dual fusion)	t(9;22)	Chronic Myeloid Leukemia
CBFB (break-apart)	16q22	Acute Myeloid Leukemia
CCND1 (break-apart)	11q13	Acute Myeloid Leukemia
CCND1/IGH, BCL2/IGH (dual fusion)	t(11;14)	Follicular lymphoma



Specimen Requirements

General

- Each specimen must be clearly labeled with at least two patient identifiers such as patient name and birth date.
- Each specimen must be accompanied by a paper test requisition including the following: First and last name, birth date, gender, physician, originating lab or clinic, clinical indication and tests ordered.
- The clinical indication is required for appropriate cell culture parameters to be chosen. Samples should be sent as soon as possible to the Cytogenetics Laboratory with same-day or overnight transport preferable. Specimen requirements for FISH correspond to the tissue type being studied (e.g., blood, bone marrow, amniotic fluid).
- Samples should never be frozen or placed on ice.

Amniotic Fluid

- 15-20 mL sterile amniotic fluid in sterile, screw-capped tubes (centrifuge tubes, Falcon 2037 or equivalent). First few mLs drawn should be discarded to reduce chance of maternal cell contamination. Indicate on Test Requisition Form if AFP and/or ACHE is requested. If prenatal interphase FISH aneuploidy screening is also requested (Aneuvysion™), a minimum of 20 mL amniotic fluid is required.
- Specimens with visible red blood may be rejected for Aneuvysion™ screening due to the increased likelihood of maternal leukocyte contamination.
- Aneuvysion™ results are typically available within 24 hours after specimen receipt at the laboratory; final written cytogenetic reports are usually available in 6 to 8 days.
- If additional tests are required, please contact the laboratory for test-specific amniotic fluid volume requirements.

Peripheral Blood

- Aseptically draw venous blood into a sodium-heparin tube and mix well (or draw blood into syringe lubricated with sodium-heparin for injection). Do not use EDTA, lithium or ammonium-heparin tubes.
- Sample size is 2-5 mL for routine, family and mosaicism studies (1 mL minimum), and 5-10 mL is required for high-resolution chromosome analysis.
- For patients also having molecular Fragile X studies, draw 2-3 mL in sodium-heparin and an additional 7-10 mL in EDTA. Contact PAML for proper ordering procedures.
- For newborns, a minimum of 0.5 mL of blood is required for a routine analysis; high-resolution chromosome analysis (band levels above 600-650) is not typically obtained and therefore not possible for newborn specimens.

Bone Marrow

Bone Marrow Aspirate / Biopsy

- Add marrow (0.5 mL minimum) immediately into prewarmed (37°C) bone marrow transport media obtained from Cytogenetics laboratory.
- If transport media is not available, a sodium heparin tube is acceptable.



Products of Conception, spontaneous abortions, fetal demise or stillbirth**Placenta**

- In cases of fetal demise, the placenta maintains cell viability longer due to maternal blood circulation; therefore, placental specimens are more likely to yield cell growth and therefore a cytogenetic result.
- 5 mm³ of placenta from near the umbilical cord insertion site containing chorionic villi.

Autopsy

- If autopsy is performed, gonad, spleen, kidney, chest wall cartilage (particularly if fetus is macerated) and other internal organs can be submitted in addition to placental tissue.
- If autopsy is not ordered, 1-3 mm³ of skin can be submitted in addition to placental tissue.
- Tendons and umbilical cord are typically not good specimens due to difficulty in cell dissociation for cell culture.
- These samples must be taken before fixative (formalin) is used! Samples should never be frozen or placed on ice!
- Blood (peripheral heart puncture or cord blood) if time of death is 2 days or less. Aseptically draw into sodium heparin tube.

Transport

- Tissues should be transported in cell culture media containing antibiotics. Kits with tissue transport media and a requisition form are available from the laboratory for convenient sampling and shipping.
- Less desirable but acceptable for shipping is the use of normal saline or Hank's Balanced Salt Solution. Unacceptable sample conditions include samples that have been frozen or placed in fixative of any kind, or samples placed in viral transport media.
- Place each tissue type in a separate tube with warmed transport media containing antibiotics obtained from the Cytogenetics Laboratory.
- Please include the approximate gestational age and fetal gender, if known, with the clinical information.
- Keep sample at room temperature or refrigerated and send to the Cytogenetics Laboratory as soon as possible.
- Refrigerate if sample cannot be shipped immediately.

