LEADERS IN GENETIC FERTILITY SCREENING™

#1 in Genetic Fertility Screening

SCREEN TODAY. PROTECT TOMORROW.
EvolveGene® was founded by world leaders in genetics and fertility discovery, with over 25+ years of experience in human reproduction, genetic screening and Assisted Reproductive Technology (ART) research.

Our research team has published over 250 clinical papers in fertility and genetic research, with over 8,000 related citations, along with over 20 worldwide patents in reproductive technology.

Our goal is to provide our valued customers with the most comprehensive fertility and reproductive genetic screening, and to offer them viable healthcare solutions for future generations.

**EVOLVE PRE-CONCEPTION SCREENS**

**EVOLVE GENETIC CARRIER SCREENS**
- Evolve FamilyReady™ Carrier Screen ......................... Cat # CFRS or Cat # CFRB

**EVOLVE FEMALE GENETIC FERTILITY SCREENS**
- Evolve Female Fertility Screen ........................................... Cat # FFGB
- Evolve Premature Ovarian Failure Screen ................................. Cat # FPOB

**EVOLVE MALE GENETIC FERTILITY SCREENS**
- Evolve Male Fertility Screen ............................................. Cat # MFGB

**EVOLVE PREGNATAL SCREENS**

**EVOLVE GENETIC NONINVASIVE PREGNATAL TESTING**
- Evolve EarlyPregnancy™ Screen ........................................... Cat # NIPT
THE EVOLVE ADVANTAGE

**Specialized and Superior Reproductive Screens**
Offering the most comprehensive preconception and prenatal screens during any reproductive stage. Through the latest, specialized technologies, such as next-generation sequencing and in-depth chromosomal analysis, we deliver the most superior reproductive screening available.

**Leading Experts in Fertility and Genetics**
EvolveGene® was established by experts in the field of human reproductive medicine, fertility and genetics with a vision of preventive and personalized healthcare. Our scientific team brings together easily accessible knowledge and puts the power in your hands through advanced and accurate genetic screening.

**Reporting Reliable Results**
EvolveGene® provides reliable results for globally prevalent and well-defined genetic issues. Our panels detect the most relevant genetic disorders and thoroughly researched genetic anomalies to bring patients one step closer to a healthy future.

**Advanced and Accurate Screening**
Genetic screening is performed at our state-of-the-art CLIA-licensed and CAP-certified clinical laboratory in the USA. It is our priority to provide the most accurate genetic screening with the highest detection rates and lowest false positive rates.

**Complimentary Genetic Counseling**
Our team of board-certified genetic counselors are ready to answer your questions to ensure the screening process is as understandable as possible. These genetic consultation services are available at no additional cost for both physicians and patients.
EVOLVEGENE® SCREENS
Accurate and Advanced Genetic Screens For Your Patients

6  EVOLVE GENETIC FERTILITY SCREENS
10 EVOLVE FAMILYREADY™ CARRIER SCREEN
16 EVOLVE EARLYPREGNANCY™ SCREEN
EvolveGene® offers the following genetic fertility screens to help determine the genetic causes of infertility in males and females.

- Evolve Female Fertility Screen
- Evolve Premature Ovarian Failure Screen
- Evolve Male Fertility Screen

Genetics is a key component of infertility problems that has largely been ignored and overlooked by both physicians and patients, until now. Genetic anomalies which influence infertility can include numerical or structural chromosome abnormalities as well as genetic mutations. Through advanced genetic technologies, EvolveGene® brings actionable results to improve the chances of reproductive success.

Professional medical societies including the American Congress of Obstetricians and Gynecologists (ACOG), the American Urological Association (AUA), and the American Society for Reproductive Medicine (ASRM) recommend females or males with infertility have genetic screening.
EVOLVE FEMALE FERTILITY SCREEN

The Most Comprehensive Female Fertility Screen on the Market

Designed by world leading geneticists and fertility experts to give any female experiencing infertility a comprehensive genetic risk assessment. Female infertility contributes to approximately 50% of all infertility cases. As many as 1 in 10 females with infertility have a genetic anomaly.

