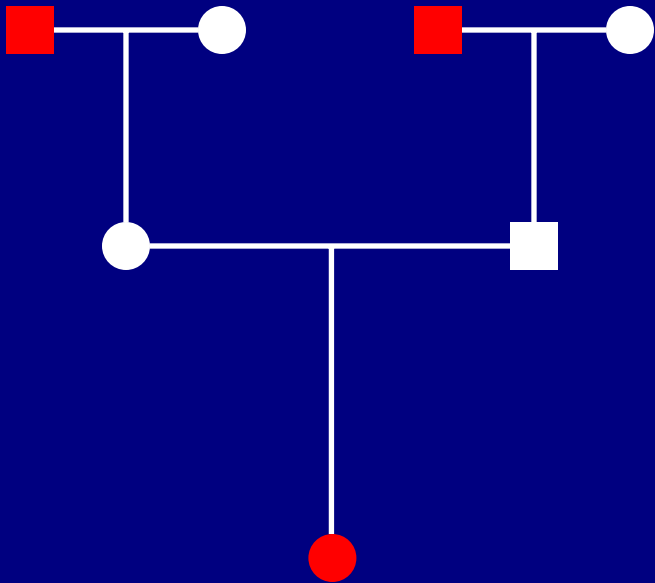


**CENTER FOR
HUMAN GENETICS
LABORATORY**

INTRODUCTION TO SERVICES



*University Hospitals Health System
Case Western Reserve University*

CENTER FOR HUMAN GENETICS LABORATORY

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Introduction

Fifty years ago, scientists were seeking the answer to a complex question: what is a gene? Much progress has been made since then. From the 1953 discovery of deoxyribonucleic acid, or DNA, the material from which genes are made, the road was paved to virtually everything that constitutes modern human genetic study. Today, physicians and scientists from University Hospitals Health System (UHHS) and Case Western Reserve University (CWRU) are on the forefront of what has been called one of the most profound developments of medical science. Through the combined efforts of our own experts and their colleagues throughout the world, we are poised on the verge of discovering not only ways to test for the presence of genetic disease but, eventually, new ways to prevent or even cure disease right at its source.

The Center for Human Genetics, a unique collaboration between clinicians of University Hospitals of Cleveland and researchers of Case Western Reserve University, is your link to this promising new era in human genetics. The Department of Genetics, <http://genetics.case.edu>, has experienced rapid growth and expansion since its formal institution in 1992. The Center for Human Genetics contains three separate, but inter-related, components: **Clinical Service, Diagnostic Laboratory, and Academic/Research**. Our interdisciplinary center brings together a multitude of medical, clinical, biochemical and molecular geneticists, genetic counselors, and researchers. This team of specialists is supported by state-of-the-art technology in the Center's laboratories that focus on prenatal screening, clinical cytogenetics, and molecular diagnostic testing. In addition, the Clinical Laboratory has an association with the many genetic research laboratories at Case Western Reserve University that study many different aspects of human, mammalian, and developmental genetics.

Who should consider consulting a specialist in genetics?

You or your patient may benefit from consulting genetics if anyone in the family has conditions such as the following:

- Mental retardation/Developmental Delay
- Birth defects (i.e. polydactyly, neural tube defects, heart defects, cleft lip/palate)
- Multiple unusual features or multiple minor anomalies
- Skeletal dysplasias or connective tissue disorders (affecting bones, tendons, or ligaments)
- Unusual growth patterns (tall, short, abnormal limb lengths)
- Disorders of internal organs (heart defects, kidney or brain abnormalities, etc)
- Ambiguous genitalia

- Neurologic disorders (hypotonia/muscle weakness, ataxia, seizures)
- Familial and non-familial cancers (multiple family members affected, early age-of onset, lymphomas, leukemia, breast/ovarian/colon cancer, etc.)
- Reproductive abnormalities (recurrent pregnancy loss, stillbirths, infertility)
- Increased risk of having a child with a genetic disorder: family history of a genetic condition, advanced maternal age, exposure to potentially harmful substances or infections during pregnancy, couples at higher risk for certain conditions (for example: Northern European and Cystic Fibrosis, Ashkenazi Jewish and Tay Sachs disease, African Americans and Sickle Cell disease)
- Known chromosomal abnormalities or genetic condition in the family
- Fetal anomalies detected by ultrasound

Why should you consult or make a referral to genetics?