Skin or Other Tissues, Children or Adult

- 1-2 mm full-thickness skin punch biopsy placed in warm tissue culture media.
- If a mosaicism analysis is desired, please clearly indicate so on the test requisition form; this may require submission of more than one biopsy from the patient.

Paraffin-Embedded Tissue**Paraffin-embedded tissue for FISH**

- Submission of an intact Paraffin-embedded tissue block is preferred.
- If intact block is not available, submit 2 to 4 slides (for each FISH probe requested) with 3- to 4-micron-thick sections cut using a distilled-water bath.
- If available, please include an H&E stained slide in which the area of interest has been clearly labeled by a pathologist. ●



🕒 Hours of Operation

- The PAML Cytogenetics Laboratory is staffed to be responsive to you and your patients' needs.
- We are available seven days a week, from 7:00 AM to 5:30 PM weekdays, and from 8:00 AM to 5:00 PM on Saturdays and Sundays.
- Voice messaging is also available for after-hours needs.
- Preliminary results on STAT cases are available 7 days a week from the Laboratory Director on call.

Turnaround Time (TAT)

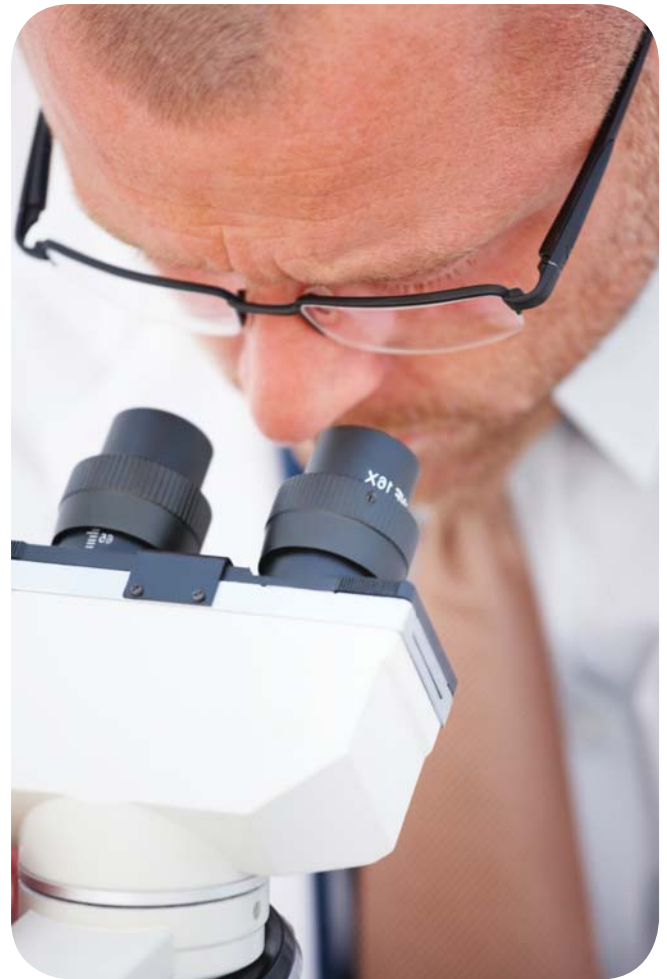
- We provide 24 to 48-hour preliminary results on bone marrow analysis requests.
- We offer a 24 to 48 hour STAT service for newborns with congenital anomalies and a turnaround time to written report of 7 days.
- Turnaround times on amniotic fluid analysis consistently average 7 days, and those of bone marrow and leukemic blood studies typically average from 5 to 10 days.
- Cytogenetics turnaround times to final written report consistently rank among the best in the industry.

Results

- Telephone results are only issued by the directors under special circumstances.
- Test results are available through an LIS interface, phoned, faxed and/or mailed upon completion of analysis.
- All abnormal prenatal results are promptly communicated by phone to the referring physician, and consultation is provided.