The Evolve Female Fertility Screen tests for the most common genetic causes of female infertility through in-depth chromosome analysis and accurate mutation analysis of 6 genes.

<table>
<thead>
<tr>
<th>MUTATION ANALYSIS</th>
<th>MUTATION EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMP15</td>
<td>Ovarian dysgenesis 2 / Premature ovarian failure</td>
</tr>
<tr>
<td>FMR1*</td>
<td>Premature ovarian failure</td>
</tr>
<tr>
<td>FSHR</td>
<td>Ovarian dysgenesis 1 / Hyperstimulation syndrome</td>
</tr>
<tr>
<td>LHB</td>
<td>Luteinizing hormone dysfunction (Hypogonadism)</td>
</tr>
<tr>
<td>LHCGR</td>
<td>Luteinizing hormone dysfunction (Hypogonadism)</td>
</tr>
<tr>
<td>ZP1</td>
<td>Oocyte maturation defect (Lack of zona pellucida)</td>
</tr>
</tbody>
</table>

**CHROMOSOME ABNORMALITIES**

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex chromosome aneuploidies</td>
<td>Dysfunctional female sexual development either before or during puberty</td>
</tr>
<tr>
<td>Mosaicism</td>
<td>May be suggestive of single gene disorders of sexual development impacting female fertility</td>
</tr>
<tr>
<td>Large chromosomal deletions</td>
<td>May be suggestive of single gene disorders of sexual development impacting female fertility</td>
</tr>
<tr>
<td>Chromosomal inversions</td>
<td>May be suggestive of single gene disorders of sexual development impacting female fertility</td>
</tr>
<tr>
<td>Chromosomal translocations</td>
<td>May be suggestive of single gene disorders of sexual development impacting female fertility</td>
</tr>
</tbody>
</table>

* FMR1-related POF is caused by triplet (CGG) repeat expansions in the FMR1 gene located on the X chromosome. The repeat expansions result in a spectrum of disorders correlated with the length of CGG repeats, including the severe intellectually disabling Fragile X Syndrome.


Advanced Chromosomal + Mutation Analysis
POF: One of the Most Common Causes of Diminished Female Fertility

Premature ovarian failure (POF) affects at least 1% of all women worldwide and contributes to a low or poor reserve of oocytes relative to a given age. The Evolve Premature Ovarian Failure Screen tests for the most common genetic causes of POF through in depth mutation analysis of 21 genes including Fragile X FMR1 repeat analysis.

Features of POF
• Oligomenorrhea or amenorrhea
• Elevated levels of serum gonadotropins
• Low estradiol levels

As many as 1 in 4 women with POF have a genetic anomaly. However, many women with POF are either misdiagnosed or not diagnosed until their mid-30s when they experience difficulty conceiving a child.

MUTATION ANALYSIS MUTATION EFFECT
NR5A1, POF1B, PSMC3IP Ovarian dysgenesis
BMP15, DIAPH2, EIF2B2, EIF2B3, FIGLA, FOXL2, GALT, GDF9, HFM1, LMNA, NOBOX Errors in folliculogenesis / oocyte maturation
CYP17A1, CYP19A1, FSHR, LHCG, POR Defects in gonadotropins / sex hormone dysfunction

* Women with FMR1 premutations are not only at a high risk of developing POF but they also have an increased risk of having a child with Fragile X syndrome due to the premutation expanding to a “full” mutation.

REF
The Evolve Male Fertility Screen detects the major genetic causes of male infertility through mosaic chromosome analysis, including Y chromosome deletions, and accurate mutation analysis of 5 genes.