A genetics evaluation can lead to a diagnosis that may explain the reasons for an individual's physical, behavioral, and/or developmental problems. This is often helpful for the family, providing them with answers to previously unanswered questions. In addition, a genetic diagnosis can provide the basis for appropriate treatment and medical management of a certain condition.

About 5% of babies are born with a birth defect or hereditary problem and many other conditions such as cancer and susceptibility to infections are being found to have a strong genetics component. This knowledge is drastically changing how genetics is playing a role in today's health care.

With rapidly advancing technology, it is nearly impossible for families (and even physicians) to keep up with new genetic testing, research, and treatments. Families with a previously diagnosed genetic condition may benefit from meeting with a geneticist and/or genetic counselor to review prognosis, inheritance, and testing options.


About Our Diagnostic Laboratory


The Center for Human Genetics includes state-of-the-art laboratories and has offered genetic screening and diagnostic testing for numerous genetic conditions for more than 25 years. The Laboratory combines clinical practice with genetic research allowing it to offer physicians and their patients advanced, innovative diagnostic testing. In addition, as an assurance of its quality, the Laboratory is certified by the College of American Pathologists (CAP) and approved by the Clinical Laboratory Improvement Amendments (CLIA).

The Laboratory consists of three related sections:


-  **Prenatal Screening Laboratory**
-  **Cytogenetics Laboratory**
-  **Molecular Diagnostic Testing Laboratory.**

These laboratories work together to offer a comprehensive genetic evaluation for each and every patient.

 The Prenatal Screening Laboratory provides testing and interpretation for the routine Triple/Quad Check usually performed between 15-24 weeks of gestation. The Triple Check uses three markers found in the mother's blood (AFP, ue3, hcG), the Quad Check adds another marker (dimeric inhibin-A). Our PSL also offers Cystic Fibrosis Screening as an option for all patients.

 The Cytogenetics Laboratory provides high quality chromosome analysis on a variety of specimens including amniocenteses, chorionic villi sampling, peripheral blood, bone marrow, tumors, and products of conception. Our Senior Cytogenetics Technologists have a combined total of more than 65 years of field expertise. The Cytogenetic Laboratory works in close conjunction with our Fluorescence in Situ Hybridization (FISH) Laboratory to detect specific abnormalities and to delineate complex karyotypes.

Our Fluorescence in Situ Hybridization Lab offers cutting edge molecular diagnostic techniques specific to many higher incidence genetic syndromes and neoplastic disorders. (page 11) Our expertise with FISH technology continues to rapidly develop and expand at our state of the art facility. FISH offers a quick turnaround time, with high levels of specificity and accuracy.

 The molecular diagnostic testing laboratory offers a variety of testing by direct DNA analyses using PCR-based methodologies, DNA hybridization, methylation analysis, sequence analysis, and other technologies. The list of tests offered at our full-service molecular laboratory continues to expand. See our test list (page 11) for an alphabetical listing of tests offered.

GENETIC COUNSELING

Genetic counseling is offered to help patients and physicians interpret test results, explain sample submission requirements, facilitate testing outside of our laboratory, and also meet with families to provide genetic counseling about testing or test results.

Please call the laboratory coordinator at (216) 983-1135 to inquire about sample requirements and/or shipping. The laboratory coordinator can facilitate necessary courier pick-ups or provide you with the laboratory's Federal Express number. Please also call the above number just prior to sending any samples.

The Laboratory can also help facilitate any available testing not listed in this brochure.

Indications for Genetic Testing

PRIMARY CARE - PEDIATRICS - INTERNAL MEDICINE - FAMILY PRACTICE

Karyotype Analysis

- § Mental retardation with unknown etiology
- § Multiple congenital anomalies
- § Dysmorphic features
- § Infertility (male or female)
- § Amenorrhea with unknown etiology
- § Short stature (male or female)
- § Abnormal or ambiguous genitalia
- § Pigmentary changes (café-au-lait spots, patches of hyper/hypo-pigmentation)
- § Hypotonia

