

Circulating tumor DNA gives treatment options for the most common ovarian cancer type

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According to a new research, circulating tumor DNA can be used detect treatment options for ovarian cancer patients who don't benefit from chemotherapy.

High-grade serous ovarian cancer (HGSOC) is the most common and aggressive subtype of ovarian cancer. The HGSOC tumors consist of several heterogeneous cell populations with a large number of mutations. This genetic variability makes it difficult to find drugs that would kill all the cancer cells, and to which the cells would not become resistant during treatment.

Over half of the patients diagnosed with high-grade serous ovarian cancer die within five years of diagnosis, that is, annually more than 150000 women globally. To improve the efficacy of HGSOC treatment, a research group from University of Helsinki, together with researchers from University of Turku and Turku University Hospital, have now studied the use of circulating tumor DNA in finding precision medicine-based treatments for the disease.

Circulating tumor DNA refers to tumor-derived cellfree DNA in the bloodstream. Circulating tumor DNA detection is a minimally invasive technique that offers dynamic "molecular snapshots" of genomic alterations in cancer.

"Analyzing circulating tumor DNA enables us to detect genomic alterations also in late stage cancers in which taking biopsies from the tumor is difficult or even impossible. In the current research, we demonstrated that circulating tumor DNA can be used to monitor the patient responses to treatment, and find drug combinations to target the Achilles' heels of the tumor's genomic profile," says research has discovered targeted therapies for the Professor Sampsa Hautaniemi, director of the Systems Oncology Research Program in the

Faculty of Medicine at University of Helsinki.

The results were published in JCO Precision Oncology.

Hautaniemi's research group has implemented a clinical circulating tumor DNA workflow to detect clinically actionable alterations in more than 500 cancer-related genes.

In the present study, the researchers analyzed 78 circulating tumor DNA samples from 12 ovarian cancer patients before, during and after the treatment using bioinformatics analysis, and inhouse Translational Oncology Knowledgebase to detect clinically actionable genomic alterations.

DNA alterations associated with clinically available drugs were detected in 58% of the patients. The treatment of one patient has already been tailored successfully based on the results. For the other patients the results may be useful if their cancer relapses.

The results demonstrate a proof-of-concept for using circulating tumor DNA to guide clinical decisions. Furthermore, the results show that longitudinal circulating tumor DNA samples can be used to identify poor-responding patients after first cycles of chemotherapy.

In addition, the researchers provide the first comprehensive, open-source circulating tumor DNA workflow for detecting clinically actionable alterations in solid cancers.

"The prognosis of ovarian cancer patients is still poor. However, the future looks brighter as genomic alterations also in ovarian cancer tumors. We are currently in the forefront of the precision



medicine for ovarian cancer. Our goal is to find out how ovarian <u>cancer</u> becomes resistant to current treatments, and use this knowledge in finding more effective precision treatments," Hautaniemi says.

More information: Jaana Oikkonen et al. Prospective Longitudinal ctDNA Workflow Reveals Clinically Actionable Alterations in Ovarian Cancer, *JCO Precision Oncology* (2019). DOI: 10.1200/PO.18.00343

Provided by University of Helsinki

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