

TEST: Fluorescence in situ hybridization (FISH)

DESCRIPTION: Fluorescence in situ hybridization (FISH) involves the hybridization of a molecular probe labeled with a fluorescent dye to target DNA. Numerous fluorescent probes are currently available. They include unique sequence probes, chromosome enumeration probes (alpha-satellite probes) and whole chromosome paint probes. A FISH analysis includes examination of 20 metaphase cells or 200 or more interphase cells, depending upon the clinical situation. Color fluorescence photomicrographs are taken of representative FISH findings.

INDICATIONS: FISH studies are used to diagnose microdeletion syndromes or demonstrate the presence of cancer gene rearrangements characteristic of certain hematologic malignancies. FISH is also used in prenatal diagnosis for rapid detection of fetal autosomal trisomies and numerical sex chromosome abnormalities. FISH studies are useful to delineate complex chromosome rearrangements. FISH is often performed in conjunction with conventional cytogenetic analysis. The CompGene cytogenetics laboratory director is available at 414-393-1000 to discuss which FISH probe would be appropriate for a particular clinical situation.

SPECIMEN REQUIREMENTS: FISH studies may be performed on metaphase and/or interphase cells of several different sample types. These include fresh amniotic fluid, bone marrow, chorionic villi, lymph node, peripheral blood, products of conception, skin, tumor, and urine samples. Paraffin embedded formalin fixed tissue sections are frequently used for FISH when a fresh specimen is not available. FISH can also be performed on fixed cell pellets. These are often available at CompGene for patients who have had metaphase chromosome analysis since any left over fixed cells are saved for possible use in the future. Usually even if a FISH analysis is requested several months later a new blood or other type sample need not be collected. Specimen requirements are as described for chromosome analysis of various tissue types. For FISH analysis of paraffin embedded tissue please send 3 unstained slides with 4-5 micron thick tissue sections. Paraffin embedded tissue that has been decalcified is not appropriate for FISH.

REFERENCE VALUE: Reference values depend upon the specific DNA probe used for a particular clinical or cytogenetic indication. Usually two fluorescent signals will be detected for any particular probe, since in the normal state all genes, except those on the sex chromosomes of a male, are present in pairs.

TURN AROUND TIME: 1 -7 days (usually 1-2 days for hematologic disorders and prenatal diagnosis and 3-5 days for constitutional disorders)

CPT CODES: 88271 - fluorescence in situ hybridization probe
88273 - fluorescence in situ hybridization analysis 10-30 cells
88275 - fluorescence in situ hybridization analysis 100-300 cells
88275 - fluorescence in situ hybridization analysis 1000 cells
88291 - interpretation and report

PROBES AVAILABLE:

prenatal diagnosis

- AneuVysion for rapid detection of trisomy 13, 18, 21, and numerical abnormalities of X and Y
- microdeletion syndrome probes (see list of probes in the following section)
- other probe combinations can be used depending upon a specific familial chromosome rearrangement or abnormal fetal ultrasound findings

constitutional microdeletion syndromes (disorders characterized by a specific constellation of birth defects and often mental retardation)

- Angelman syndrome
- Cri du chat syndrome
- DiGeorge syndrome/velo-cardio-facial syndrome (22q11.2 deletion)
- Kallmann syndrome
- Miller-Dieker syndrome
- Prader-Willi syndrome
- Smith-Magenis syndrome
- steroid sulfatase deficiency
- velo-cardio-facial syndrome/DiGeorge syndrome
- Williams syndrome
- Wolf-Hirschhorn syndrome
- deletion 1p36 syndrome
- Phelan-McDermid syndrome (deletion 22q13 syndrome)
- sex reversal disorders involving loss or gain of the SRY gene

