PREMIER GENOMICS
PRENATAL

# ACOG/ACMG ECS CARRIER SCREENING PANEL

| DISEASE (GENE) | POPULATION | DETECTION RATE | PRE-TEST CARRIER RISK (NO FAMILY HISTORY) | POST-TEST CARRIER RISK (WHEN RESULT NEGATIVE) | CLINICAL CHARACTERISTICS | IMPACT |
|---|---|---|---|---|---|---|
| Bloom Syndrome (BLM) | Ashkenazi Jewish | 97% | 1 in 107 | 1 in 3520 | Short stature, light sensitivity, increased cancer risk, distinctive facial features, learning and/or intellectual disability, male infertility, premature menopause in women. | |
| | General Population | <10% | <1 in 500 | <1 in 555 | | |
| Canavan disease (ASPA) | Ashkenazi Jewish | 98% | 1 in 55 | 1 in 2700 | Destruction of myelin sheath leads to muscle weakness, developmental delay, and mental disability. | |
| | Caucasian | 50% | < 1 in 500 | <1 in 1000 | | |
| Cystic Fibrosis (CFTR) | African American | 81% | 1 in 61 | 1 in 316 | Excessive mucus production, coughing, wheezing, breathing difficulty, persistent lung infections, abdominal pain, slow growth, male infertility. | |
| | Ashkenazi Jewish | 97% | 1 in 24 | 1 in 767 | | |
| | Asian | 55% | 1 in 94 | 1 in 183 | | |
| | Caucasian | 93% | 1 in 25 | 1 in 343 | | |
| | Hispanic | 78% | 1 in 58 | 1 in 248 | | |
| Familial Dysautonomia (IKBKAP) | Ashkenazi Jewish | 99% | 1 in 31 | 1 in 3100 | Affects nerve cells. Early/infants: feeding problems, poor growth, lack of tears, unstable blood pressure, susceptible to infections. Childhood: less sensitive to temperature and pain, decreased ability to taste, poor balance, fracture risk, blood pressure unstable. | |
| | General population | 10% | 1 in 500 | 1 in 555 | | |
| Familial Hyperinsulinism (ABCC8) | General population | 14% | 1 in 350 | 1 in 430 | Hypoglycemia, enlarged liver/liver disease, build up of lactic acid, affect on breathing, heart, lethargy, seizures, cognitive issues. Due to body's inability to break down a class of amino acids. Some have milder presentation. | |
| | Finnish | 60% | 1 in 100 | 1 in 256 | | |
| | Ashkenazi Jewish | 87% | 1 in 52 | 1 in 400 | | |
| Fanconi Anemia Group C (FANCC) | Ashkenazi Jewish | 99% | 1 in 100 | 1 in 9900 | Impaired bone marrow, short stature, physical and organ malformations, leukemia and other cancer risks. | |
| | General population | 10% | 1 in 300 | 1 in 333 | | |
| Fragile X (FMR1) | General population | >99% | 1 in 260 | <1 in 26000 | Intellectual disability, loose connective tissue, distinctive facial features, autism, behavioral issues. | |
| Galactosemia (GALT) | General population | 61% | 1 in 210 | 1 in 540 | Abnormal galactose metabolism. Untreated may lead to death in infancy. Treated (lactose restricted diet) still may lead to speech, motor and developmental problems. Most females- premature ovarian failure. | |
| | Ashkenazi Jewish | 95% | 1 in 227 | 1 in 4500 | | |
| | Irish | 89% | 1 in 107 | 1 in 980 | | |
| | African | 62% | 1 in 78 | 1 in 207 | | |
| Gaucher disease (GBA) | Ashkenazi Jewish | 90% | 1 in 15 | 1 in 140 | Bone pain, fractures, bruising, enlarged liver and spleen, anemia. | |
| | General population | 30% | 1 in 200 | 1 in 285 | | |
| Glycogen Storage Disease Type 1A (G6PC) | Ashkenazi Jewish | 96% | 1 in 64 | 1 in 1600 | Low blood sugar, high uric acid, high lipids. Short stature. Accumulation of glycogen and fat in liver and kidneys. Can lead to liver/kidney damage, brain function changes, and seizures. | |
| | Hispanic | 50% | 1 in 220 | 1 in 435 | | |
| | Japanese | 88% | 1 in 345 | 1 in 2800 | | |
| Hemoglobinopathies (HBB) | General population | 99%‡ | € | € | Blood disorders including sickle cell, affecting the structure of hemoglobin. | |
| Joubert Syndrome Type 2 (TMEM216) | General population | 19% | 1 in 715 | 1 in 882 | Brain malformation, intellectual disability, extra digits, low muscle tone, abnormal breathing, unique facial features, can lead to vision loss, kidney/liver disease, endocrine problems. | |
| | Ashkenazi Jewish | 99% | 1 in 92 | 1 in 9100 | | |
| Lipoamide dehydro-genase deficiency (DLD) | General population | 27% | 1 in 500 | 1 in 670 | Lactic acidosis, breathing and heart rhythm issues, enlarged liver, low muscle tone, lethargy, difficulty feeding, intellectual disability, short lifespan. | |
| | Ashkenazi Jewish | 99% | 1 in 94 | 1 in 9300 | | |
| Maple Syrup Urine Disease Type 1B (BCKDHB) | General population | 48% | 1 in 350 | 1 in 680 | Progressive neurodegerative disorder resulting from the accumulation of 3 amino acids that are poorly catabolized. Poor growth and feeding, cognitive issues, lethargy. If not identified and treated in early infancy, can be fatal. | |
| | Ashkenazi Jewish | 95% | 1 in 100 | 1 in 2000 | | |