DNA/FISH testing

- § Mental retardation with unknown etiology, especially males
- § Hypotonia
- § Multiple congenital anomalies
- § Abnormal Behaviors
- § Seizures
- § Leukemia/Cancers
- § Breast cancer in Ashkenazi Jewish population
- § Colon cancer in Ashkenazi Jewish population
- § Heart defects
- § Ambiguous genitalia
- § History of thrombosis (clotting) or strokes
- § Abnormal liver studies, liver disease

OBSTETRICS - INFERTILITY

Karyotype Analysis

- § Couples with two or more miscarriages
- § Male and female infertility
- § Family history of chromosome abnormality including translocations
- § Products of conception: stillborn children or spontaneous miscarriages
- § Abnormal Triple/Quad Check
- § Abnormal Ultrasound

DNA Testing

- § Family history of thrombosis (risk increases during pregnancy)

HEMATOLOGY - ONCOLOGY

Karyotype Analysis

- § Leukemia
- § Myelodysplastic/Myeloproliferative conditions/disorders
- § Lymphoma
- § Neuroblastoma
- § Pre/post treatment and/or transplant

DNA Testing

- § History of thrombosis
- § Hereditary Hemochromatosis

NEUROLOGY

- § Seizures
- § Ataxia/Gait disturbances
- § Hearing/vision loss
- § Dementia/Personality changes
- § Mental retardation
- § Myoclonus
- § Spasticity
- § Numbness
- § Abnormal MRI/EEG
- § Dysarthria / speech abnormalities

PRENATAL TESTING

Triple Check/Quad Check (AFP, estriol, hCG, Inhibin)

- § Available for all pregnancies, assesses risk for open neural tube and ventral wall defects, trisomy 21 (Down syndrome), trisomy 18, and pregnancies at risk for certain complications

Amniotic Fluid AFP and ACHE

- § Amniotic Fluid AFP routine for all pregnancies to detect open neural tube or ventral wall defect
- § ACHE testing to confirm elevated amniotic fluid AFP

Karyotype Analysis

- § Advanced Maternal Age (>35 years)
- § Abnormal Triple Check/Quad Check Results
- § Abnormal Ultrasound findings
- § Family history of chromosome abnormalities

DNA Testing

- § Fragile X testing if mother is a premutation carrier
- § Heart defects
- § Testing of fetus for genetic condition in family

Prenatal Screening Laboratory

Our **Prenatal Screening Laboratory** is one of the larger labs of its kind in the country. This Laboratory provides testing and interpretation for the routine Triple Check usually performed between 15-24 weeks of gestation. The Triple Check uses three markers found in the mother's blood called alpha-feto protein (AFP), unconjugated estriol (ue3) and human chorionic gonadotropin (hcG).

The Quad Check adds another marker, dimeric inhibin-A. Using all four of these makers, the Quad Check result can help more accurately determine a fetal risk of open neural tube or ventral wall defects, Down syndrome, Trisomy 18, and a few other pregnancy complications. An abnormal Triple Check or Quad Check is also often helpful to determine if an ultrasound or amniocentesis is warranted.

The laboratory also offers the routine amniotic fluid AFP (AFAFP) assay. If an AFAFP level is elevated, the laboratory will facilitate acetylcholinesterase (ACHE) testing which detects over 99% of open neural tube defects and open abdominal wall defects. Triple Check and AFAFP results are usually completed in 1-2 days, Quad Check results in 2-3 days.

Required Information for analysis

Page 12 is a copy of a requisition for the Prenatal Screening Laboratory. Please contact us to obtain additional requisitions by email, fax or traditional mail. Please complete the requisition in its entirety, including the following:

- § Patient's name
- § Patient's date of birth
- § Patient's insurance or billing information
- § Patient's weight (this can affect the values)
- § Date of ultrasound (if the patient has had an ultrasound)
- § Gestational age (preferably by ultrasound, but last menstrual period can be used as well).
 The Triple Check can be performed between 15-25 weeks gestation.
- § Patient's ethnicity or race (as certain ethnic groups have different cut-off values)
- § Date of the blood draw
- § Whether there is a family history of neural tube defects
- § Whether the patient is diabetic
- § Whether it is a twin or singleton pregnancy

Sample Requirements

A single red top tube of blood or serum separator tube is required for analysis. The sample can be stored in a refrigerator for 1-2 days and should be shipped at room temperature.

