THE PATHCARE NEWS

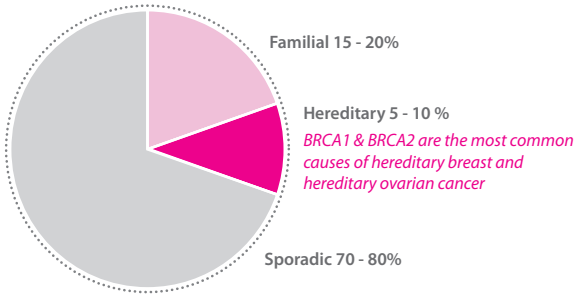
GENETIC TESTING FOR BREAST AND OVARIAN CANCER

PathCare is proud to offer both in-house and international send-away genetic testing for breast and ovarian cancer.

PathCare *BRCA1* and *BRCA2* Genetic Testing

Our molecular laboratory offers genetic testing using Sanger and Next Generation Sequencing technologies. We pride ourselves in offering these tests according to international best practice standards and interpretation of variants based on professional society guidelines.

Causes of breast cancer



1. PathCare *BRCA1* and *BRCA2* Founder Mutation Testing

There are specific variants (mutations) in the *BRCA1* and *BRCA2* genes that have been shown to be particularly prevalent in the Ashkenazi Jewish, Afrikaner and black South African populations. Founder mutation testing is a first tier, cost-effective option for patients that belong to these population groups.

A total of 7 founder mutations (3 Ashkenazi Jewish, 3 Afrikaner and 1 South African) in the *BRCA1* and *BRCA2* genes are tested for directly.

Over 2700 likely pathogenic or pathogenic variants have been described in *BRCA1* and over 3000 in *BRCA2* (ClinVar). Therefore, **a negative result for a founder mutation test does not exclude a *BRCA1* or a *BRCA2* mutation.** If your patient tests negative, more comprehensive testing is strongly recommended in cases with a strong suspicion of a genetic predisposition. Comprehensive testing may also be used to exclude a *BRCA1/BRCA2* mutation for treatment purposes.

2. PathCare Comprehensive *BRCA1* and *BRCA2* Sequencing

Comprehensive testing should identify all known pathogenic variants as well as potentially novel variants.

Our team of scientists, genetic counsellors and medical geneticist are involved in scrutinising identified variants to determine pathogenicity and compiling reports that are useful for clinical interpretation.

3. Family Variant Testing

If testing has been performed in a patient and a specific variant has been identified in the *BRCA1* or *BRCA2* gene, testing for the specific familial variant can be performed.

A copy of the family member's report needs to be attached to the request form.

Often this is predictive testing (for an unaffected individual), therefore genetic counselling is highly recommended.

As the running costs of genetic tests depend directly on the referral numbers, it is difficult to compete with international laboratories in terms of cost. For this reason, we have looked at international send-away options in order to make genetic testing accessible to patients and families as referred by their managing clinician or genetic counsellor.

Invitae – International Send-away Services

PathCare offers a referral service to Invitae Laboratory in the USA. Invitae offers an extensive genetic test menu over a broad range of clinical areas, including hereditary cancer - https://www.invitae.com/en/physician/category/CAT000015/

Invitae offers testing via single-gene or multi-gene panels at a fixed patient-pay price, with the additional benefits of re-requisitioning a sample for additional genes at no extra cost, and free-of-charge family variant testing to first-degree relatives, if requested within 90 days of the report.

The cost of any Invitae panel (regardless of the number of genes tested) is **250 US Dollars (cost in Rands is dependant on the exchange rate)**. As this is a patient-pay option, Invitae bills the patient directly for these tests. PathCare charges an international courier fee (R811) and handling fee (R500) which is paid upfront when providing the sample. The total cost of testing is therefore approximately R5000.

Saliva samples are sent to Invitae in specialised Saliva Collection Kits. These can be arranged for your patient at their closest PathCare depot. Please let our genetics team know if you are ordering this option for your patient and we will facilitate the sample collection.

The turnaround time for Invitae tests is **10-21 calendar days (14 days on average)** once the sample arrives at their laboratory.

