Breast cancer is still most common women cancer and second most common cancer in the world with estimated over 2 million of new cases yearly. Over the years substantial research was performed with the aim to establish personalized lifelong risk scores for breast cancers based on patients' genetic background (germline mutations). However, the effectiveness of the genetic based risk scores is limited and leaves majority of the breast cancer cases unexplained. Moreover, with the advent of the new technologies such as Next Generation Sequencing it becomes clear that additional high penetrance genes increasing risk of cancer are unlikely to be identified.

At the same time, studies of epidemiology of the breast cancer have identified various lifestyle and environmental risk factors such as: age, hormonal and reproductive factors, body mass index (BMI) or physical activity. The molecular mechanism through which those factors modulate cancer risk remain largely unknown but there is consensus in the field that vast majority of environmental exposures are unlikely to induce genetic changes that in turn could result in increased cancer susceptibility. It is therefore plausible that environmental factors modulate cancer risk by altering gene expression through epigenetic mechanisms such as DNA methylation. Especially, that there is a large body of evidence indicating that disruption of the epigenetic mechanisms of the gene expression regulation contributes if not initiates cancer and other diseases such as diabetes or psychiatric disorders.

Current large-scale studies aiming to identify epigenetic changes induced by the environmental exposure are frequently performed because epigenetic profiling data for the large number cohorts has become recently available from various other studies. Those studies do not focus on specific exposures only explode available data, mainly because the recruitment of the donors to the large-scale studies was not designed specifically to study epigenetic effects of the specific exposures

Those study do not focus on specific exposures because the recruitment of the subjects was not designed to study epigenetic effects of the specific exposures. Despite large data sets those studies frequently fail to identify the epigenetic biomarkers of the exposure or report contradicting results.

Contrary to that approach, in this proposal we will firstly study genome wide epigenetic changes in carefully selected groups of women for which our preliminary and already published studies indicated increased risk of breast cancer. And secondly, use the identified epigenetic changes to complement current genetic based risk scores and improve breast cancer risk management.

Overall, our study is built on hypothesis driven research that may significantly contribute to the knowledge in the field. At the same time, the composition of the work packages gives us a chance to contribute to translational cancer research and identify epigenetic biomarker candidates that can potentially improve breast cancer risk prediction models. The genome wide data collected in the project will serve as a reference methylation profiles for other prospective studies. We will deposit the data in dedicated data base and made them available to scientists for the use as controls in other studies of the influence of environmental factors on the epigenome. To our knowledge, this will be first data base of this kind for polish population what will also potentially allow us to take part in national and international projects established to study influence of environmental factors on cancer risk.