**MUTATION ANALYSIS**

<table>
<thead>
<tr>
<th>MUTATION</th>
<th>EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>AR</td>
<td>Androgen insensitivity syndrome</td>
</tr>
<tr>
<td>CATSPER1</td>
<td>Decrease sperm mobility / lack of sperm hyperactivity</td>
</tr>
<tr>
<td>CFTR*</td>
<td>Congenital bilateral absence of the vas deferens</td>
</tr>
<tr>
<td>FSHR</td>
<td>Defect in spermatogenesis - Hypogonadism</td>
</tr>
<tr>
<td>LHCGR</td>
<td>Leydig cell dysfunction</td>
</tr>
</tbody>
</table>

**CHROMOSOME ABNORMALITIES**

<table>
<thead>
<tr>
<th>ABNORMALITY</th>
<th>EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex chromosome aneuploidies (e.g. Klinefelter syndrome)</td>
<td>Dysfunctional male sexual development either before or during puberty</td>
</tr>
<tr>
<td>AZFa</td>
<td>Sertoli-cell-only syndrome</td>
</tr>
<tr>
<td>AZFb</td>
<td>Defect in spermatogenesis: Absent azoospermia factors</td>
</tr>
<tr>
<td>AZFc</td>
<td>Defect in spermatogenesis: Absent azoospermia factors</td>
</tr>
<tr>
<td>AZFd</td>
<td>Oligospermia with anomalies of sperm morphology</td>
</tr>
<tr>
<td>Large chromosomal deletions</td>
<td>Azoospermia / oligospermia with anomalies of sperm morphology / motility</td>
</tr>
<tr>
<td>Chromosomal inversions</td>
<td>Azoospermia / oligospermia with anomalies of sperm morphology / motility</td>
</tr>
<tr>
<td>Chromosomal translations</td>
<td>Azoospermia / oligospermia with anomalies of sperm morphology / motility</td>
</tr>
</tbody>
</table>

* Testing for the 39 most common CFTR mutations, including the core panel of mutations recommended by the American College of Medical Genetics (ACMG).
EVOLVE FAMILYREADY™ CARRIER SCREEN

Comprehensive Screening for the Most Relevant Disorders

**Evolve FamilyReady™ Carrier Screen**
Designed and developed by leading geneticists for reliable and advanced carrier screening of genetic disorders for all ethnicities.

- **Testing for 720 Variants in 148 genes**
- **Deletion/Duplication Analysis for CFTR, DMD, HBA1, HBA2, and MECP2**
- **Spinal Muscular Atrophy (SMA) and Fragile X Syndrome Analysis**

### Del/Dup Analysis

### NGS

### Genotyping

![Genotyping Results]

**Next Generation Sequencing + Genotyping + Deletion/Duplication Analysis**
Using genotyping, next generation sequencing, and deletion-duplication analysis, the Evolve FamilyReady™ Carrier Screen provides the most complete, in-depth genetic coverage for carrier screening available with accurate data-proven results.

**Evolve FamilyReady™ Carrier Screen Panel**
Advanced gene sequencing or targeted mutation analysis of close to 150 autosomal recessive and X-linked genes, including deletion/duplication analysis on select genes.

<table>
<thead>
<tr>
<th>AUTOSOMAL RECESSIVE GENES</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCC8, ACADM, ACADS, ACADVL1, ACAT1, AGA, AGXT, AIRE, ALDH3A2, ALDOB, ALPL, ARSA, ARSB, ASL, ASPA, ASS1, ATM, ATP7B, BBS1, BBS10, BCKDHA, BCKDHB, BCS1L, BLM, BTD, CAPN3, CBS, CFTR, CLN3, CLN5, CLN8, CLRN1, CNGB3, CPT1A, CPT2, CTNS, CTSC, CTSK, CYP1B1, CYP21A2, DBT, DHCRR7, DLD, DPYD, EDAR, F11, FAH, FANCC, FH, FKTN, G6PC, GAA, GALC, GALNS, GALT, GBA, GCHD, GHRHR, GJB2, GJB6, GLB1, GNE, GNPATB, GPIX, GP9, GRHPR, GUSB, HADHA, HBA1, HBA2, HBB, HEXA, HEXB, HFE, HMOX1, HSDB47, IDUA, IKBAP, IVD, LAMA3, LAMB3, LAMC2, LIPH, MANZBI, MCOLN1, MEFV, MLCI, MMAA, MMAB, MMACHC, MPI, MUT, NAGLU, NBN, NER, NLRP7, NPC1, NPC2, NPHS1, NPHS2, OPA1, PAH, PANK2, PCDH15, PEX1, PEX7, PPKD1, PMM2, POMGNT1, PPT1, PROP1, PYGM, RMRP, SACS, SERPINA1, SGCA, SGCB, SGC0, SGSH, SLC12A6, SLC17A5, SLC19A2, SLC22A5, SLC22A6, SLC26A2, SLC26A4, SLC37A4, SMNI, SMPS1, TH, TMEM216, TPPI, TTC17, TTPA, TYR, VPS13B, WISP3, WRN</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>X-LINKED GENES</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHM, DMD, FMR1, F9, GLA, G6PD, IDS, MECP2, OTC, RS1</td>
</tr>
</tbody>
</table>
Accurate and In-depth Genetic Carrier Screening Available Globally