cancer gene rearrangements

- acute leukemia gene rearrangements

- BCR/ABL gene rearrangement brought about by the t(9;22)(q34;q11.2) translocation characteristic of chronic myelogenous leukemia and acute lymphoblastic leukemia
- ETO/AML1 gene rearrangement brought about by the t(8;21)(q22;q22) translocation of acute myelogenous leukemia
- PML/RARA gene rearrangement brought about by the t(15;17)(q22;q21) translocation diagnostic of acute promyelocytic leukemia
- MYC gene rearrangements brought about by the t(8;14)(q24;q32), t(2;8)(p12;q24) and t(8;22)(q24;q11) translocations characteristic of Burkitt's leukemia/lymphoma
- MLL gene rearrangements involving band 11q23 of acute monocytic, acute myelomonocytic and acute mixed lineage leukemia
- TEL/AML1 gene rearrangement brought about by the t(12;21)(p13;q22) translocation of acute lymphoblastic leukemia
- CFBF gene rearrangements brought about by inversion inv(16)(p13q22) and deletion del(16)(q22) characteristic of acute myelomonocytic leukemia with eosinophilia
- monosomy 5/deletion 5q of secondary acute myelogenous leukemia with dysplasia
- monosomy 7/deletion 7q of secondary acute myelogenous leukemia with dysplasia
- EVI1 gene rearrangement brought about by the inv(3q21q26) or t(3;3)(q21;q26) of secondary acute myelogenous leukemia with dysplasia

- chronic lymphocytic leukemia chromosome rearrangements

- CLL panel for trisomy 12, deletion 11q, deletion 13q, and deletion 17p

- chronic eosinophilia

- FIP1L1/PDGFR α gene rearrangement and other rearrangements of the PDGFR α gene, rearrangements of PDGFR β gene and FGFR1 gene

- **lymphoma** gene rearrangements

- ALK gene rearrangements brought about by the t(2;5)(p23;q35) translocation and other variant translocations of anaplastic large cell lymphoma
- BCL6 gene rearrangements brought about by the t(3;14)(q27;q32) translocation and other translocations involving the BCL6 gene in follicular or diffuse large B-cell lymphoma
- MYC gene rearrangements brought about by the t(8;14)(q24;q32), t(2;8)(p12;q24) and t(8;22)(q24;q11) translocations characteristic of Burkitt's leukemia/lymphoma
- BCL1/IGH gene rearrangement brought about by the t(11;14)(q13;q32) translocation characteristic of mantle cell lymphoma
- IGH/BCL2 gene rearrangement brought about by the t(14;18)(q32;q21) translocation and other translocations involving the BCL2 gene of follicular or diffuse large B-cell lymphoma
- MALT1 gene rearrangements brought about by the t(11;18)(q21;q21) translocation and other translocations of MALT lymphomas
- IGK for rearrangements of the kappa light chain gene locus
- IGL for rearrangements of the lambda light chain gene locus

- **myelodysplasia** chromosome rearrangements

- monosomy 5/deletion 5q
- monosomy 7/deletion 7q
- monosomy 20/deletion 20q
- monosomy Y
- trisomy 8
- deletion 12p and deletion 17p can also be performed

- **multiple myeloma** chromosome rearrangements

- BCL1-MYEOV1/IGH gene rearrangement brought about by the t(11;14)(q13;q32) translocation
- IGH/FGFR3 gene rearrangement brought about by the cytogenetically cryptic t(4;14)(p16;q32) translocation
- MULTIPLE MYELOMA panel includes IGH/FGFR3 gene rearrangement, deletion 13q, and deletion 17p (MYEOV1/IGH gene rearrangement, IGH/MYB gene rearrangement, (CCND3/IGH brought about by the t(6;14)(p21;q32) translocation, IGH/MAFB brought about by the t(14;20)(q32;q12) translocation, and trisomy 5, 9, 11 and 15 can also be performed)

- **solid tumors**

- EWSR1 gene rearrangements brought about by the t(11;22)(q24;q12) translocation and variant translocations of **Ewing sarcoma and other neuroectodermal tumors**
- deletions of 1p36, 1q25, 19p13 and 19q13 seen in **oligodendrogliomas**
- SYT gene rearrangement brought about by the t(X;18)(p11.2;q11.2) translocation characteristic of **synovial sarcoma**
- CHOP gene rearrangement brought about by the t(12;16)(q13;p11) translocation characteristic of **myxoid liposarcoma**
- FKHR gene rearrangement brought about by the t(2;13)(q35;q14) translocation characteristic of **alveolar rhabdomyosarcoma**
- EGFR gene amplification for invasive **colon cancer, mesothelioma, others**

delineation of complex chromosome rearrangements

Probes used (centromere probes, telomere probes, unique sequence probes) depend upon the clinical and cytogenetic situation and usually are selected by the CompGene cytogenetic laboratory director.