Cytogenetics Laboratory

The **Cytogenetics Laboratory** routinely performs chromosomal analysis on amniotic fluid, chorionic villi samples (CVS), peripheral blood, cord blood, skin, bone marrow, and other tissues. This analysis can detect substantial extra or missing genetic material, thus ruling out such things as Down syndrome, chromosomal translocations, and other cytogenetic problems. Such testing may be warranted for high-risk pregnancies (abnormal triple check/quad check, abnormal ultrasound, women over the age of 35), miscarriages, children that are stillborn, children with dysmorphic features, or when there is a family history of a chromosomal abnormality. In addition, cytogenetics can also be performed on bone marrow and/or blood for a number of different cancers to help diagnose particular types of cancer, determine prognosis to help select a treatment, and determine if an individual is benefiting from a recent therapy.

Any abnormal results are immediately called and faxed to the referring physician with recommendations for appropriate follow-up. Experienced professionals can answer questions and can direct calls to obtain test results. Cytogenetic results are usually available in 8-10 days with preliminary results often available in 4-6 days.

The Cytogenetics Laboratory also works in close association with the Fluorescence In-Situ Hybridization (FISH) Laboratory on prenatal and postnatal specimens. FISH can confirm the presence or absence of certain small regions of chromosomes not detected by routine cytogenetics. Please see page 11 for a complete listing of the FISH testing that is currently available.

Aneuvysion, a commonly prescribed prenatal FISH test can be performed on an amniocentesis to detect aneuploidy in chromosomes 13, 18, 21, X, and Y. These results can be ready in 24-48 hours. This test is often appropriate when the patient is of late gestational age, or Trisomy 13, 18, 21 (Down syndrome), Turner syndrome, or ambiguous genitalia is suspected. Also, if an elevated risk of any of these conditions is detected during routine Triple Check or Quad Check testing, Aneuvysion may be requested.

Sample Requirements

At least 3-5ccs of blood or 2ccs of bone marrow in a green top (sodium heparin) tube is required for a karyotype (chromosome analysis) or any FISH test. Please note that some tests (Fragile X, Prader-Willi and Angelman syndromes) require both a purple top and green top tube, as these tests require cytogenetics/FISH analysis and Molecular DNA testing. The sample can be stored at room temperature for 1-2 days and can be shipped at room temperature.

Tissues from miscarriages or a fetal demise should be sent in HBSS media or sterile saline. Do **NOT** freeze or fix specimens. Preferred tissues for miscarriages are (in order of preference): chorionic villi, membrane, or sac. Preferred tissues of a fetal demise are (in order of preference): lung, deep muscle, achilles tendon, kidney, skin, chorionic villi. Please label each specimen and do not include more than 1-2 cubic centimeters of each tissue.

Molecular (DNA) Diagnostic Laboratory

The Molecular Diagnostic Laboratory offers a variety of testing to help diagnose genetic conditions that cannot be diagnosed by routine cytogenetics. By using technology such as PCR and Southern blot analyses, the Molecular laboratory can detect specific DNA mutations for particular genetic conditions. Please see the page 11 for a list of testing that is currently available.

Sample Requirements

At least 3-5ccs of blood in a purple top (EDTA) tube is required for molecular tests. Please note that some tests (Fragile X, Prader-Willi and Angelman syndromes) also require a green top tube for the associated cytogenetic component.

INDICATIONS FOR COMMON MOLECULAR TESTS

Angelman Syndrome

Mental retardation
Ataxia
Seizures
Erratic arm movements (hand flapping)
Unprompted laughter
Lack of speech

Breast Cancer

(BRCA1/2 in Ashkenazi Jewish)
A significant family history of breast and/or ovarian cancer
Breast and/or ovarian cancer before the age of 40

Familial Adenomatous Polyposis

(APC/I307K mutation in the Ashkenazi Jewish)
Personal or Family history of colorectal polyps and/or cancer

Fragile X Syndrome

Mental retardation, especially in males
Long, thin face, protruding jaw, and large ears
Macroorchidism (large testes)
Autistic-like and other behavioral problems
Mitral valve prolapse

Hereditary Hemochromatosis

Liver dysfunction
Endocrine dysfunction
Skin hyper-pigmentation
Cardiomyopathy
Arthropathy

