Can DNA a simple cervical cell swabs be used for early detection of ovarian cancer?

Abstract for laypersons

Ovarian Cancer is the leading cause of death from gynecological cancers with approx. 350 deaths every year. The high death rate is due to unspecific symptoms in early disease stages, resulting in late diagnosis. It is of high priority to find new biomarkers which can be measured precisely early in the disease course. Ovarian cancer is characterized by cellular changes. One such cellular event is changes in methylation on the DNA of the cell. Previous research suggest DNA methylations has a strong potential as cancer biomarkers.

The purpose of the project is, with DNA methylation, to make diagnostics possible and thereby contribute to increased survival of patients with ovarian cancer. Our aims are:

1) To make comprehensive methylation profiling of *tumor tissues* to facilitate differentiation of patients with benign tumors and early and late stages of OC;
2) To investigate if the methylation profile in the cancer tissue can be obtained in *cervical cell swabs* from the same patients, and consequently be used for early diagnostics in a potential ovarian cancer screening.
3) a) To test the identified methylation candidates in cervical cell swabs in a larger cohort of women with a *pelvic mass* referred to hospital for surgery.

   b) Finally, to perform a validation in a large cohort of cervical cell swabs collected from the *national screening program*, to clarify the potential of implementation in current ovarian cancer routine diagnostics.

We apply a new technology to examine the methylation of 850.000 methylation sites simultaneously. We are the first to do methylation analysis in this scale on ovarian cancer patients. The discovery study includes 64 patients with ovarian cancer and 32 controls with benign pelvic tumors. DNA methylations in tumor tissue and concordant cervical cell swaps will be investigated and establish the basis for potential methylation markers to be tested in cervical cell swaps from women referred to hospital due to a pelvic mass (200 ovarian cancer patients and 100 controls). Finally, tested biomarkers will be validated in cervical cell swaps collected through the National cervical screening program. Currently around 25 women have developed ovarian cancer after their routine cervical sample was taken. It is anticipated that approximately 10 more women will have had a diagnosis of ovarian cancer before we are ready to validate candidate methylation markers. A control group consisting of 10 women for each ovarian cancer patient will be selected. The current data is based on results from Mermaid III, made possible by *a large donation from the Candys Foundation*. The preliminary data are very promising, showing that DNA methylations can differentiate ovarian cancers from benign ovarian tumors. The perspective of the study is to include identified methylation markers, which can be detected in cervical cell swaps, in the Danish screening program for cervical cancer.

Our goal is earlier and improved diagnosis of ovarian cancer with new biomarkers. According to the Danish gynecological cancer database, earlier detection of ovarian cancer can improve the average survival of 40-45% to approximately 90 % among ovarian cancer patients.