BRCA Gene Testing in Ovarian Cancer

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- **Around 7,500 women are diagnosed with ovarian cancer in the UK each year.[1] This makes ovarian cancer the 6th most common cancer in women.[1]**
- **The laboratory offers testing of the BRCA1 and BRCA2 genes for women with ovarian cancer to help guide their treatment and management.**
- **These genes are involved in repairing damaged DNA, specifically double stranded breaks. Certain mutations, also known as variants, in the BRCA1 or BRCA2 gene can prevent them from functioning in the repair of DNA. When the DNA is not repaired, damage can accumulate, and the cell is more likely to become cancerous. If there is too much damage the cell will die.**

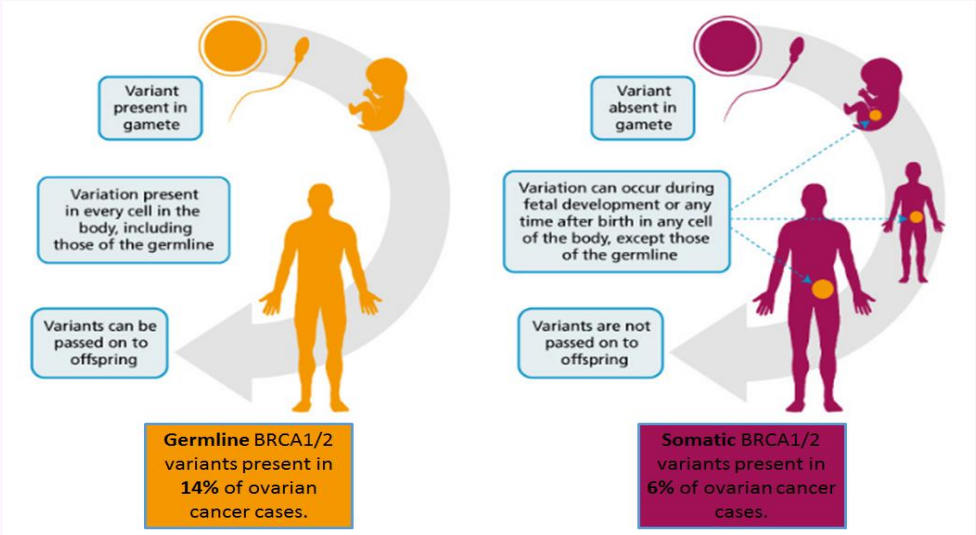

Figure 1: Germline and somatic variants. Adapted figure. [2,3]

Everyone has two copies of both the BRCA1 and BRCA2 genes. Some individuals will carry a germline (or hereditary) variant, others may acquire a variant during their lifetime (somatic variant). The laboratory can test for both germline and somatic variants in ovarian cancer patients.

Pathogenic BRCA1/2 variants may improve response to treatment with PARP-inhibitors

PARP is a protein found in our cells, it stands for **p**oly-**A**DP **r**ibose **p**olymerase. Its normal function is to repair single stranded DNA breaks enabling cell survival.

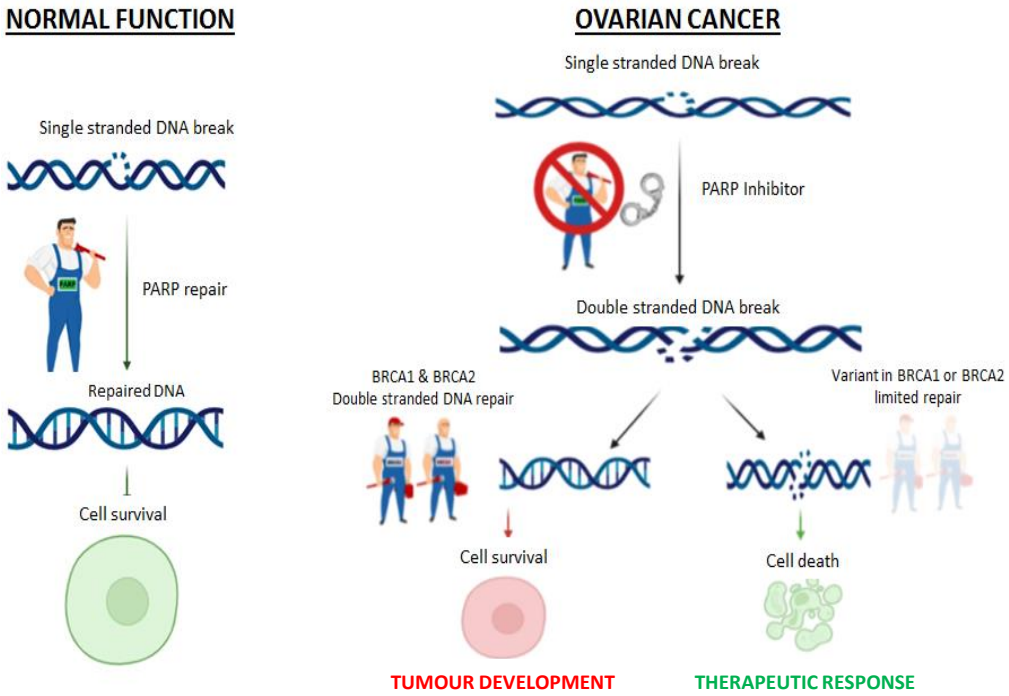

Figure 2: If PARP is blocked by an inhibitor, single stranded breaks are not repaired and form double stranded breaks. BRCA1/2 genes help to repair the double stranded breaks, enabling the cells to survive. Cancer cells with pathogenic BRCA1/2 variants have an impaired ability to repair the double stranded breaks causing further damage and cell death.

Importance of Germline testing

- Offered to women for whom there is clinical suspicion of a hereditary cause of ovarian cancer, increasing the risk of recurrence.
- Positive patients can undergo risk-reducing surgery & attend screening clinics.
- Predictive testing can be offered to unaffected relatives.
- Reduces risk of & enables earlier detection of additional cancers, improving prognosis.

References: 1) Cancer Research UK, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/ovarian-cancer#heading-Zero, Accessed [December][2021]. 2) Ji Nam, et al. 2020. doi: 10.1186/s12885-020-6693-y. 3) NHS Health Education England, https://www.genomicseducation. hee.nhs.uk/cancer-genomics/, Accessed [December][2021].