1. Invitae Breast and Gynae Cancers Guidelines-Based Panel

This comprehensive panel analyses 20 genes (including *BRCA1* and *BRCA2*) associated with a significantly increased lifetime risk of hereditary breast, ovarian and other gynaecological cancers. All genes on this panel have published management guidelines.

This option is not only more cost-effective, but also more comprehensive, particularly if the patient's family history is not necessarily suggestive of *BRCA*-related hereditary breast and ovarian cancer syndrome (HBOC).

2. Invitae Breast Cancer STAT Panel

This panel analyses 9 well-established genes associated with a significantly increased risk of developing breast cancer. This panel may be requested when an accelerated turnaround time (TAT) is needed to facilitate urgent surgical and management decisions. The TAT for this panel is **5-12 calendar days (7 days on average)** once the sample arrives at Invitae. One can expect a report within 2 weeks of sample collection.

This test is appropriate for breast cancer patients with upcoming cancer-related breast surgeries and/or treatment where genetic testing may inform decisions such as lumpectomy versus mastectomy, single versus double mastectomy, or use of other treatments (such as use of PARP-inhibitors or other chemotherapy treatments).

If a patient tests negative for the genes analysed on this panel, their sample may be re-requisitioned for the full 20 gene Breast and Gynae panel or other appropriate panel at no additional charge within 90 days.

3. Invitae Family Variant Testing

Testing can be performed on family members of a patient where a pathogenic or likely pathogenic variant has been identified. Invitae offers this service free-of-charge to first degree relatives of the patient within 90 days of their report. At PathCare, we understand that this service can be very beneficial for families and we waive the international courier fee and handling fee for these samples.

The original report from Invitae (including the RQ number) will need to accompany these samples. Adequate genetic counselling is recommended, as this testing may be offered to at-risk unaffected family members.

Genetic Counselling

It is internationally recognised and strongly recommended that genetic testing be offered in the context of appropriate pre- and post-test genetic counselling by a genetics professional.

Please contact our genetics team for the contact details of an HPCSA-registered genetic counsellor who can arrange to see your patient. We understand that there are limited genetic counselling services in South Africa, however, most genetic counsellors would be able to arrange telephonic/Skype consultations if necessary.

Please feel free to contact our genetics team if you have any questions on 021 596 3655 or geneticconsult@pathcare.org

Quick Guide To Testing

(Please use the PathCare familial Cancer Screening request form for all requests.)

Laboratory	PathCare			Invitae		
Test	*BRCA1* and *BRCA2* **Founder mutation** testing	**Comprehensive** *BRCA1* and *BRCA2* Sequencing and Del/Dup analysis	**Known family** variant/mutation testing	**Breast and Gyn Cancers Guidelines-Based Panel** (20 genes)	**Breast Cancer STAT Panel** (9 genes)	**Family variant/ mutation testing**
Description	7 common founder mutations in the South African population 3 – Afrikaner mutations 3 – Ashkenazi Jewish mutations 1 – South African mutation	Comprehensive testing should detect all known pathogenic and novel mutations in these genes	Testing for a known mutation in the family	Breast and gynaecological cancer genes	Breast cancer genes	Testing for a known mutation in the family
When to order?	This is a first line test for patients with relevant ancestry. **This is NOT a comprehensive test.**	Patients who do not fall into a founder population group. Patient whose founder mutation test came back negative.	Following adequate pre-test genetic counselling. Attach copy of original report from family member.	Patients who require comprehensive genetic screening, or whose family history fits a genetic cancer predisposition syndrome other than HBOC.	This panel is ideal for patients who require results quickly, e.g. for surgical decision making.	Following adequate pre-test genetic counselling. Attach copy of original report from family member.
Cost* (Standard tariff)	~R2 668	~R12 369	~R2 007	$250 + R1311 international courier and handling fee	$250 + R1311 international courier and handling fee	Free of charge
Turnaround time	~5 days	6-8 weeks	2 weeks	~10-21 days	~5-10 days	~10-21 days
Test code	PPCRBRCA	PPCRBRCAFS	PPCRKSV	PMMGPBGCA	PMMGPOTHR	PINVITAEFAM
Sample type	EDTA 4ml whole blood			Saliva		

** Costs are subject to change. Please contact the PathCare genetics team for confirmation of current prices.*