Impact of Genetic Disorders
Evolve FamilyReady™ Carrier Screen is a comprehensive genetic carrier screen for the most medically relevant genetic disorders that can significantly impact the health of an individual. The genetic disorders can be categorized into 3 groups, note genetic disorders can belong to one, two, or all three categories.

- Can be managed early in life and are treatable: 68 genetic disorders (e.g. PKU and Wilson Disease)
- Chronic and require lifelong management: 135 genetic disorders (e.g. Sickle Cell Anemia and Duchenne Muscular Dystrophy)
- Life-threatening with no curative treatments: 98 genetic disorders (e.g. Cystic Fibrosis and Fragile X Syndrome)

We detect nearly two times as many carriers in people of Ashkenazi Jewish descent compared with the general population. Therefore, it is highly recommended that all couples with ANY Jewish ancestry, including interfaith couples, have carrier screening performed prior to a pregnancy.

Society Guidelines and Recommendations
Assessing a patient’s carrier status is becoming an integral part of reproductive health. Both the American Congress of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics (ACMG) recommend all women have some form of genetic screening if they are of reproductive age. Research has shown that patients, especially those undergoing fertility care, have used information from carrier screening to make a clinical decision regarding their reproductive health.

REF //
Benn P. et al. (2014) Obstetricians and gynecologists’ practice and opinions of expanded carrier testing and noninvasive prenatal testing. Prenat Diagn. 34:145-152.
Carrier Screening is a type of genetic testing that can determine if individuals are carriers of genetic mutations that can lead to serious inherited recessive disorders or X-linked disorders in their children.

Anyone can be a carrier of a genetic disorder. It’s important to know who is a carrier since there are different genetic inheritance patterns. Each child inherits one copy of a gene from each parent. 80% of children born with a genetic recessive disorder were born to parents who had no family history. Autosomal recessive disorders impact genes on chromosome pairs 1 - 22. X-linked disorders impact the 23rd pair of chromosomes (e.g. the sex chromosome), specifically the X chromosome.

**X-Linked Inheritance: Female Carrier**
When a female is a carrier for an X-linked disorder, if she has a daughter, there is a 50% chance she will be a carrier. If she has a son, there is a 50% chance he will be affected by the X-linked disorder. An example of an X-linked disorder is Hemophilia.

**Autosomal Recessive Inheritance: Both Parents Carriers**
If both parents are carriers, there is a 25% chance with each pregnancy for sons or daughters to be affected with the genetic disorder. An example of an autosomal recessive disorder is Spinal Muscular Atrophy.

**X-Linked Inheritance: Male Carrier**
When a male is a carrier for an X-linked disorder, if he has a daughter, there is a 100% chance she will be a carrier. If he has a son, there is virtually a 0% chance he will be affected by the X-linked disorder. An example of an X-linked disorder is G6PD Deficiency.

**The Risk of Genetic Disorders**
Genetic disorders, when taken collectively, impact more individuals than common chromosomal disorders (e.g. Down Syndrome) and neural tube defects (e.g. Spina Bifida), which have both been routinely screened for in pregnancy for decades.

- Genetic Disorders: 1 in 280 live births
- Down Syndrome: 1 in 800 live birth
- Neural Tube Defects: 1 in 1,000 live births

Ethnicity Changes The Chance Of Being A Carrier

Some genetic disorders are more common in certain populations. As the chart below demonstrates, your patient’s ethnicity alone can put them at an increased risk of being a carrier of a severe recessive genetic disorder.