🗨️ Consultation Services

Directors are available to answer questions and provide clinical consultation regarding testing, testing menu, and associated issues affecting patient care (See Page 4 for names and numbers of directors). ●



Shipping and Supplies

- Shipping kits with transport media are supplied for your use with bone marrow, solid tissue, solid tumor and lymph node specimens. Order transport kits through PAML Supply at 1-800-541-7891 (Ext. 8997) or online at www.paml.com/Supply/
- All specimens should be sent at room temperature with appropriate absorbent material following federal shipping guidelines.
- Specimens for cytogenetics should not be exposed to extreme heat or cold.
- Transport is usually available by courier at your facility. If courier service is not available in your area, please send specimens via overnight transport (FedEx, UPS, or DHL).
- Custom Requisitions containing your client information are available for clients that send cytogenetics to PAML on a routine basis. Contact your PAML Marketing Representative.

SHIPPING AND STORAGE TIPS

- 1 Store transport tubes at 4 degrees C until use.
- 2 Bring media to room temperature (20 degrees C) immediately prior to specimen collection.
- 3 Ship specimens at room temperature, protected from extreme cold or heat.

SUPPLIES:



1731K
Bone Marrow
Specimen Kit



1732K
Solid Tissue
Specimen Kit

Note: These boxes contain two layers of foam and will hold up to 12 tubes for transport.



1729 Box
Cytogenetics Specimen
Transport Kit



1731 Solid Transport Tube
Bone Marrow Media
(Pink Label)



1732 Solid Transport Tube
Tissue Specimen Media
(Yellow Label)



1333 Bag Ziploc Room Temp.
Green with 3 x 6, Absorbant

**0551 Cytogenetics
Request Form**



Neoplastic FISH Probes

Clinically validated FISH probes as of March 2010



**Neoplastic DNA FISH Probes: Probes can be used for either interphase or metaphase analysis.
Probes are considered analyte-specific reagents.**