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|---|---|---|---|---|---|---|
| Mucolipidosis Type IV (MCOLN1) | Ashkenazi Jewish | 96% | 1 in 89 | 1 in 220 | Delayed development of mental and motor skills, intellectual disability, and limited or absent speech, hypotonia, and vision loss. | |
| | General Population | <10% | <1 in 500 | <1 in 555 | | |
| Niemann-Pick Disease Type A/B (SMPD1) | Ashkenazi Jewish | 97% | 1 in 161 | 1 in 3834 | Enlarged liver and spleen, growth and developmental delay, low muscle tone, rigidity, lung disease. | |
| | General Population | 20% | 1 in 250 | 1 in 312 | | |
| Phenylketonuria (PAH) | General Population | 33% | 1 in 100 | 1 in 156 | Inability to break down the amino acid, phenylalanine. Accumulation may lead to intellectual disability, seizures and behavioral problems. Treatment- low protein diet. | |
| | Irish | 46% | 1 in 34 | 1 in 63 | | |
| Spinal Muscular Atrophy (SMN1) | African American | 71% | 1 in 66 | 1 in 121 | Most common inherited cause of infant mortality, low muscle tone, muscle weakness/wasting, and feeding problems. Type 2 is the most common with a 2 year life expectancy. | |
| | Ashkenazi Jewish | 90% | 1 in 41 | 1 in 350 | | |
| | Asian | 93% | 1 in 53 | 1 in 628 | | |
| | Caucasian | 95% | 1 in 35 | 1 in 632 | | |
| | Hispanic | 91% | 1 in 117 | 1 in 1061 | | |
| | Northern European | 95% | 1 in 35 | 1 in 632 | | |
| Tay Sachs (HEXA) | Ashkenazi Jewish | 98%* | 1 in 27* | 1 in 1300 | Progressive neurological disorder; muscle weakness, cherry red spot in the eye, seizures, blindness, early death; in a small number, less severe, present in adulthood. | |
| | General population | 46%* | 1 in 300* | 1 in 554 | | |
| | US French Canadian | 47%* | 1 in 73* | 1 in 136 | | |
| Usher Syndrome Type 1F (PCDH15) | Ashkenazi Jewish | 31% | 1 in 700 | 1 in 1018 | Hearing loss at birth, progressive vision loss (retinitis pigmentosa) beginning in childhood, balance issues. | |
| | General population | 75% | 1 in 147 | 1 in 590 | | |
| Usher Syndrome Type 3A (CLRN1) | General population | 69% | 1 in 500 | 1 in 1600 | Progressive hearing loss and vision loss (retinitis pigmentosa) beginning in teens. Complete loss of hearing in middle age. Some with balance issues. | |
| | Ashkenazi Jewish | 98% | 1 in 120 | 1 in 6000 | | |

‡ Detection rate of HBB mutations tested for is 99%. € Detection and carrier rate for Hemoglobinopathy disease type varies by ethnicity.
* Excludes HEXA pseudodeficiency alleles: c.739C>T (p.R247W) and c.745C>T (p.R249W)

**References:** Available upon request.

## A Pan-ethnic approach to carrier screening: 21 inherited disorders, 20 recessive and Fragile X syndrome

- Most individuals carry alterations in genes.
- Children are born with inherited conditions, even when these conditions don't run in their family.
- This occurs because each parent without the disease carries only one abnormal copy of a gene for the same inherited condition, and their child inherits both abnormal copies of a gene from each parent. This is called recessive inheritance. If both parents are carriers, there is a 25% chance (1 in 4) they will have a child with a recessive condition.
- Our panel tests for recessive mutations for common genetic conditions found in diverse populations.

## Screening consistent with American Congress of Obstetrics and Gynecology (ACOG) and American College of Medical Genetics and Genomics (ACMG)

- Offer all women considering or currently pregnant Spinal Muscular Atrophy (SMA) and Cystic Fibrosis (CF) Carrier Screening.
- Population Diversity, strategy: pan-ethnic/ expanded carrier screening.
- Consistent with a standard/consistent approach to screening to be applied to all patients.
- If found to be a carrier, test spouse/partner.

## Carrier screening benefits

- Better manage pregnancy
- Plan for medical intervention/treatment at birth
- Informed decision making
- Risk for disorder in future pregnancies

| LEGEND | |
|---|---|
| | **Life** = Shortened life expectancy |
| | **CNS** = Impacts brain/ spinal cord |
| | **Diet** = Change in diet may improve symptoms |
| | **Meds** = Therapeutic Medications may reduce symptoms * |
| | **Hearing** = Hearing loss |
| | **Vision** = Vision loss |

* (https://www.centerwatch.com/drug-information/fda-approved-drugs/therapeutic-area/34/genetic-disease)