Connexin 26 Testing and/or AGID

Sensorineural or other Hearing Loss
Deafness

Medium-Chain Acyl-CoA Dehydrogenase (MCAD) Deficiency

Intermittent hypoglycemia
Hyper-ammonemia
Carnitine Deficiency
Excretion of certain fatty acids in urine
Vomiting, lethargy, coma, and/or death
Often misdiagnosed as SIDS

Mitochondrial Disorders

(MELAS, MERRF, NARP/Leigh Syndromes)
Myopathy
Hearing loss
Epilepsy, ataxia, or spasticity
Eye abnormalities
Abnormal lactate or pyruvate levels

Prader-Willi Syndrome

Severe hypotonia
Mental retardation
Obesity/hyperphagia
Abnormal genitalia

SRY/Testis Determining Factor

Ambiguous or abnormal genitalia
Discrepant gender identification

Thrombosis Panel

(Factor V Leiden, MTHFR, Prothrombin)
Thrombosis events
Stroke / Premature cardiovascular disease
Elevated homocysteine levels
Pre-eclampsia

Uniparental Disomy

Translocations or mosaicism involving chromosomes 6, 7, 14 and 15

FISH Diagnostic Laboratory

Our **Fluorescence in Situ Hybridization Lab** offers cutting edge molecular diagnostic techniques specific to many higher incidence genetic syndromes and neoplastic disorders. Our expertise with FISH technology continues to rapidly develop and expand at our state of the art facility. FISH offers a quick turnaround time, with high levels of specificity and accuracy. Please see page 11 for a comprehensive listing of available FISH tests.

Sample Requirements

As with routine cytogenetics, FISH testing requires at least 3-5ccs of **blood** or 2ccs of **bone marrow** in a green top (sodium heparin) tube. For other admissible tissue types, please reference the sample requirements section of the Cytogenetics Laboratory.

INDICATIONS FOR COMMON FISH TESTS

AneuVysion (supplemental amniocentesis test)
Allows for rapid count of chromosomes
13, 18, 21, X and Y
Used in later gestation pregnancies or after
abnormal ultrasound

Bcr-Abl
Confirms translocation t(9;22) found in chronic
myelogenous leukemia (CML)

Cri-du-Chat Syndrome (5p- syndrome)
Cat-like cry in infancy
Mental retardation
Multiple congenital anomalies
Heart defects

DiGeorge/Velocardiofacial Syndromes (22q11)
Velopharyngeal insufficiency / cleft palate
Hypernasal speech
Heart defects (prenatal or postnatal)
Learning disabilities
Absent or hypoplastic thyroid gland
Immune deficiency (abnormal T cell function)
Psychiatric disorders

Miller-Dieker Syndrome (17p13)
Lissencephaly
Mental retardation
Facial dysmorphism

PML-RARA
Confirms translocation t(15;17) found in
promyelocytic leukemia (PML)

Retinoblastoma (13q14)
Detects deletion in 5-10% of patients
Unilateral or bilateral eye tumors

Rubinstein-Taybi Syndrome (16p13.3)
Broad thumbs and Toes
Mental retardation
Hypoplastic maxilla
Beaked nose
Detects up to 25% of patients

Smith-Magenis Syndrome (17p11)
Abnormal and self-injurious behaviors
Abnormal sleep patterns
Hoarse Voice
Mental retardation
Facial dysmorphisms

**Steroid Sulfatase Deficiency
(X-linked ichthyosis)**
Dry, flaky or scaly skin
Cataracts
Can have very low ue3 (estriol) levels by triple check

Williams Syndrome (7q11.23)
Distinctive "cocktail" personality
Prominent lips
Hoarse voice
Mental retardation
Heart defects (pulmonary hypoplasia
Stellate pattern in iris

Wolf-Hirschorn Syndrome (4p-)
Mental retardation
Failure to thrive
Retarded growth
Seizures
Facial dysmorphism

List of FISH tests offered:

Syndromes:

1p36 Deletion syndrome
Angelman Syndrome
Aneuvysion (prenatal testing for 13,18,21,X,Y)
Cri-du-chat Syndrome (5p-)
Kallman Syndrome
Miller-Dieker Syndrome
Prader-Willi Syndrome
Retinoblastoma
Rubinstein-Taybi Syndrome
Smith-Magenis Syndrome
Sotos Syndrome
Steroid Sulfatase Deficiency
- (STS, X-linked ichthyosis)
Velocardiofacial/DiGeorge Syndrome
William Syndrome
Wolf-Hirschorn (4p-) Syndrome