Toll Free: 1-800-541-7891

GENE REARRANGEMENT PROBES (alternate name)	TRANSLOCATION / LOCATION	DISEASE	PURPOSE
258B3, MYB, 252P19	6q13, 6q23, 6q27	Lymphoma, Myeloma, Waldenstrom's	Deletion 6q / monosomy 6
ALK (break-apart)	2p23, t(2;5) or variant	Anaplastic large cell lymphoma	ALK Gene rearrangement
ETO/AML1 (RUNX1/RUNX1T1)	t(8;21)	AML M2	Gene fusion, reciprocal translocation
ATM	11q22.3	CLL	ATM deletion
BCL2/IGH (dual fusion)	t(14;18)	Follicular or DLBCL	Gene fusion, reciprocal translocation
BCL6 (break-apart)	3q27	DLBCL	BCL6 gene rearrangement
BCR/ABL1 (dual fusion)	t(9;22)	CML, AML or ALL	Gene fusion, reciprocal translocation
CBFB (break-apart)	16q22	AML M4, Eos	inv(16) or t(16;16)
CCND1 (break-apart)	11q13	Mantle cell lymphoma	CCND1 Gene rearrangement
CCND1/IGH (BCL1/IGH) (dual fusion)	t(11;14)	Mantle cell lymphoma	Gene fusion, reciprocal translocation
CEP4, CEP10, CEP17	chr. 4, 10, 17 centromere	ALL in pediatric	Hyper- or hypodiploidy
CEP8	Trisomy 8	Myeloid disorders and CML, AML, MPD	Trisomy 8
FIP1L1, CHIC2, PDGFRA (break-apart/deletion)	4q12 rearrangement	Hypereosinophilia/mast cell disease	Chromosome rearrangement
CHOP (DDIT3) (break-apart)	12q13, t(12;16) or t(12;22)	Liposarcoma	CHOP gene rearrangement
D13S319, LAMP1	13q14, 13q34	CLL, MM, MPD, MDS	Deletion13q / monosomy 13
D20S108	20q12	Myeloid disorders	Deletion 20q
D7S486	7q31	Myeloid disorders	Deletion 7q / monosomy 7
DEK/CAN (dual fusion)	t(6;9)	AML	Gene fusion, reciprocal translocation
EGFR	7p12	Non-small cell lung cancer, glioma	Amplification status
EGR1	5q31	Myeloid disorders	Deletion 5q / monosomy 5
ELL, ENL	19p13.1, 19p13.3 t(11;19)	ALL or AML	Identify gene on 19p involved in t(11;19)
ETV6 (break-apart)	12p13	Pediatric precursor B-ALL	ETV6 gene rearrangement
ETV6/RUNX1 (TEL/AML1) (dual fusion)	t(12;21) (cryptic)	Pediatric precursor B-ALL	TEL/AML fusion
EWSR1 (break-apart)	t(11;22) or variant	Ewing sarcoma	EWSR1 gene rearrangement
FGFR (break-apart)	8p12	Myeloproliferative disorders, MPD; EMS	FGFR1 gene rearrange., amplification
FGFR3/IGH (dual fusion)	t(4;14)	Multiple myeloma	Gene rearrangement
FKHR (break-apart)	t(2;13) or variant	Rhabdomyosarcoma	FKHR gene rearrangement
FUS (break-apart)	16p11	Liposarcoma, L-G Fibrinixoid sarcoma	FUS gene rearrangement
IGH (break-apart)	14q34	Lymphoma, MM, HCL	IGH gene rearrangement
MAF/IGH (dual fusion)	t(14;16)	Multiple myeloma	Gene rearrangement
MALT1 (break-apart)	t(11;18) or variant	MALT lymphoma	MALT1 gene rearrangement
MLL (break-apart)	11q23	Leukemias	Rearrange., amplifications or deletion
MYC (enumeration)	8q24	Solid tumors, leukemias	Amplification
MYC (break-apart)	8q24	lymphoma	c-MYC gene rearrangement
MYC/IGH (dual fusion)	t(8;14)	Burkitt's lymphoma	Gene rearrangement
MYCN (N-MYC)	2p23-24	Neuroblastoma	Amplification status
NUP98 (break-apart)	11p15	AML	Gene rearrangement
PAX5	9p13	ALL, Lymphoma	t(9;14)(p13;q32),
PDGFRA (FIP1L1-CHIC2-PDGFR)	4q12 deletion/translocation	Hypereosinophilia/mast cell disease	CHIC2 deletion, FIP1L1-PDGFR fusion
PDGFRB (break-apart)	5q33	Myeloproliferative disease	Gene rearrangement
PML/RARA (dual fusion)	t(15;17)	AML M3	PML/RARA fusion
RARA (break-apart)	17q12-21	AML M3	RARA gene rearrangement
RB1	13q14	Retinoblastoma	Deletion
SIL-TAL1	1p32	T-cell ALL	SIL sub-deletion or TAL1 translocation
SHPRH, MYB, CEP6	6q24/6q23/6q10	Myeloma, Waldenstrom's	Deletion 6q / monosomy 6
SYT (SS18) (break-apart)	t(X;18) t(18q11.2)	Synovial sarcoma	Gene rearrangement
TCF3/PBX1 (dual fusion)	t(1;19)(q23;p13)	B-cell ALL	TCF3/PBX1 fusion
TCRAD (break-apart)	14q11	T-cell ALL, PLL	inv(14)(q11q32)
TP16	9p21	T-cell lymphoblastic leukemia	Deletion
TP53	17p13	Solid tumors, leukemias, MM	Deletion
TP58	1p36	Neuroblastoma, glioblastoma	Deletion 1p36
WT1*	11p15	Wilms tumor	Deletion
Panels of Probes:			
BCR/ABL 1, ETV6/RUNX1, MLL, CEP4, 10, 17		Acute lymphocytic leukemia, pediatric ALL	
AML1/ETO, PML/RARA, CBF, MLL		Acute myeloid leukemia classification	
ATM/TP53, D13S319/CEP12		Chronic lymphocytic leukemia prognosis	
MLL, D13S319, TP53, FGFR3/IGH, MAF/IGH, CCND1/IGH		Multiple myeloma prognosis	
EGR1, D7S486, CEP8, D20S108		Myeloid dysplastic syndrome (MDS)	
FIP1L1/CHIC2/PDGFR, PDGFRB, FGFR1		MPD, Myeloid and lymphoid neoplasm with eosiniphilia	
1p/19q, PTEN, EGFR, TP16		Glioma diagnosis and prognosis, therapy response	
Chromosome Enumeration Probes: Centromere probe for chromosomes 7, 8, 9, 12, 21, X, and Y are the most useful for assessment of clinically relevant chromosome gain/loss of these chromosomes in hematologic malignancies and for following patients with sex mismatched BMT.			
FDA - Approved Kits			Amplification
HER2, CEP17	17q21.1	Breast, ovarian, gastric cancer	

Form B



Form available online at www.paml.com (Forms and Brochures).

