Genomic Diagnostics

LEADING THE WAY TO IMPROVE HEALTH

Core Genetic Carrier Screen

FOR MEDICAL PROFESSIONALS

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Carrier screening

Carrier screening is genetic testing performed to determine whether individuals or couples have a genetic variant (mutation) that may affect their chance of having a child with a genetic condition. Genomic Diagnostics' Core Genetic Carrier Screen tests for three relatively common genetic conditions in general populations: cystic fibrosis (CF), fragile X syndrome (FXS), and spinal muscular atrophy (SMA). These conditions were chosen based on their inclusion in local and international genetic screening recommendations for patients considering conception[1,3].

Many children affected by these conditions are born to families with no history of disease due to the relatively rare nature of the conditions and inheritance patterns - autosomal recessive or X-linked in the included conditions. The value of carrier screening for CF and SMA has therefore been recognised for all patients in some countries such as the United States[1], with the value of FXS also being recently recognised in Australian research[2].

Importantly, if couples are found to be carriers of these conditions, they can consider several reproductive options including:

- natural pregnancy, with or without prenatal diagnosis
- preimplantation genetic diagnosis (PGD) with in vitro fertilization (IVF) to test and then transfer embryos that are free of the condition
- the use of a sperm or egg donor
- adoption

Background

What is Cystic Fibrosis?

Cystic fibrosis is an autosomal recessive genetic condition caused by a malfunction in the exocrine system responsible for producing saliva, sweat and mucus. This can result in a variety of symptoms, from mild (pancreatic sufficient) to severe (pancreatic insufficient), affecting mostly the respiratory and digestive systems.

What is Fragile X syndrome?

Fragile X syndrome is an X-linked genetic condition causing intellectual disability, behavioural and learning challenges and various physical characteristics. It is also the most common single gene cause of autism worldwide (accounting for up to 5% of all cases) and the most common genetic cause of intellectual disability in males. Although fragile X syndrome occurs in both sexes, males are generally affected with greater severity than females.

What is Spinal Muscular Atrophy?

Spinal muscular atrophy (SMA) is an autosomal recessive condition that results in the loss of motor neurones in the spinal cord and is classified as a motor neurone disease. The primary symptom is weakness of the voluntary muscles. In the most common form of SMA, due to pathological variants on chromosome 5, there is wide variability in age of onset, symptoms and progression rate.

How common are these conditions?

These three conditions combined are amongst the most commonly carried pathogenic variants in European populations.

	CARRIER FREQUENCY	NUMBER OF LIVE BIRTHS
Cystic Fibrosis	1 in 25	1 in 2,500
Fragile X	1 in 150	1 in 4,000 males (1 in 8,000 females)
Spinal Muscular Atrophy	1 in 40	1 in 6,000 – 10,000

Which Cystic Fibrosis variants are identified by the test?

Since the discovery of the CFTR gene in 1989, more than 1900 disease-causing variants have been described. Many of these variants have been described only in one patient and/or family. Routine testing for all possible variants is not cost effective and therefore testing is confined to the most common pathogenic variants.

Genomic Diagnostics' Core Genetic Carrier screen consists of a panel of common CFTR gene variants accounting for >90% of disease-causing variants in the Australian population.

References:

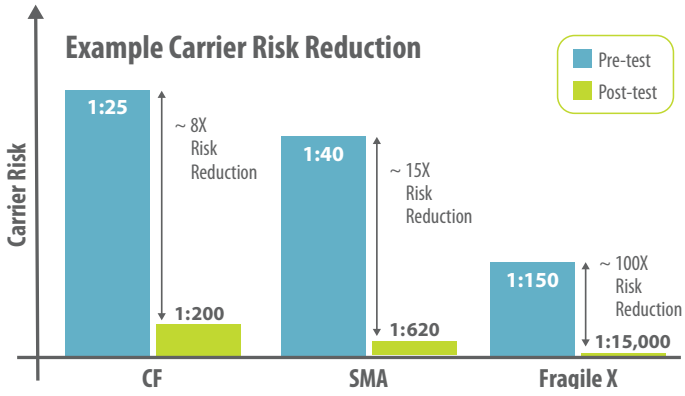
1. ACOG Committee Opinion, No. 690, March 2017. "Carrier Screening in the Age of Genomic Medicine".
2. Metcalfe, S.A. Genetics In Medicine, 2017. "Informed decision making and psychosocial outcomes in pregnant and non-pregnant women offered population fragile X carrier screening".
3. Prenatal screening and diagnosis of chromosomal and genetic abnormalities in the fetus in Pregnancy. RANZCOG. C-obs 63.

