Utility of global methylation as a diagnostic approach for patients with ovarian cancer.

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Background: The mortality rate of ovarian cancer is high, since symptoms are relatively unspecific until advanced disease, and a majority of patients develop resistance to treatment. Early diagnosis would be a decisive breakthrough to improve survival. Epigenetics is the study of heritable changes in gene expression caused by mechanisms other than changes in the DNA. One such epigenetic mechanism is DNA methylation, and cancer is characterized by ’methylation imbalance.’ Previous reports indicate that changes in DNA methylation can be used diagnostically, and that they may predict resistance to treatment. The objective of this study is to characterize global methylation profiles and identify methylation sites specific for ovarian cancer, with the purpose of improving prediction of drug resistance, diagnostics and screening for women with ovarian cancer.

Materials and Methods: As part of the MERMAID III study we will do a discovery and validation investigation to determine the utility of DNA methylation as a putative biomarker for ovarian cancer. We will investigate global DNA methylation profiles in ovarian cancer patients selected from the pelvic-mass cohort, which at this point include more than 3.500 patients. A well-established array technology will be used in the discovery phase and the newest array, Infinium MethylationEPIC, will be applied. 850.000 cancer relevant areas of the DNA from 60 ovarian cancer patients and 30 controls (borderline or benign tumors and normal tissue) will be investigated. Corresponding tissue, blood and smear-samples from each patient will be analyzed. Methylation results will be correlated with clinical data, and potential epigenetic markers will be validated by sequencing based analysis of 200 cancer patients and 100 controls.

Results and Conclusion: The perspective of the study is to improve survival and treatment by earlier diagnosis and better prediction of drug resistance. Besides from identifying markers for diagnosis and prediction, we aim to discover methylation markers for ovarian cancer which can be detected in a cervix smear and thereby potentially be used in the already implemented national screening program for women. Moreover, our data will improve the understanding of the cause of the disease and may contribute to development of new therapies in the future.

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