Phone: 509-434-1050

Fluorescence In Situ Hybridization (FISH) Reflex Testing Hematological Neoplastic Specimens

Toll Free: 509-541-7891 Ext. 1050

Fax : 509-747-2388

PATIENT NAME	BIRTH DATE	ACCESSION NUMBER
CLINICAL INDICATION	CYTOGENETIC RESULT	

Testing: Check boxes for entire panel or specific probes needed.

Diagnosis	Subtype	Probes Loci / Chromosome Abnormalities	Probe Loci / Chromosome Abnormalities
<input type="checkbox"/> AML		<input type="checkbox"/> AML / ETO t (8;21)	
		<input type="checkbox"/> PML / RARA t (15;17)	
		<input type="checkbox"/> CBFB inv (16) / t (16;16)	
		<input type="checkbox"/> MLL 11q23 rearrangements	
<input type="checkbox"/> B-Cell Lymphoma	Burkitt, Burkitt-like, large B-Cell	<input type="checkbox"/> MYC 8q24 rearrangement	
	Burkitt / Diffuse large B-Cell	<input type="checkbox"/> MYC/IGH t (8;14)	
	Follicular / Diffuse large B-Cell	<input type="checkbox"/> BCL2/IGH t (14;18)	
	Follicular / Diffuse large B-Cell	<input type="checkbox"/> BCL6 3q27 rearrangements	
	MALT1	<input type="checkbox"/> MALT 18q21 rearrangements	
	Mantle Cell	<input type="checkbox"/> CCND1/IGH t (11;14)	
<input type="checkbox"/> CML		<input type="checkbox"/> BCR/ABL1 t (9;22)	
<input type="checkbox"/> CLL/SLL Panel		<input type="checkbox"/> ATM/TP53 11q or 17p/p53 deletion	<input type="checkbox"/> CCND1 / IGH t (11;14)
		<input type="checkbox"/> D13S319/13q34/CEP12 -13/13q / +12	
<input type="checkbox"/> ALL-Pediatric		<input type="checkbox"/> ETV6/RUNX1 t (12;21)	<input type="checkbox"/> TP16/CEP9 -9/9p deletion or +9
		<input type="checkbox"/> MLL 11q23 rearrangements	<input type="checkbox"/> BCR / ABL1 t (9;22)
		<input type="checkbox"/> CEP4/CEP10/CEP17 Hyper or hypodiploidy	<input type="checkbox"/> PBX1/TCF3 t (1;19)
<input type="checkbox"/> ALL-Adult		<input type="checkbox"/> BCR/ABL1 t (9;22)	<input type="checkbox"/> ELL/ENL 19p rearrangements
		<input type="checkbox"/> MLL 11q23 rearrangements	
<input type="checkbox"/> MDS/AML Panel		<input type="checkbox"/> EGR1 / D5S630 -5/5q deletion	<input type="checkbox"/> CEP8 +8
		<input type="checkbox"/> D7S486 / Cep7 -7/7q deletion	<input type="checkbox"/> D20S108 20q deletion
<input type="checkbox"/> MM/MGUS Panel If IGH +, FGFR3 -, reflexes additionally to:		<input type="checkbox"/> TP53 / Cen17 TP53 / 17p deletion	<input type="checkbox"/> D13S319/13q34 -13/13q deletion
		<input type="checkbox"/> FGFR3/IGH t (4;14)	<input type="checkbox"/> MLL 11q23 rearrangements
		<input type="checkbox"/> CCND1/IGH t (11;14)	<input type="checkbox"/> MAF/IGH t (14;16)
<input type="checkbox"/> Hypereosinophilia / Eosinophilia / Mastocytosis		<input type="checkbox"/> FIP1L1-CHIC2-PDGFR4 4q12 rearrangements	
		<input type="checkbox"/> PDGFRB 5q33 rearrangements	
		<input type="checkbox"/> FGFR1 8p12 rearrangements	
<input type="checkbox"/> Bone Marrow Transplant (opposite sex donor)			<input type="checkbox"/> CEPX, CEPY
<input type="checkbox"/> Other recommended probe:			

Please indicate the desired test(s) and fax your request back to the lab with a physician signature. An addendum report will be issued when the FISH analysis is complete.

Fax : 509-747-2388

Test Ordered By:	Phone:	Date:
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Physician Signature:



Form available online at www.paml.com (Forms and Brochures).

