

Breast cancer is among the most frequent types of cancer and the main causes of cancer-related deaths among women. Worldwide, about 1.5 million women are diagnosed with breast cancer annually and approximately one-third of them will die due to this malignancy. Prognosis of this malignancy, in addition to treatment efficacy, greatly depends on the stage of the disease at diagnosis. Therefore, many developed countries (including Poland and Norway) introduced mammography screening programs aimed at middle-aged women. However, because of several disadvantages of imaging techniques supplementary molecular markers that could help early detection of breast cancer are highly desired. Moreover, though several risk factors of breast cancer are known they are associated only with a fraction of breast cancer cases. Hence, knowledge of new molecular factors associated with increased risk of breast factors would apparently contribute to the reduction of cancer mortality and other health problems related to this malignancy.

Blood metabolomics is a very powerful approach to reveal systemic conditions existing in a patient body, particularly those related to disease development and progression. Therefore blood metabolome is an emerging source of cancer biomarkers. However, little is known about metabolites that could be associated with cancer-promoting conditions and/or existence of preclinical cancer, i.e. potential biomarkers feasible for breast cancer risk assessment and early detection. The current proposal concerns the possibility to estimate the risk of breast cancer based on a novel combination of molecular features with anthropometric and lifestyle-related features. We hypothesize that disease-related features of metabolism could be detected in serum, reflecting cancer-promoting conditions (e.g. chronic inflammation) and/or existence of early “preclinical/ symptomless” stages of the disease. We assume that such features (metabolites) could be detected in the serum of individuals who were diagnosed with breast cancer a few years after blood sample collection yet were considered “healthy” at that time. Hence, the general hypothesis driving this proposal states that the combination of a serum metabolome profile and lifestyle-related risk factors would allow building a joint classification model for stratification of breast cancer risk in a healthy population.

Two complementary analytical metabolomics tools based on mass spectrometry and magnetic resonance spectroscopy will be used, which increases the possibility to detect and identify molecular components associated with breast cancer. Sample and data repository from a large population-based study performed in Trøndelag region of Norway (HUNT2) will be involved, which provides a unique opportunity to work with a sufficiently large cohort of individuals where relevant medical, anthropometric and lifestyle data, as well as a longterm followup, are available. Furthermore, a reference group of women with actual (clinical) cancer (breast cancer and other solid cancers) will be recruited to the study. Specific aims of the proposal include: (i) to identify serum metabolome signature that discriminates individuals who were diagnosed with breast cancer a few years after donating serum from women who remained free of breast cancer, (ii) to compare the serum metabolome signature of a “high risk of breast cancer” with serum metabolome features of female patients with actual (clinical) breast cancer and other types of malignancies, (iii) to build a classification model for the stratification of breast cancer risk in the population of healthy women, which will combine features of the serum metabolome and features associated with anthropometric and lifestyle-related risk factors.

The proposal provides a unique possibility to explore the underlying biological mechanisms in early breast cancer development, and possibly identify molecular targets to hinder cancer progression. Moreover, the project could contribute to pre-diagnostic management, early diagnosis and successful treatment of breast cancer, which is to issues with high health and socio-economic impact in both participating countries.