Test performance

This test screens for the most common genetic changes associated with FXS, CF and SMA. The assay can detect:

- >90% of cystic fibrosis carriers
- 99% of fragile X carriers
- 95% of spinal muscular atrophy carriers

The test cannot detect everyone who is a carrier as rarer pathogenic variants cannot be detected by the assay. Therefore, the use of this assay in a carrier screening setting can significantly reduce the risk of a couple having an affected child but cannot remove this risk completely.



Assumptions:

1. Caucasian population - frequencies will vary for other ethnic groups.
2. Calculations are based on reported test sensitivity CF: 90% SMA: 95% and Fragile X: 99%

When should patients be tested?

The ideal setting for carrier screening is preconception, in order to have the most time to deal with all possible testing outcomes. However, testing can also be used in an antenatal setting.

Genetic counselling

If the couple are shown to be carriers for any of these conditions, then genetic counselling is recommended to provide more information and enable detailed discussion regarding their options and potential impacts of any decisions.

Testing options

The two testing options are to either initially test the female partner, and to only test her partner if she is found to be a carrier or, for fastest results, test both partners at the same time. Please note details on the request form if the patient has a family history of any of these conditions or is pregnant.

Arranging Core Genetic Carrier Screening

Step 1: Patient consultation

- Discuss carrier screening with your patient as recommended by clinical guidelines
- Order Core Genetic Carrier Screening on a standard request form, noting any family history or pregnancy

Step 2: Prepare for collection

- Patient is required to pay for their Core Genetic Carrier Screening prior to having their blood taken
- Payment occurs online at genomicdiagnostics.com.au
- Patient notes their receipt number on the request form

Step 3: Sample collection

- Patient attends collection centre with their signed request form
- Blood is collected
- Core Genetic Carrier Screening performed

Step 4: Result discussion

- Results are delivered to you by your preferred method
- Reproductive partners of carriers identified will be tested free of charge for SMA or CF (as detected in partner), details must be noted on request form
- Genetic counselling is provided for couples and individuals who are identified as carriers.

Autosomal recessive inheritance: A mode of inheritance such that an individual must have a pathogenic variant in both copies of the specific disease gene, usually one inherited from each parent, to express the genetic condition.

X-linked inheritance: A mode of inheritance in which a pathogenic variant on the X chromosome causes the expression of the genetic condition. Males are typically affected, as they only have one X chromosome, whereas females may show variable expression of the condition due to differences in X chromosome inactivation: As fragile X is a dominant variant, females can be affected, but at approximately half the rate of males (50% chance of female receiving normal allele from mother). Variants are typically inherited from a mother who is an unaffected carrier.

Why choose Genomic Diagnostics?

We're one of Australia's longest running specialist DNA testing laboratories.

We bring you depth of knowledge and experience, state of the art facilities and dedicated scientists and pathologists who care about what they do.

Quality and Accreditation

Our laboratory has held continuous accreditation to all relevant medical testing standards for all the tests we do. We pride ourselves on providing you with quality results and expert testing advice that you can rely on.

We're Convenient

We're part of the SDS network of pathology laboratories across Australia, which means wherever your patients are, there's a collection centre nearby.

Dedicated, friendly and knowledgeable Customer Care team

Our customer care team specialise in taking enquiries. With extensive experience in the field, they're on hand to provide you with the right advice, or direct your enquiry, based on your requirements.

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For more information, contact us at info@genomicdiagnostics.com.au

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