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Identification of mutations in DNA damage response and repair genes in genitourinary cancers

Abstract

In Belarus, genitourinary (GU) cancers are in the top 10 causes of newly diagnosed malignancies in men, prostate cancer (PC) being the first most common, and bladder cancer (BC) being the sixth most common. More than a third of all cases of PC and BC are found in their late stages associated with a poor prognosis. Standard treatments for advanced tumors are not effective for all patients and responses are rarely durable. To date, no clinically validated predictive markers for therapeutic efficacy exist for patients with GU cancers.

The characterization of the genomic landscape of advanced PC and BC identified a significant number of germline and somatic mutations in DNA damage response and repair genes. Similar to BRCA-deficient breast and ovarian cancer, these mutations may be responsible for increased sensitivity to DNA damaging agents and poly(ADP)ribose polymerase inhibitors. However, it is still unclear which alterations and of which genes, besides BRCA1/2, involved in DNA repair pathway may be targeted by these drugs.

Therefore, more studies are needed to identify a mutational spectrum of DNA repair genes in GU cancers in order to establish biomarkers for selection of patients for specific anticancer therapy. The best approach for comprehensive analysis of a large number of genes in a single test is a next-generation sequencing assay. Generating high quality NGS data and analyzing them requires proper training on methodology and utilization of sophisticated bioinformatics workflows.

Hence, the main objectives of the proposed project are acquiring practical skills and expertise in targeted next-generation sequencing technology, implementing them for identification of DNA repair gene pathogenic mutations in GU cancers, and evaluation of their potential correlation with anticancer therapy efficacy and prognosis.