CAF/25/78 - Characterising the Endometrioid Ovarian Cancer Population Through Risk Stratification and Novel Multiomic Analyses

Ovarian cancer is a common cause of cancer deaths in women. There are multiple types of ovarian cancer. Each type has unique characteristics, including how they respond to treatment. The most common type is high-grade serous (70% of patients), followed by endometrioid ovarian cancer (EnOC; 10% of patients).

Compared with other ovarian cancers, EnOC is often diagnosed in younger women. Some EnOC are very aggressive (termed ‘high-risk’), while others are successfully treated with our usual treatment approaches (so-called ‘low-risk’). A lack of research means we cannot easily discriminate high-risk from low-risk EnOC. Recently, systems for identifying high- versus low-risk EnOC have been proposed to solve this challenge, using information like gene mutations to help categorise cancers.

A classification system used for endometrial (or womb) cancer has been applied to EnOC, mainly because EnOC and endometrial cancer share similarities. Although this system works well for a minority of women with EnOC, studies suggest it is not a useful system for ≈85% of EnOC patients.

Two other custom-made classifications for EnOC exist, both designed by a team in Edinburgh. These come from studying the cancer’s genetic information, alongside cancer cell surface molecules that detect hormones (called ‘hormone receptors’). One such receptor, called the ‘progesterone receptor,’ is particularly important. These two classification systems work relatively well, but neither is perfect.

This project aims to build on this previous work to improve EnOC patient classification. To do this, we will take 100 patient samples already collected in Edinburgh, with genetic sequencing performed from previous work. We will add 50 new patient samples to the study and expand our molecular understanding of all 150 samples. The bigger the number of samples we have, the more reliable the classifications will be when other cancer centres use them.

The extra information we will gain includes ‘gene expression analysis’, where we look beyond simple gene mutations and examine how each gene is being used by cancer cells. We will also perform ‘methylation analysis’, which is another way to assess the activation and deactivation of cancer cell genes. Importantly, as one of these tests has not been performed in EnOC before, we hope they will give us completely new information about EnOC behaviour. This will be beneficial as it may improve our existing high- and low-risk classifications, or recommend a new system altogether. This project may also help us discover new treatments, including those involving our immune system, like in other cancers. We already have all of the patient samples required for this testing, which is a big advantage.

In summary, this study will help us to classify EnOC, supporting us to explain to patients the risk of their cancer coming back after treatment. In those at high risk of their cancer returning, we hope to identify new targets and use these to design new treatments. If we can identify women with low-risk EnOC, we may be able to avoid giving them chemotherapy after surgery, as they are less likely to need it. This would avoid long-term side effects.