Phone: 509-434-1050

Fluorescence In Situ Hybridization (FISH) Reflex Testing Constitutional Disorders

Toll Free: 509-541-7891 Ext. 1050

Fax : 509-747-2388

PATIENT NAME	BIRTH DATE	ACCESSION NUMBER
CLINICAL INDICATION	CYTOGENETIC RESULT	

Testing: Check boxes for specific probes needed.

Constitutional Diagnosis	FISH Probes	Locus
<input type="checkbox"/> Allagile Syndrome	<input type="checkbox"/> JAG1	20p11.23 deletion
<input type="checkbox"/> Angelman Syndrome	<input type="checkbox"/> UBE3A	15q11.2 deletion
<input type="checkbox"/> Beckwith-Wiedemann Syndrome	<input type="checkbox"/> IGF2	11p15.5 duplication
<input type="checkbox"/> CHARGE Syndrome	<input type="checkbox"/> CHD7 CHARGE, 668C3	8q12 deletion
<input type="checkbox"/> Congenital Diaphragmatic Hernia	<input type="checkbox"/> CDH1	15q26 micro-deletion
<input type="checkbox"/> Cri du Chat	<input type="checkbox"/> D5S23, D5S721	5p15.2 deletion
<input type="checkbox"/> DiGeorge / VCF Syndrome	<input type="checkbox"/> TUPLE 1 or D22S75	22q11.2 deletion
<input type="checkbox"/> 22q11.2 duplication Syndrome	<input type="checkbox"/> TUPLE 1 or D22S75	22q11.2 duplication
<input type="checkbox"/> Familial Adenomatous Polyposis/MR	<input type="checkbox"/> APC	5q22q31 deletion
<input type="checkbox"/> Kallman Syndrome	<input type="checkbox"/> KALL	Xp22.3 deletion
<input type="checkbox"/> Langer-Gideon/Multiple Exostosis 1 and 2	<input type="checkbox"/> EXT 1 <input type="checkbox"/> EXT 2	8q24.1 deletion 11p11.2 deletion
<input type="checkbox"/> Miller-Dieker Syndrome	<input type="checkbox"/> D17S379	17p13.3 deletion or duplication
<input type="checkbox"/> Neurofibromatosis, Type 1	<input type="checkbox"/> NF1	17q11.2 deletion
<input type="checkbox"/> Prader-Willi Syndrome	<input type="checkbox"/> SNRPN/CEP 15	15q11.2 deletion
<input type="checkbox"/> DUP15q11q13 Syndrome	<input type="checkbox"/> UBE3A	15q11q13 duplication
<input type="checkbox"/> Rubenstein-Taybi Syndrome	<input type="checkbox"/> CREBBP (CBP)	16p13.3 deletion
<input type="checkbox"/> Smith-Magenis Syndrome	<input type="checkbox"/> D17S25	17p11.2 deletion
<input type="checkbox"/> Soto's Syndrome	<input type="checkbox"/> NSD1	5q35 deletion
<input type="checkbox"/> 3q29 micro deletion Syndrome	<input type="checkbox"/> RP11 470E12	3q29 micro-deletion
<input type="checkbox"/> Trichorhinophalangeal. Type 1	<input type="checkbox"/> TRPS1	8q24.2 deletion
<input type="checkbox"/> Yp; Xp or Yp; autosome translocation	<input type="checkbox"/> SRY	Yp11.2
<input type="checkbox"/> Williams Syndrome	<input type="checkbox"/> ELN	7q11.23 deletion or duplication
<input type="checkbox"/> Wilm's Tumor / Aniridia (WAGR)	<input type="checkbox"/> WT1 <input type="checkbox"/> PAX6	WT1 (11p13) deletion PAX6 (11p13) deletion
<input type="checkbox"/> Wolf-Hirschorn Syndrome	<input type="checkbox"/> 4p16.3	4p16.3 deletion
<input type="checkbox"/> X-linked Ichthyosis (Steroid Sulfatase differentiation)	<input type="checkbox"/> STS (Steroid Sulfatase)	Xp22.3 deletion
<input type="checkbox"/> X inactivation center	<input type="checkbox"/> XIST	Xp13.2 deletion
<input type="checkbox"/> Subtelomeric rearrangement	<input type="checkbox"/>	
<input type="checkbox"/> Other recommended probe:		

Please indicate the desired test(s) and fax your request back to the lab with a physician signature. An addendum report will be issued when the FISH analysis is complete.