Cancers:

CLL (13q,11q,17p, trisomy 12)
Deletion 5q
Deletion 7q
Deletion 13q
Inverted 16; t(16;16)/del 16 (AML-M₄)
MLL involvement (11q23)
Monosomy 7
Multiple Myeloma (13q,17p,14q)
Sex Chromosomes (X/Y) Transplant
t(4;14) (Myeloma)
t(8;14) (Burkitt's lymphoma)
t(9;22) (BCR-ABL fusion for CML and ALL)
t(11;14) (Lymphoma)
t(11;22) (Ewing Sarcoma)
t(12;21) (TEL-AML1 fusion for ALL-pediatric)
t(15;17) (PML-RARA fusion for APL)
t(14;18) (Lymphoma)

Additional Testing:

Cryptic Rearrangement (Telomeric Studies)
M-FISH (identify /delineate marker chromosome)
Sex chromosome determination (X/Y)
Submicroscopic Deletions

List of Molecular tests offered:

Aminoglycoside-induced Deafness
Angelman Syndrome (Methylation Studies)
APC I307K
Chimerism (Pre/Post Transplant Studies)
Connexin 26 (sequencing)
Cystic Fibrosis Carrier Testing (41 mutations)
Cystic Fibrosis poly (T) variant
DNA Extract and Store
Factor V Leiden Mutation
Factor V HR2 Mutation
Familial Colon Cancer (FAP, Ashkenazi I1307K)
Fragile X Syndrome
Hereditary Hemochromatosis
Identity Testing
LCHAD Deficiency
MCAD Deficiency
MELAS Analysis
MERRF Analysis
Mitochondrial Panel (MELAS, MERRF, NARP)
MTHFR Gene Mutation C677T
NARP/LEIGH Syndrome
Prader-Willi Syndrome (Methylation Studies)
Premature Ovarian Failure
Prion Disease (Mutation Analysis)
Prothrombin G20210A
Russel Silver (UPD 7)
SRY/TDF
Thrombosis/Thrombophilia Panel
- (Factor V, MTHFR, Prothrombin)
Transient Neonatal Diabetes (UPD 6)
Translocation Carrier
Uniparental Disomy Studies
- (6, 7, 14, 15)
X Inactivation Pattern
Y deletion for male infertility
Zygosity testing

Center for Human Genetics Laboratory

University Hospitals of Cleveland/Case Western Reserve University
10524 Euclid Avenue, 6th Floor
Cleveland, OH 44106 Tel: (216) 983-1135 Fax (216) 983-1144

Prenatal Genetic Requisition Form

Medical Record Number _____

PATIENT INFORMATION

Name (Last, First) _____ Phone (H) (____) _____ DOB ____/____/____

Address _____ (W) (____) _____ SS# ____-____-____

City/State/Zip _____

Ethnicity: Caucasian (NW European, SW European) Ashkenazi Other Jewish Hispanic Asian African American
 Native American Other _____

REFERRING PHYSICIAN

Name _____ Other Physician: _____

Phone: _____ Fax: _____ Genetic Counselor _____

BILLING INFORMATION

Bill: Insurance Referring Institution Patient Other Party

Please attach any appropriate billing information

SPECIMEN INFORMATION

Amniotic Fluid _____ cc's (1st cc's separated Y / N) (Gravida _____ Para _____) CVS

Products of Conception (specify) _____ Tissue (specify) _____ Cord Blood _____ cc Other (specify) _____

Date specimen collected _____ Time Collected _____ Where drawn (institution): _____

INDICATIONS FOR TESTING

Pregnant: Y / N Gestational age: _____ weeks Gender by U/S: Male / Fem / Unkn. Twins: Y / N

