INFORMATION FOR CLINICIANS IN WOMEN’S REPRODUCTIVE MEDICINE

PRECONCEPTION/PRENATAL GENETIC TESTING SERVICES

BAYLOR MIRACA HAS BEEN A PIONEER IN CHROMOSOMAL MICROARRAY TESTING AND IN RESEARCH, DISCOVERY, AND IMPLEMENTATION OF THE HIGHEST QUALITY OF GENETIC TESTING FOR OVER 40 YEARS.
Baylor Miraca Genetic Laboratories (BMGL) is an industry leader in implementation of new technology and genetic testing services in reproductive women’s care. The wide breath of BMGL's innovative genetic testing services continue to expand to provide the most comprehensive genetic testing services relevant to current and future 21st century medicine.

BMGL comprehensive genetic reproductive services include:

PRECONCEPTION:
- **GeneAware** (expanded carrier testing)
- Parental Blood Chromosome analysis
- Parental Chromosomal Microarray (CMA)

Prenatal:
- **GeneAware** (expanded carrier testing)
- Noninvasive Prenatal Testing (NIPT)
- FISH/prenatal aneuploidy testing (13, 18, 21, X, Y)
- Prenatal chromosome analysis, AFAFP and ACHE
- Prenatal Chromosomal Microarray (targeted or expanded)
- Prenatal Whole Exome Sequencing
- Prenatal Noonan Spectrum Disorder Testing
- Gene Specific Screening and/or Sequencing
  (ex. Cystic Fibrosis, Fragile X, Spinal Muscular Atrophy)
- Genetic Mutation Analysis for Hundreds of Distinct Genetic Disorders

PRODUCT OF CONCEPTION/ FETAL DEMISE/AUTOPSY:
- Chromosomal Microarray (CMA)
- Whole Exome Sequencing
- Single Gene Mutation Analysis
Prenatal Chromosomal Microarray (CMA) Testing

We were a pioneer in developing and offering chromosomal microarray services, and we remain an industry leader in the implementation of new technology for this and other services. The Baylor Miraca Genetics Laboratories (BMGL) offer a variety of testing for Prenatal Chromosomal Microarray, Analysis. BMGL has been a leading provider of clinical array testing for over 10 years. Now that the National Institute of Health (NIH) Prenatal CMA trial is complete, we want to be your Prenatal CMA lab of choice. BMGL offers many advantages to help patients, physicians and counselors with CMA studies.

I. CMA–Targeted
This Prenatal array is very similar to what was used in the NIH trial and is ideal for physicians, counselors and patients who want detection of all well characterized, deletion and duplication syndromes. It also includes additional deletion/duplication syndromes that were not yet characterized when the NIH array was designed. This array includes 105,000 oligonucleotides and has a very low rate of variants of unknown significance.

II. CMA-Targeted + Limited Karyotype Analysis
This option includes the Limited array as described above plus a 5 cell chromosome analysis to rule out rearrangements not detected by microarray such as balanced translocations, inversions and triploidy. The benefits of the limited karyotype are lower cost and a quicker turnaround time.

III. CMA – Expanded
BMGL also offers an EXPANDED prenatal array. This array offers exon by exon coverage for over 1700 genes. In our experience, this array detects more genetic disorders, without significantly increasing the variant of unknown significance rate lead to difficult counseling situations. The EXPANDED array is recommended for families who want the highest level of chromosomal microanalysis possible (understanding no single test can assess for every possible genetic outcome).

IV. CMA-Expanded + Limited Karyotype Analysis
This option includes the Expanded array as described above, plus a 5 cell chromosome analysis to rule out rearrangements not detected by microarray such as balanced translocations, inversions and triploidy. The benefits of the limited karyotype are lower cost and a quicker turnaround time.

Services
1. Insurance contracts with all of the major providers. This provides for the least out of pocket expense to the patient.
2. Flexible payment plans.
3. BMGL will perform prior authorization at the request of the patient, physician, or counselor.
4. Industry leading turnaround time as a product of optimizing direct amnio and CVS analysis (80% if results are reported in 5-7 calendar days).
5. BMGL custom designed arrays avoid regions of uncertainty, providing results of uncertain clinical significance in less than 1% of cases.
6. Large group of lab directors and clinicians with extraordinary experience in interpreting and signing out prenatal arrays. We have signed out more than 4000 prenatal arrays since 2007, both as clinical care leaders and as part of the NIH study.
7. Parental studies at no cost BMGL requests that blood samples on both parents be submitted together with the fetal specimen in order to improve turnaround time and reduce parental anxiety where possible.
Test Offered

Aneuploidy FISH, G-banded Chromosomal Analysis, Noonan Panel, Prenatal Chromosomal Analysis (CMA), and Prenatal TRIO Whole Exome Sequencing. For additional testing information please see quick reference guide tab.