Most people cannot state their ethnicities correctly. With that in mind, our Evolve FamilyReady™ Carrier Screen panel has been expertly developed to include the most relevant genetic disorders for all ethnic groups.

<table>
<thead>
<tr>
<th>POPULATION</th>
<th>GENETIC DISORDER</th>
<th>CARRIER FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>Beta-Thalassemia</td>
<td>1 in 75</td>
</tr>
<tr>
<td></td>
<td>Cystic Fibrosis</td>
<td>1 in 61</td>
</tr>
<tr>
<td></td>
<td>Sickle Cell Disease</td>
<td>1 in 10</td>
</tr>
<tr>
<td>Ashkenazi Jewish</td>
<td>Cystic Fibrosis</td>
<td>1 in 24</td>
</tr>
<tr>
<td></td>
<td>Gaucher Disease</td>
<td>1 in 15</td>
</tr>
<tr>
<td></td>
<td>Tay-Sachs Disease</td>
<td>1 in 25</td>
</tr>
<tr>
<td>Asian</td>
<td>Alpha-Thalassemia</td>
<td>1 in 20</td>
</tr>
<tr>
<td></td>
<td>Beta-Thalassemia</td>
<td>1 in 50</td>
</tr>
<tr>
<td></td>
<td>Cystic Fibrosis</td>
<td>1 in 94</td>
</tr>
<tr>
<td>European</td>
<td>Cystic Fibrosis</td>
<td>1 in 25</td>
</tr>
<tr>
<td>French Canadian</td>
<td>Tay-Sachs Disease</td>
<td>1 in 30</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>Beta-Thalassemia</td>
<td>1 in 40</td>
</tr>
<tr>
<td></td>
<td>Cystic Fibrosis</td>
<td>1 in 58</td>
</tr>
<tr>
<td>Mediterranean</td>
<td>Beta-Thalassemia</td>
<td>1 in 25</td>
</tr>
<tr>
<td></td>
<td>Cystic Fibrosis</td>
<td>1 in 29</td>
</tr>
</tbody>
</table>
LEADERS IN GENETIC FERTILITY SCREENING

COMPLIMENTARY GENETIC COUNSELING

Ready To Answer All Your Questions
EvolveGene® offers free genetic counseling with a board-certified genetic counselor for all of our genetic screens, ensuring you have access to expert and compassionate services.

During sessions, results will be explained in the context of the patient’s fertility, family, and medical history. Our team of trained and board certified genetic counselors are on hand to make certain genetic screening is empowering and see to it that your patients can facilitate reproductive health decisions based on their results.

Counseling Components
- Understandable Results Disclosure
- Medical History
- Discussion of Reproductive Options
- Fertility History
- Residual Risk Assessments
- Family History
- Genetics Education
RELIABLE RESULTS TO YOUR PATIENTS

Genetic Fertility Screening
Reveals genetic causes that contribute to infertility in your patients and guides medical management. Couples may still be able to attempt natural pregnancies with the assistance of fertility centers or elect to pursue pre-conception reproductive options.

FamilyReady™ Carrier Screening
Provides information to help your patients plan and make informed decisions for the healthiest family possible. Carriers may use the information to help plan for a child with a genetic disorder or elect to pursue pre-conception reproductive options.

Pre-Conception Reproductive Options
• IVF +Pre-Genetic Diagnosis (PGD) to screen for and transfer mutation-free embryos
• Use sperm or egg donors that do not carry specific genetic disorder
• Adoption
• Continue a pregnancy with more knowledge and a better plan
**EVOLVE EARLYPREGNANCY™ SCREEN**

**Reliable and Non-invasive Prenatal Screen from 10 Weeks Gestation**

**Technologically Superior & Scientifically Sound**

The Evolve EarlyPregnancy™ Screen is a highly accurate non-invasive prenatal test (NIPT) that screens for multiple fetal chromosomal aneuploidies using a single tube of maternal blood. It provides significantly better risk indication than traditional prenatal screens resulting in fewer false positives, and poses no risk of miscarriage or fetal damage normally associated with invasive procedures.