- | | | | |
|--|--|--|--|
| <input type="checkbox"/> Abnormal Triple Check
DS risk 1: _____
NTD risk 1: _____
MSAFP: (high) _____ MoM
Tri 18 risk 1: _____ | <input type="checkbox"/> Choroid Plexus Cyst
<input type="checkbox"/> Cystic Hygroma
<input type="checkbox"/> D&E
<input type="checkbox"/> Dandy Walker Malformation
<input type="checkbox"/> Diaphragmatic Hernia
<input type="checkbox"/> Duodenal Atresia
<input type="checkbox"/> Echogenic Bowel
<input type="checkbox"/> Echogenic Intracardiac Focus
<input type="checkbox"/> Encephalocele | <input type="checkbox"/> Gastroschisis / Omphalocele
<input type="checkbox"/> Heart Defect (list type below)
<input type="checkbox"/> Hydrocephalus
<input type="checkbox"/> Hydrops
<input type="checkbox"/> IUFD
<input type="checkbox"/> IUGR
<input type="checkbox"/> Microcephaly
<input type="checkbox"/> Neural tube defect (list below)
<input type="checkbox"/> Nuchal Translucency | <input type="checkbox"/> Oligo / Polyhydramnios
<input type="checkbox"/> Pyelectasis
<input type="checkbox"/> Recurrent Pregnancy Loss
<input type="checkbox"/> Short femur
<input type="checkbox"/> Single Umbilical Artery
<input type="checkbox"/> Spontaneous Abortion
<input type="checkbox"/> Translocation Carrier
<input type="checkbox"/> Ventriculomegaly |
|--|--|--|--|

Other _____

CHECK TEST REQUESTED

Chromosome Analysis / Karyotype (Amniotic fluid AFP done automatically unless otherwise specified) No AFP

FISH

- | | | |
|--|--|---|
| <input type="checkbox"/> AneuVysion (prenatal screen for abnormalities of X,Y,13,18,21) Need extra (>3cc) amniotic fluid | <input type="checkbox"/> DiGeorge/Velocardiofacial Syndrome
<input type="checkbox"/> Miller-Dieker Syndrome (Lissencephaly)
<input type="checkbox"/> STS (X-linked ichthyosis) | <input type="checkbox"/> Williams Syndrome
<input type="checkbox"/> Wolf-Hirschhorn (4p-) Syndrome
<input type="checkbox"/> Other _____ |
|--|--|---|

Molecular:

- | | | |
|---|--|---|
| <input type="checkbox"/> Cystic Fibrosis Carrier Screening (41 mutations) | <input type="checkbox"/> Factor V Leiden | <input type="checkbox"/> Uniparental Disomy: chromosome # _____ |
| <input type="checkbox"/> Family History of CF | <input type="checkbox"/> MTHFR | <input type="checkbox"/> Other _____ |
| <input type="checkbox"/> Patient/Couple is pregnant | <input type="checkbox"/> Prothrombin 20210 | |

ADDITIONAL TESTS REQUESTED ON AMNIOTIC FLUID/CVS CELLS (to be sent to another lab)

- | | | |
|--|---|--|
| <input type="checkbox"/> Cystic Fibrosis | <input type="checkbox"/> Parvovirus | <input type="checkbox"/> Toxoplasmosis |
| <input type="checkbox"/> Cytomegalovirus (CMV) | <input type="checkbox"/> RH-D genotyping (histocompatibility) | |
| <input type="checkbox"/> Herpes I/II | <input type="checkbox"/> Sickle Cell Analysis | <input type="checkbox"/> Other _____ |

Special Instructions:

Save cells temporarily for the following reason: _____

SPECIMEN INFORMATION

Peripheral Blood Cord Blood from liveborn Other _____
 DNA Cord Blood from stillborn/demise
 Tissue _____ Cord Blood from ongoing pregnancy

*Collection date _____
 Phlebotomist _____
 Institution _____

PATIENT INFORMATION

Name (Last, First): _____

DOB: ____/____/____ Medical Record Number: _____

Sex: Male Female Ambiguous Unknown **Pregnant:** Yes / No Gestational age: _____

Ethnicity: Caucasian (N. and S. European) Ashkenazi Jewish Hispanic Asian Afr. American Other: _____

Address: _____ Phone: _____

City, State, Zip: _____ SS #: ____/____/____

REFERRING PHYSICIAN

Name _____ Phone: _____ Fax: _____

Name & Phone of person completing requisition: _____ Informed consent obtained (if appropriate)

BILLING INFORMATION

Bill: * Insurance Referring Institution Check enclosed for \$ _____

* If Insurance will be billed, please attach a copy of current insurance card (front and back), which should include:
 Patient Name, Insurance Provider address & phone #, Policy #, Group #, Relationship to Patient