Shipping information

Ship the sample at room temperature to the laboratory by overnight express. Specimen should arrive in the laboratory within 48 hrs of sample date. Specimen cannot be frozen. Ship the sample at room temperature to the laboratory by overnight express. Specimen should arrive in the laboratory within 48 hrs of sample date. Specimen cannot be frozen. Ship at room temperature in an insulated container by overnight courier. Do not heat or freeze. Sample must arrive within 48 hrs.

Turnaround Time

7-10 days
Chorionic Villus Sampling (CVS)

Chorionic villus sampling (CVS) is available as a method of prenatal diagnosis of chromosomes and genetic disorders for women who are less than 14 weeks pregnant. This test can be performed earlier than amniocentesis, which is usually performed between 15 and 20 weeks, thereby offering results earlier in the pregnancy.

Who should consider CVS?

CVS is offered to women age 35 or older at the time of delivery, individuals who have had a child with a chromosome abnormality, individuals who have a chromosome translocation, and couples at risk for a prenatally diagnosable genetic disease (e.g., hemophilia or sickle cell disease). CVS may also be offered when certain abnormalities are seen on ultrasound or when first trimester screening or non-invasive prenatal testing has identified an increased risk for certain chromosome or fetal anomalies. CVS is also available to any woman interested in having diagnostic prenatal testing performed.

When is CVS performed?

CVS is traditionally performed between 11-14 weeks after a woman’s last menstrual period (during the first trimester).

What can be detected through CVS?

Chromosome abnormalities, such as Down syndrome, can be detected through CVS. If indicated, some genetic diseases can be diagnosed through DNA or enzyme analysis. Prenatal chromosomal microarray analysis (CMA) allows for detection of additional chromosome abnormalities not detectable through standard chromosome analysis. See the prenatal CMA brochure for more details about this testing. CVS cannot detect neural tube defects such as spina bifida. Therefore, it is recommended that all women who undergo CVS consider having their blood drawn at 15-18 weeks of pregnancy for a spina bifida screening test (maternal serum AFP assay). This can be arranged through your obstetrician. Many women also wish to pursue a level II ultrasound at 18-20 weeks for further information regarding the physical development of the fetus. No method of prenatal testing can guarantee a baby will be born without birth defects or genetic disease. It is also important to remember that 2-3% of all children are born with a birth defect or intellectual disability regardless of whether or not a woman had prenatal testing during her pregnancy. Prenatal testing can only identify certain problems for which a couple is known to be at risk. Unfortunately, there are many conditions for which prenatal diagnosis is not yet routinely available. Prenatal DNA analysis often requires that the specific familial genetic change has been identified. Unfortunately, there are many conditions for which prenatal diagnosis is not yet routinely available.

How accurate are the results from CVS?

Chromosome results from CVS are greater than 99% accurate. Occasionally some results need to be clarified through blood tests on the parents, ultrasounds, amniocentesis, or fetal blood sampling.
When will I receive my test results?
Chromosome and CMA results are typically available 2 weeks after the procedure. Preliminary results are typically available within 48 hours. Special studies for other genetic diseases may take longer.

What are the advantages of CVS?
The greatest advantage of CVS is timing and the amount of disorders that are detectable with this testing. Since CVS is performed during the first trimester of pregnancy, the results from the CVS are available earlier than are amniocentesis results.

How Do I Learn More?
All the information can be discussed in greater detail during a genetic counseling session or with your physician. It can be helpful to schedule an appointment for genetic counseling prior to the CVS procedure. The genetic counselor/healthcare provider will not only discuss the procedure in greater detail, but will also determine whether additional testing is appropriate and ensure that all of your concerns are addressed. The genetic counselor is also available to follow-up with you after the results of the CVS become available.

Test Offered
Aneuploidy FISH, G-banded Chromosomal Analysis, Noonan Panel, Prenatal Chromosomal Analysis (CMA), and Prenatal TRIO Whole Exome Sequencing. For additional testing information please see quick reference guide tab.