Fax : 509-747-2388

Test Ordered By:	Phone:	Date:
Physician Signature:	CPT CODES TO BILL: 88291x _____ 88271x _____ 88273x _____ 88283x _____	

Form D

Form available online at www.paml.com (Forms and Brochures).

Phone: 509-434-1050

Fluorescence In Situ Hybridization (FISH) Reflex Testing Solid Tumor Specimens

Fax : 509-747-2388

PATIENT NAME	BIRTH DATE	ACCESSION NUMBER
CLINICAL INDICATION	CYTOGENETIC RESULT	

Testing: Check boxes for specific probes needed.

Tumor Type	FISH Probes	Locus
<input type="checkbox"/> Breast Cancer	<input type="checkbox"/> HER2/CEP17	17q11.2-q12
<input type="checkbox"/> Oligodendroglioma	<input type="checkbox"/> 1p/19q, PTEN, EGFR,, TP16	1p25, 19q13, 10q23, 7p12, 9p21
<input type="checkbox"/> EWING'S SARCOMA	<input type="checkbox"/> EWSR1	22q12
<input type="checkbox"/> LIPOSARCOMA	<input type="checkbox"/> CHOP	12q13
<input type="checkbox"/> LIPOSARCOMA	<input type="checkbox"/> FUS	16p11
LYMPHOMA SUBTYPE:		
<input type="checkbox"/> Anaplastic Large Cell	<input type="checkbox"/> ALK	2p23
<input type="checkbox"/> Burkitt	<input type="checkbox"/> MYC/IGH	t (8;14)(q24;q32)
<input type="checkbox"/> Diffuse Larger Cell	<input type="checkbox"/> BCL2/IGH <input type="checkbox"/> BCL6	t (14;18)(q32;q21) 3q27
<input type="checkbox"/> Follicular	<input type="checkbox"/> BCL2/IGH	t (14;18)(q32;q21)
<input type="checkbox"/> MALT	<input type="checkbox"/> MALT1	18q21
<input type="checkbox"/> Mantle Cell	<input type="checkbox"/> CCND1/IGH	t (11;14)(q21;q32)
<input type="checkbox"/> Uncharacterized	<input type="checkbox"/> IGH	14q32
<input type="checkbox"/> NEUROBLASTOMA	<input type="checkbox"/> MYCN	2p24.1
<input type="checkbox"/> RETINOBLASTOMA	<input type="checkbox"/> RB1	13q14
<input type="checkbox"/> RHABDOMYOSARMA	<input type="checkbox"/> FKHR	13q14
<input type="checkbox"/> SYNOVIAL SARCOMA	<input type="checkbox"/> SYT (SS18)	18q11.2
<input type="checkbox"/> Wilm's Tumor / Aniridia (WAGR)	<input type="checkbox"/> WT1 <input type="checkbox"/> PAX6	WT1 (11p13) deletion PAX6 (11p13) deletion
<input type="checkbox"/> Other recommended probe:		

Please indicate the desired test(s) and fax your request back to the lab with a physician signature. An addendum report will be issued when the FISH analysis is complete.

Fax : 509-747-2388

Test Ordered By:	Phone:	Date:
Physician Signature:	CPT CODES TO BILL: 88291x _____ 88271x _____ 88273x _____ 88283x _____	

Cytogenetics Request Form

PAML Cytogenetics Laboratory

P.O. Box 2687 | Spokane, WA | 99220



PAML Cytogenetics Laboratory

110 West Cliff Avenue
Spokane, WA 99204

Phone: 509-434-1050

Toll Free: 509-541-7891 Ext. 1050

Fax : 509-747-2388

Form available online at www.paml.com (Forms and Brochures).

PATIENT NAME	SEX	DATE OF BIRTH (Required)
FINANCIALLY RESPONSIBLE PERSON	RELATIONSHIP TO PATIENT	
ADDRESS OF FINANCIALLY RESPONSIBLE PERSON		
INSURANCE	POLICY / GROUP NO.	
REFERRING PHYSICIAN		
REFERRING HOSPITAL / LAB		
DATE SAMPLE DRAWN	TIME SAMPLE DRAWN	
CLINICAL INDICATION (SAMPLE CANNOT BE PROCESSED WITHOUT THIS)		

All Specimens Should Accompany a Requisition Form with Detailed Clinical Indications for Study.

