New subtypes identified in difficult-to-treat ovarian cancer

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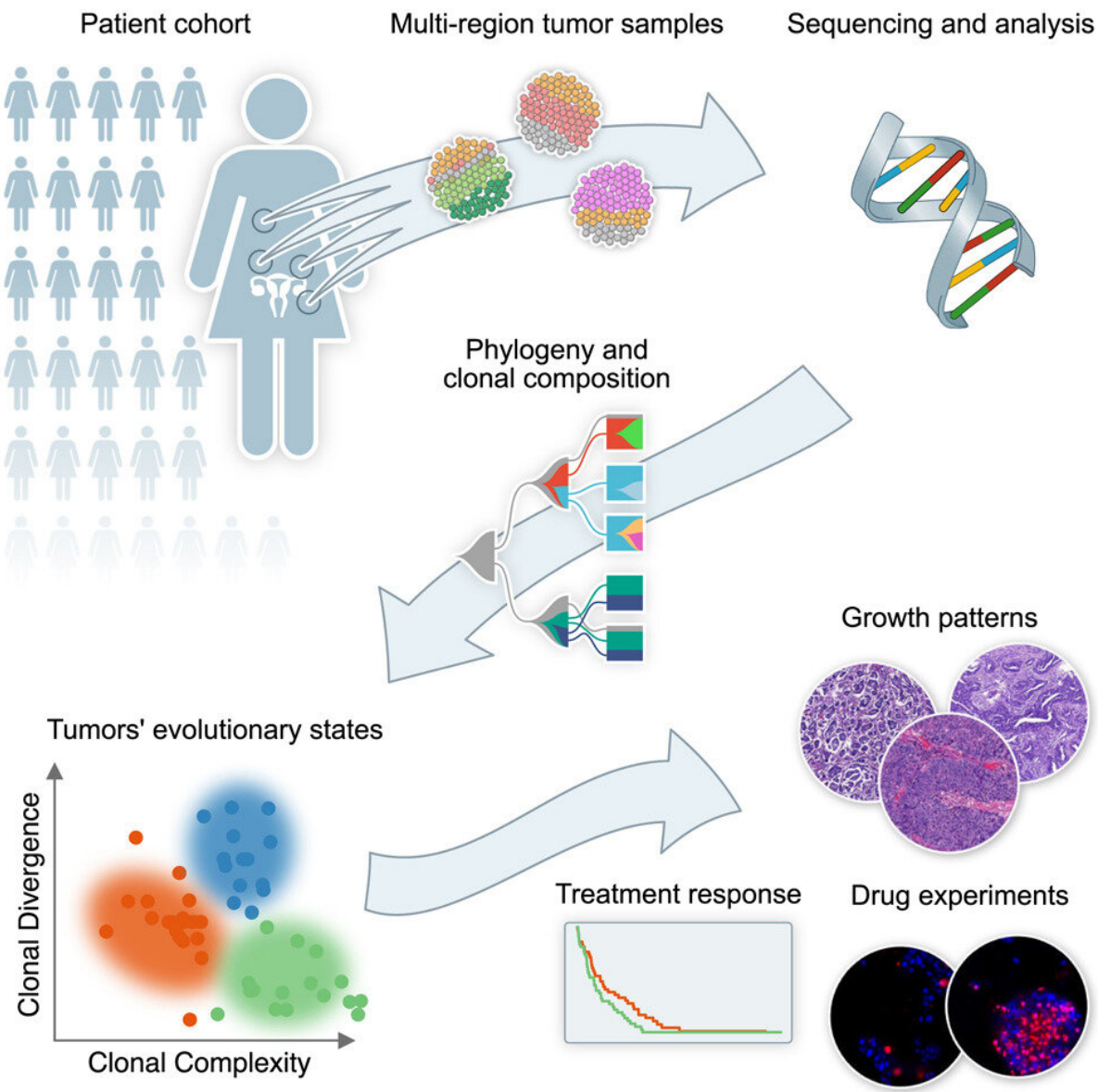

Graphical abstract. Credit: *Cancer Cell* (2023). DOI: 10.1016/j.ccell.2023.04.017

Every year, approximately 400 women die of ovarian cancer in Finland, while the corresponding figure for Europe overall is more than 40,000. Ovarian cancer is a genetically very heterogeneous disease, which makes it exceptionally difficult to study and treat. The prognosis is particularly poor in ovarian high grade serous carcinoma (HGSC), a subtype of ovarian cancer. Fewer than 40% of patients with this subtype survive five years after their diagnosis.

The researchers were able to classify HGSC tumors into three groups on the basis of genomic changes. The groups differ in the intracellular signaling pathways, the ways in which the tumors grow, and response to treatment. The findings can help therapies to become more accurate and help patients with HGSC.

The results of the joint study carried out by the University of Helsinki, Turku University Hospital, HUS Helsinki University Hospital, the University of Turku and the University of Copenhagen were published in *Cancer Cell* in May.

"Prior studies have not identified generally accepted subgroups of HGSC tumors that would enable targeted treatment in the same way as, for example, in breast cancer. Our study is a step forward in identifying effective targeted therapies," says Professor of Systems Biology Sampsa Hautaniemi from the University of Helsinki.

Three signaling pathways

The researchers analyzed genomics data on cancer tumors collected in the DECIDER project from 148 patients with HGSC treated and

recruited in Turku University Hospital. Depending on the stage of development, they divided the tumors into three evolutionary states: evolving, maintaining and adaptive. The classification was based on the tumors' pattern of spread and their development in metastases. Depending on the group, the cancer populations grew up in combinations of either genetically different or clonal cells. These combinations either continued to evolve in metastases or remained unchanged.

The researchers identified signaling pathways characteristic of each tumor group, which make these tumors biologically distinct.

"There are targeted drugs already in clinical use for many of them. We demonstrated that a single signaling pathway, PI3K/AKT, is particularly important for certain patients. While the importance of this pathway has been known, it was not known who are most likely to respond to treatment targeted at this signaling pathway. Based on our findings, we are better able to identify the subset of patients likely to benefit from such treatment," says Postdoctoral Researcher Jaana Oikkonen from the University of Helsinki.

Tumor evolution should be investigated

The study approaches the issue from the perspective of tumor evolution, or how the tumor develops and spreads into new metastases. This approach is currently important in research on HGSC as the knowledge available is largely based on studies with small sample or patient numbers.

"The dataset we analyzed was one of the largest, if not the largest, to date in terms of HGSC tumor samples. This is yet another indication of the capacity for top-level research in Finland in spite of our small population," Hautaniemi says.

"Our findings bring order to the genomic chaos of HGSC. Now, the entire research field will advance faster, making it easier to target therapies. Of course, there is still work to be done. Further research is being carried out on, for instance, what would be the easiest way to classify patients into the three groups identified," says Postdoctoral Researcher Alexandra Lahtinen from the University of Helsinki.

More information: Alexandra Lahtinen et al, Evolutionary states and trajectories characterized by distinct pathways stratify patients with ovarian high grade serous carcinoma, *Cancer Cell* (2023). DOI: 10.1016/j.ccell.2023.04.017

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