Shipping information
Ship the sample at room temperature to the laboratory by overnight express. Specimen should arrive in the laboratory within 48 hrs of sample date. Specimen cannot be frozen. Ship the sample at room temperature to the laboratory by overnight express. Specimen should arrive in the laboratory within 48 hrs of sample date. Specimen cannot be frozen. Ship at room temperature in an insulated container by overnight courier. Do not heat or freeze. Sample must arrive within 48 hrs.

Turnaround Time
7-10 days
Amniocentesis

Amniocentesis is typically offered to women who are greater than 15 weeks pregnant. Amniocentesis is a method of prenatal diagnosis of chromosomes and genetic disorders that has been performed for over 30 years. Women who are less than 15 weeks pregnant may wish to consider pursuing a chorionic villus sampling (CVS) procedure instead of amniocentesis.

Who Should Consider Amniocentesis?
Amniocentesis is generally offered to women age 35 or older at the time of delivery, individuals who have had a child with a chromosome abnormality, individuals who have a chromosome translocation, couples at risk for a prenatally diagnosable genetic disease (e.g., hemophilia or sickle-cell disease), and individuals with a child or other close family member with a neural tube defect (spina bifida or anencephaly). Amniocentesis may also be offered when certain abnormalities are seen on ultrasound or when maternal serum screening or non-invasive prenatal testing has identified an increased risk for certain chromosome or fetal anomalies. Amniocentesis is also available to any woman interested in having diagnostic prenatal testing performed.

When Is Amniocentesis Performed?
An amniocentesis is typically performed between 15-20 weeks after a woman’s last menstrual period. It can, however, be performed later if necessary.

What Can Be Detected Through Amniocentesis?
Chromosome abnormalities (such as Down syndrome) can be detected through amniocentesis. The majority of neural tube defects can be detected by elevated levels of AFP in the amniotic fluid. Some specific genetic diseases can be diagnosed by DNA or enzyme analysis if indicated. Prenatal chromosomal microarray analysis (CMA) can also be performed and allows for detection of additional chromosome abnormalities not detectable through standard chromosome analysis. See the prenatal CMA brochure for more details about this testing.

How Accurate Are The Results from Amniocentesis?
Chromosome results are greater than 99% accurate. Amniotic fluid AFP is 96% accurate in detecting open neural tube defects. Occasionally, some results need to be clarified through blood tests on the parents, ultrasound, a repeat amniocentesis, or fetal blood sampling. No method of prenatal testing can guarantee a baby will be born without birth defects or genetic disease. It is also important to remember that 2-3% of all children are born with a birth defect or intellectual disability regardless of whether a woman had prenatal testing during her pregnancy. Prenatal DNA analysis often requires that the specific familial genetic change has been identified. Unfortunately, there are many conditions for which prenatal diagnosis is not yet routinely available.

How Long Do The Results Take?
Chromosome, amniotic fluid AFP, and prenatal CMA results are typically available within two weeks. Preliminary results are typically available within 48 hours. Special studies for other genetic diseases may take longer.
How Do I Learn More?

All the information can be discussed in greater detail during a genetic counseling session or with your physician. It can be helpful to schedule an appointment for genetic counseling prior to the amniocentesis procedure. The genetic counselor/healthcare provider will not only discuss the procedure in greater detail, but will also determine whether additional testing is appropriate and ensure that all of your concerns are addressed. The genetic counselor is also available to follow-up with you after the results of the amniocentesis become available.

Test Offered

Chromosomal Microarray Analysis (CMA) and Chromosome Analysis (Limited or Full) + AFP + / - Aneuploidy FISH, Chromosomes / AFAFP and Aneuploidy FISH, Chromosome Analysis, and AFAFP ONLY, Chromosomal Microarray Analysis (CMA) ONLY, Chromosomal Microarray Analysis (CMA) AND / OR Chromosome Analysis + AFAFP AND Molecular / Biochemical testing, Single Gene Molecular / Biochemical testing ONLY, Prenatal Noonan Panel and Prenatal COL1A1 & COL1A2 Panel. For additional testing information please see quick reference guide tab.

Shipping information

Ship the sample at room temperature to the laboratory by overnight express. Specimen should arrive in the laboratory within 48 hrs of sample date. Specimen cannot be frozen. Ship the sample at room temperature to the laboratory by overnight express. Specimen should arrive in the laboratory within 48 hrs of sample date. Specimen cannot be frozen. Ship at room temperature in an insulated container by overnight courier. Do not heat or freeze. Sample must arrive within 48 hrs.