This method analyzes cell-free fetal DNA present in maternal serum to detect fetal chromosome aneuploidies. The cell-free fetal DNA found is derived primarily from the placenta and represents approximately 10% of total DNA circulating in the maternal blood by 10th week gestational age.

**Simple, Fast, & Reliable**

- Requires just one routine blood draw from the expectant mother
- Results in 5 - 7 days after sample receipt
- Very low technical failure rate at 0.1%
- Accurate & Accurate Results

Evolve EarlyPregnancy™ Screen is powered by the deepest massively parallel sequencing approach and superior analysis algorithm. It provides more reliable results, fewer redraws, faster turnaround times than other methods, hence, reducing anxiety for your patients. When you recommend prenatal screen, you and your patients can have confidence in our EarlyPregnancy™ Screen to deliver reliable and actionable results.

**Test Options**

The EarlyPregnancy™ Screen reports on the most prevalent Trisomies*:

- Trisomy 21 (Down syndrome)
- Trisomy 18 (Edwards syndrome)
- Trisomy 13 (Patau syndrome)

*The overall sensitivity and capability of this assay allows for use in twin pregnancies.

**Additional options available upon request**

Patients can discuss the additional opt-in panels in more detail during their genetic counseling consultation or with their healthcare provider.

**Sex Chromosome Disorders:**

- Monosomy X (Turner syndrome)
- Trisomy X (Triple X syndrome)
- XXY (Klinefelter syndrome)
- XYY (Jacobs syndrome)

**Trisomies:**

- Trisomy 9
- Trisomy 16

**Microdeletions:**

- 22q11.2 deletion syndrome
- 1p36 deletion syndrome
- Prader-Willi syndrome
- Angelman syndrome
- Cri du chat syndrome
- Wolf-Hirschhorn syndrome

You can focus on patient care while we focus on the science.

---

**REF**

**Best Results When Ordered Before 24 Weeks Gestation**

Performance Metrics in Most Prevalent Chromosomal Aneuploidies

<table>
<thead>
<tr>
<th>CHROMOSOME ANEUPLOIDIES</th>
<th>DETECTION RATES (%)</th>
<th>FALSE POSITIVE RATES (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>&gt; 99.1</td>
<td>0.2</td>
</tr>
<tr>
<td>18</td>
<td>97.4</td>
<td>0.4</td>
</tr>
<tr>
<td>13</td>
<td>87.5</td>
<td>&lt; 0.1</td>
</tr>
</tbody>
</table>

**On March 1, 2016, the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) issued a joint Practice Bulletin including Cell-free DNA screening or NIPT as part of the screening options for all pregnancies, to allow for patients to make an informed choice based on their values and goals. According to the bulletin, all pregnant women should be offered aneuploidy screening or diagnostic testing (with informed consent), regardless of maternal age or risk factors. It is also recommended that the option should be discussed with women who achieved IVF pregnancies following preimplantation genetic screening.**
Leading Innovative Genetic Research
At EvolveGene®, we are continuing our 25+ years of experience in the field of reproductive medicine in conjunction with our distinguished scientific team composed of leading embryologists, geneticists and fertility experts to bring meaningful research backed products and services to the field. Through our experience, expertise and passion we are committed to advancing the field of infertility care and reproductive medicine and helping to improve reproductive success around the world.

Non-Invasive Genetic Screening through “Liquid Biopsy”
EvolveGene® is currently undertaking IRB-approved research projects led by our scientific team aimed at developing novel solutions for non-invasive genetic screening in the field of In Vitro Fertilization (IVF).
BECOME AN EVOLVE CLINIC MEMBER TODAY

Membership is Free & Benefits Include:

• Free Evolve kits available to your clinic
• Free subscription to our Fertility Genetics Magazine and Newsletters
• Free Educational Speakers (Scientific, Technical, and Genetic Counseling) available for educational programs and training with your patients and staff.

If you are interested in making your clinic part of the Evolve membership program please email us at Support@EvolveGene.com.

RELIABLE, FAST, & STRAIGHTFORWARD GENETIC SCREENING