TEST REQUESTED

CYTOGENETIC ANALYSIS: Routine Analysis High-Resolution Mosaicism Family Study

FISH Probe(s) Requested: _____

OTHER: _____

TYPE OF SPECIMEN

PERIPHERAL BLOOD SOLID TISSUE TYPES: _____

BONE MARROW OTHER: (please describe) _____

AMNIOTIC FLUID: _____

COMPLETE FOR ALL AMNIOTIC FLUIDS AND POC'S AS APPROPRIATE

GESTIONAL AGE (WKS LMP):

GESTIONAL AGE (BY ULTRASOUND): AFP: YES NO

G P SAB ACHE: YES NO

COMPLETE FOR ALL BONE MARROWS

PREVIOUS BONE MARROW ASPIRATIONS (DATE):

PREVIOUS CYTOGENETIC STUDIES (DATE): CASE # IF KNOWN:

MEDICATION (PAST AND PRESENT):

RADIATION THERAPY:

CHEMOTHERAPY:

Sample Report

Name: **Last Name, First Name**
DOB/Sex: 1/1/1952/F



Cytogenetics Report

Case #:	G10-3783	Med. Rec. #:	01011952FL
Location:	S18 (PA) /	Billing #:	01011952FL
Physician:	{None}	Collected:	5/30/2010
Client:	PAML	Received:	5/30/2010
Copy To:	{None}	Completed:	6/3/2010
Other Inst:	{None}		

Specimen Type: Bone Marrow Aspirate

Clinical Indication: R/o Mantle Cell Lymphoma

Result: 46,XX,der(3)t(3;8)(q29;q12),-6,+add(8)(p11.2),t(11;14)(q13;q32),-13,add(15)(q26),+mar[6]/46,XX[13].nuc ish 11q13(CCNDx3),14q32.3(IGHx3)(CCND1 con IGHx2)[38/300]/11q13(CCNDx4),14q32.3(IGHx4)(CCND1 con IGHx3)[24/300]

Abnormal Female Karyotype

Abnormal FISH result, positive for CCND1-IGH fusion, t(11;14)

Interpretation: Cytogenetic analysis shows the presence of a complex abnormal cell clone characterized by a reciprocal translocation between chromosomes 11 and 14, unbalanced translocation between 3q and 8q, monosomy of chromosomes 6 and 13, gain of a derivative chromosome 8, additional material on 8p and 15q and the presence of a marker chromosome. Thirteen normal cells were found during the course of study.

FISH (Fluorescence In Situ Hybridization) was performed using the CCND1 and IGH gene probes, specific for the t(11;14) associated with Mantle Cell Lymphoma. Of a total of 300 interphase nuclei examined, 12.6% showed 2 fusion signals and 8% contained 3 fusion signals. These abnormal results confirm cytogenetic findings and are consistent with the presence of CCND1-IGH gene fusion and clonal evolution resulting in gain of an additional derivative chromosome in a sub-set of abnormal cells.

The t(11;14) is highly associated with Mantle cell Lymphoma including the leukemic phase of the disease. Clinical and hematopathology correlation is required.

This test was developed and its performance characteristics determined by the Cytogenetics Division of PAML. The U.S. Food and Drug Administration (FDA) has not approved or cleared this test. However, FDA approval or clearance is currently not required for clinical use of this test. This test is used for clinical purposes, it should not be regarded as investigational or for research but is not intended to be used as the sole means for clinical diagnosis or patient management decisions. PAML Cytogenetics laboratory is authorized under Clinical Laboratory Improvement Amendments of 1988 (CLIA) to perform high-complexity testing.

Cytogenetic Analysis Summary:

Number of cells analyzed:	19
Number of Cultures used for Analysis:	3
Number of Cells Karyotyped at Microscope:	11
Number of Hard Copy Karyotypes:	8
Extra Cells examined/scored:	none
Banding Level:	350-400
Banding Method:	GTW

FISH Analysis Summary:

Number of Cells Analyzed:	300 ea
Cells Analyzed:	Interphase
Probes Utilized:	CCND1/IGH
Source and Lot Number:	Abbott, 414871
Control Probe Utilized:	database

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TRI-CITIES LABORATORY
TREASURE VALLEY LABORATORY
ALPHA MEDICAL LABORATORY
MOUNTAINSTAR CLINICAL LABORATORIES
COLORADO LABORATORY SERVICES
CALIFORNIA LABORATORY ASSOCIATES

*For more information, please contact your local marketing representative or
call Toll Free: 509-541-7891 Ext. 1050*