Turnaround Time

7-10 days
Prenatal Whole Exome Sequencing Trio

Prenatal Whole Exome Sequencing Trio (Prenatal WES Trio) is a new offering by Baylor Miraca Genetics Laboratories. In general, the test is used when prenatal imaging detects an anomaly that strongly suggests that there is an underlying genetic etiology. Prenatal WES Trio is often considered only after fetal chromosome microarray analysis has been non-diagnostic. The test is ordered by a physician and must be accompanied with a consent form and detailed clinical information.

### Test Details

<table>
<thead>
<tr>
<th>Test Code:</th>
<th>1622</th>
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**Clinical Report:**

- **Fetal report includes:**
  - Pathogenic or likely pathogenic variants in disease genes related to the prenatal indications.
  - Variants in disease genes unrelated to the prenatal indications but likely to cause significant disorders during childhood.

- **Parental report includes (if requested):**
  - Pathogenic variants in genes included in the ACMG policy statement regarding recommendations for reporting of incidental findings will be reported as medically actionable.
  - Carrier status for autosomal recessive conditions will include disorders recommended for reproductive screening by professional societies such as ACMG or ACOG.
  - For information on gene coverage, please check our Whole Exome Sequencing Version 3 Coverage Search Tool at [https://www.bcm.edu/research/medical-genetics-labs/exome.cfm](https://www.bcm.edu/research/medical-genetics-labs/exome.cfm)

### Technical Information

- **Methodology:** Exome Capture and Next Generation Sequencing; Sanger Sequencing

### Sample

- **Specimen Type:** Cultured amniocytes or cultured CVS

### Requirements:

Prior to ordering the test, please call the lab @ 1-800-411-GENE (4363) or 713-798-6555 to discuss the test indication and sample requirements with a genetic counselor. For more details consult our website at www.BMGL.com or call us at the number listed above.

### Shipping information

Ship at room temperature in an insulated container by overnight courier. Do not heat or freeze.

### Turnaround Time

3 weeks (excluding cell culture time)
## Quick Reference Guide

### Optimal Prenatal Genetics Specimen Requirements

<table>
<thead>
<tr>
<th>Test Categories</th>
<th>Amniotic Fluid</th>
<th>Chorionic Villi Sampling (CVS)</th>
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<tbody>
<tr>
<td>Chromosomal Microarray Analysis (CMA) and Chromosome Analysis (Limited or Full) + AFP + / - Aneuploidy FISH*</td>
<td>30cc in two or three 15cc screw-top polypropylene tubes (Discard first 2cc)</td>
<td>30-35 mg in 15cc screw-top tube with sterile transport media</td>
</tr>
<tr>
<td>CHROMOSOMAL MICROARRAY ANALYSIS (CMA) ONLY*</td>
<td>15-20cc in two 15cc screw-top polypropylene tubes (Discard first 2cc)</td>
<td>15-20mg in 15cc screw-top tube with sterile transport media</td>
</tr>
<tr>
<td>Chromosomes / AFAFP and Aneuploidy FISH</td>
<td>20-25cc in two 15cc screw-top polypropylene tube (Discard first 2cc)</td>
<td>25-30mg in 15 cc screw-top tube with sterile transport media</td>
</tr>
<tr>
<td>Chromosome Analysis and AFAFP ONLY</td>
<td>15-20cc in two 15cc screw-top polypropylene tubes (Discard first 2cc)</td>
<td>15-20mg in 15cc screw-top tube with sterile transport media</td>
</tr>
<tr>
<td>Chromosomal Microarray Analysis (CMA) AND / OR Chromosome Analysis + AFAFP AND Molecular / Biochemical testing</td>
<td>30cc in two or three 15cc screw-top polypropylene tubes (Discard first 2 cc)</td>
<td>Call to discuss case before sending.</td>
</tr>
</tbody>
</table>

**SPECIAL CONSIDERATIONS FOR PRENATAL CMA SAMPLES:**

- Amniotic Fluid Samples collected before 16 weeks gestation cannot be used for Direct DNA prep – such samples will be cultured.
- Cultured fetal specimens >3 weeks old may yield uninterpretable results

**SUBOPTIMAL SPECIMENS LIKELY TO CAUSE LONGER TURN AROUND TIMES:**

- AF sample collected < 16 wks or > 26 wks
- AF pellet with RBC present or micropellet
- AF sample < 15 ml volume
- Cystic Hygroma Fluid
- Bloody or discolored AF sample
- CVS < 10 mgs, after cleaning

*5cc EDTA blood samples from both parents are required.