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Sonic Genetics

Information for Doctors

Disease risks for carriers

Reproductive carrier screening involves examining a person's genes to determine whether they have one or more mutations that could place their child at risk of a serious inherited disorder. The purpose of such testing is to identify the risks for a future child, rather than identifying the risk of a future disorder for the parent who is tested.

For that reason, Sonic Genetics provides reproductive carrier screening for severe autosomal recessive and X-linked disorders that present in childhood and for which there are limited therapeutic options. By restricting the screen to recessive disorders, we reduce the chance of identifying genetic information that could have implications for a parent's future health.

Risks of a carrier being affected

Healthy individuals can be asymptomatic carriers of one or more mutations that cause recessive disorders. In the past, it was assumed that carriers of both autosomal and X-linked recessive disorders would remain unaffected because they have both a normal and a mutated copy of the relevant gene. As genetic testing has become more widespread, it has become clear that there are certain recessive disorders for which further assessment or advice for a carrier may be appropriate.

If a person is identified as a carrier of a disorder for which there may be future medical implications, this possibility is noted in the test report provided by Sonic Genetics. Genetic counselling may then be indicated for that person to review the implications regarding their own risk of a future disorder; click here for a list of providers. Such counselling is not provided by Sonic Genetics unless the couple is at high reproductive risk of having an affected child.

The table below summarises information about genes with recessive mutations for which there are risks for carriers (advice is limited to only include genes with documented evidence that carriers are at risk of a clinically significant disorder). Please note that this field is changing as new information is published.

Gene	Disorder in child	Carrier frequency[1]	Risks to carrier[2]	References[3]
ATM[4]	**Ataxia telangiectasia** is an autosomal recessive disorder that causes cerebellar ataxia, telangiectases, immune defects and predisposition to develop cancer.	1 in 100 people	Female carriers are at up to 4-fold increased risk of breast cancer. Earlier and more frequent breast cancer screening may be indicated. There may be an increased risk of other cancers. The risk of cancer for male carriers is also increased, but to a lesser degree.	15928302 16998505 1961222 26662178 22585167 20301790
BLM[4]	**Bloom syndrome** is an autosomal recessive disorder that causes growth deficiency, telangiectases, abnormal skin pigmentation and predisposition to develop cancer.	1 in 800 people	Some reviews have concluded that there is insufficient evidence of a risk to carriers, while others suggest that carriers have an increased risk for cancer, particularly of the breast and colon.	NBK1398 23225144 12242432 19945966 26778106 26358404 18210922 12702560

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Gene	Disorder in child	Carrier frequency[1]	Risks to carrier[2]	References[3]
DMD[4]	**Duchenne muscular dystrophy** is an X-linked recessive disorder that causes progressive weakness of skeletal and cardiac muscle in affected boys.	1 in 2,500 people	Approximately 20% of female carriers have mild muscle weakness. Approximately 8% of female carriers have cardiomyopathy evident on ultrasound examination, but published figures vary widely.	NBK119
FH[4]	**Fumarase deficiency** is an autosomal recessive disorder that causes profound psychomotor delay and brain malformations.	1 in 1,000 people	Approximately three quarters of carriers develop benign cutaneous leiomyomata. Uterine fibroids are present in most affected female carriers. Carriers are also at 10–16% lifetime risk of developing renal cancer (c/f 1% in general population.	20301430
FMR1[5]	The **fragile X syndrome** is an X-linked recessive disorder due to mutation that varies in size and effect across generations. It causes moderate intellectual disability in affected males, and can cause mild intellectual disability in females.	1 in 250 women 1 in 1,000 men	Female carriers of a pre-mutation are at 10–30% risk of premature ovarian failure (c/f 1% in general population). There is a comparable risk of developing a tremor/ataxia in male carriers, and a lower risk of tremor/ataxia in female carriers (c/f 2% in general population).	16247297
GLA[4]	**Fabry disease** is an X-linked recessive disorder in which affected males have varying combinations of severe limb pain, angiokeratomas, cataracts, renal failure and cardiomyopathy.	1 in 25,000 people	Some female carriers can experience less severe manifestations of these clinical features.	NBK1292
NBN[4]	The **Nijmegen breakage syndrome** is an autosomal recessive disorder that causes microcephaly, growth retardation, immunodeficiency and predisposition to cancer.	1 in 158 people	Female carriers have an overall lifetime risk of developing breast cancer of up to 30% (c/f 10% in general female population). The risk for other cancers is uncertain and may be increased 1.5- to 4-fold.	NBK1176
OTC[4]	**Ornithine transcarbamylase deficiency** is an X-linked recessive disorder that causes hyperammonaemia and encephalopathy.	1 in 1,000 women	Some female carriers can experience a less severe form of the disorder. This may be evident as episodes of erratic behaviour, delirium, reduced level of consciousness, headaches, vomiting, seizures or simply an aversion to high-protein foods.	NBK154378
RTEL1[4]	**Dyskeratosis congenita** is an autosomal recessive disorder that causes abnormal skin pigmentation, dysplastic nails, bone marrow failure and predisposition to develop cancer.	1 in 50 people	Carriers may have short telomeres, and there are a few case reports of carriers with some clinical features of dyskeratosis congenita.	23329068

1. Carrier frequencies are approximate and for healthy people from a general West European population.
2. Risks are indicative and may be altered by other clinical or environmental factors.
3. Citations are referenced as PubMed IDs; access through ncbi.nlm.nih.gov/pubmed.
4. This gene is only included in the expanded reproductive screening panel.
5. This gene is included in our 3-gene screen (cystic fibrosis, spinal muscular atrophy, fragile X syndrome) and expanded carrier screen.

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