TEST INDICATION
 (Check at least one)

- Amenorrhea (primary or secondary 626.0)
- Ambiguous genitalia
- Autism
- Behavior Abnormalities
- Cleft lip and/or palate
- Deep vein thrombosis
- Developmental delay
- Dysmorphic Features (list below)
- Failure to thrive
- Family hx of chromosome abnormality
- Family hx of clotting disorder
- Family hx of mental retardation
- Hearing loss
- Heart Defect (list type below)
- Hypotonia
- Infertility
- Iron storage disorder
- Mental retardation
- Mult. Congenital Anomalies (list below)
- Pulmonary embolism
- Recurrent pregnancy loss
- Seizures
- Short stature
- Stroke
- Other _____

CYTOGENETIC TESTS
 (Green top tube-Sodium Heparin)

- CHROMOSOME ANALYSIS, HIGH RESOLUTION
 (also known as karyotype or cytogenetics)
 - ' With five-cell, lower resolution preliminary result called within 48-72 hours (extra charge, done for newborns only)
 - ' With extra 10 counts for sex-chromosome mosaicism (used with Q. 45,X or Q. 47,XXY)
- FISH with selected probe(s)
 - ' 1p Deletion Syndrome
 - ' Angelman Syndrome
 - ' Cri-du-Chat Syndrome
 - ' DiGeorge/VCF Syndrome
 - ' Miller-Dieker Syndrome
 - ' Prader-Willi Syndrome
 - ' Retinoblastoma
 - ' Rubinstein-Taybi Syndrome
 - ' Prader-Willi Syndrome
 - ' Smith-Magenis Syndrome
 - ' Sotos Syndrome
 - ' STS(X-linked Ichthyosis)
 - ' Williams Syndrome
 - ' Other Probe _____
- FISH with all SUBTELOMERE PROBES
- Other _____

MOLECULAR TESTS
 (Purple Top tube—EDTA)

- Aminoglycoside-induced Deafness
- Connexin 26 (sequencing)
- Cystic Fibrosis (41 mutations) (need ethnicity)
 - ' Patient/Couple is pregnant
 - ' Family history of CF
- DNA Extract & Store (specify indication)
- Factor V Leiden Mutation (ICD9=286.3)
- Factor V HR2 Mutation (ICD9=286.3)
- Familial Colon Cancer (FAP, Ashkenazi I1307K mut.)
- Fragile X Syndrome (chromosome analysis required - order under Cytogenetic Tests)
- Hereditary Hemochromatosis
- Methylation - Chr. 15
 - ' Angelman Syndrome
 - ' Prader-Willi Syndrome
- MTHFR (ICD9=286.3)
- Prothrombin 20210 (ICD9=286.3)
- Thrombosis Panel (ICD9-286.3) (Factor V, MTHFR, Prothrombin)
- Uniparental Disomy, Chrom.# _____
- Y deletion for male infertility
- Zygosity
- Other _____

Other Laboratory Information

RESEARCH STUDIES

The Department of Genetics at Case Western Reserve University is one of the top ten federally funded genetics research institutions in the country. Current research includes studies on identification of protein mutations related to Skeletal Dysplasia and Osteoarthritis, small nuclear ribonucleoproteins (snRNPs) and their connection to Spinal Muscular Atrophy, and a variety of projects related to the influence of familial factors on neoplasm development. Many previous innovative research projects have resulted in the formulation of new diagnostic clinical tests.

ADDITIONAL INFORMATION

If you have questions about specimen requirements or shipping and handling, you may contact the laboratory coordinator directly at (216) 983-1135. We would also ask that you call this number just prior to sending any samples. We can provide you with detailed sample requirements by request.

We have seven Genetic Counselors on staff to answer any specific patient or physician questions about testing or results. We can also help facilitate genetic testing not offered by our laboratory. If you have a question about any tests not listed on the following pages, please call the main laboratory number at (216) 983-1134 to help locate and arrange testing.

We can usually arrange for a courier to pick-up samples on a routine basis or when needed. It is best to send samples overnight Monday-Thursday.

The hours for the Laboratory are from 8:30 am -5:00 pm Monday-Friday. All off hours inquiries left in the main lab voicemail box will be returned promptly the next business day.