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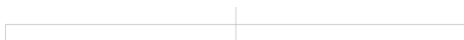
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## Genetics and prostate cancer

Overview by Ms Vicki Kiesel

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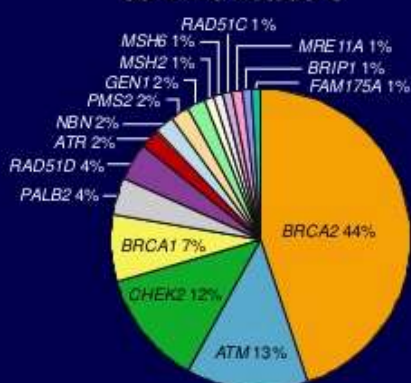
Profile

The IMPACT study

Prostate Cancer gene testing guidelines

## Germline Mutations in Prostate Cancer: 1 in 10

Distribution of Presumed Pathogenic Germline Mutations



- 11.8% (82/692) of men with metastatic prostate cancer inherited a germline DNA repair mutation vs 4.6% of 499 men with localized disease

Presumed Pathogenic Germline Mutations in Metastatic Cases (N = 692)

Gene	No. of Mutations	% of Men
BRCA2	37	5.35
ATM	11	1.59
CHEK2*	10	1.87
BRCA1	6	0.87

\*n = 534; data censored for metastatic cases with inadequate sequencing.

Prostate cancer is the most common cancer among men in the UK, with 13% of men being diagnosed at some point in their lives. While the majority of all prostate cancer occur by chance, it is estimated that 5-9% of all prostate cancers, and about 12% of metastatic\* prostate cancers, are hereditary. In general, men who have a father, brother or son (first degree relative) with prostate cancer, are at twice the risk of developing prostate cancer, while men with two first degree relatives have 5 times the risk compared to the general population.

\* "Cancer that is not confined to the prostate gland but has spread to other parts of the body"

Typically, prostate cancer is very slow growing and left undiagnosed or untreated would not shorten a man's life; this type of prostate cancer is seen very commonly in older men. However, in some men prostate cancer can be aggressive and develop more quickly: in these situations early diagnosis and treatment is important. Regularly screening, for example with PSA can help identify these men at earlier stages.

Men may have an increased risk of prostate cancer, and genetic testing may be helpful, if they have the following signs in their families:

- Relatives with early onset prostate cancer (diagnosed before age 55)
- 3 first degree relatives (brother, son, father) diagnosed with prostate cancer
- Ashkenazi Jewish ancestry and breast, ovarian or prostate cancer
- Prostate cancer and two relatives with breast or ovarian cancer
- Prostate cancer and male breast cancer, or ovarian cancer or bilateral breast cancer
- Prostate cancer and early onset bowel or womb cancer (before age 50)
- Prostate cancer and 2 relatives with bowel or womb cancer

Genetic testing can look for changes (mutations) in several different genes which are known to cause an increased risk of prostate cancer. Mutations in the BRCA1 and BRCA2, HOXB13, ATM, CHEK2 and Lynch Syndrome genes are associated with higher risk of prostate cancer and are inherited in an autosomal dominant pattern which means one copy of the altered gene in each cell is sufficient to increase a person's chance of developing cancer. In other words, if a parent has a mutation in one of these genes their children have a 50% risk of inheriting the genetic mutation and therefore being at increased risk of prostate cancer. Genetic mutations for prostate cancer can be inherited from both the mother and the father's side of the family.

The table below summarises the risk of prostate cancer associated with known genes:

Mutated Gene	Increased lifetime risk of Prostate cancer
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BRCA1	7 – 25%
BRCA2	19 – 60%
HOXB13	33 – 60%
Lynch Syndrome	12-52%
ATM and CHEK2	Moderate risk

For men who have been diagnosed with prostate cancer, genetic testing may be helpful as it may alter their treatment, particularly for those men with BRCA1/BRCA2 mutations who may benefit from platinum-based therapy while men with Lynch syndrome may find Pembrolizumab beneficial. It should be noted that while it is expected that there are approximately 31,000 men in the UK with BRCA1 and BRCA2 mutations, currently very few have been identified. There are current studies underway such as the IMPACT study which is further investigating prostate cancer genes, and the best way to screen for prostate cancer.

Theranostics treatment for advanced prostate cancer

Where to access theranostic therapy

Prostate cancer treatment – Immunotherapy

Prostate cancer – Assessing response to treatment



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