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FUNCTIONAL BIOMARKERS OF PLATINUM CHEMOTHERAPY AND PARP INHIBITOR RESPONSE

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Value Proposition: *Robust and reliable biomarker to accurately predict patient response to PARP inhibitors and platinum chemotherapy for high grade serous ovarian cancer.*

Technology Description

Researchers at Washington University in St. Louis have developed an automated, functional assay for determining platinum and PARPi resistance in HGSOC tumors. Most patients diagnosed with high-grade serous ovarian cancer (HGSOC) undergo first-line platinum therapy and PARP inhibitor maintenance therapy. However, the degree to which HGSOC patients respond to platinum and PARPi depends on the tumor's homologous recombination (HR) status. Existing assays to determine HR deficiency rely on genetic testing (e.g. BRCA1/2) or evaluation of genomic instability markers, but they reflect past events and may not adequately capture the present HR capacity of the tumor. Using several biomarkers involved in HR, including RAD51, this new assay can predict resistant patient cohort with high specificity and sensitivity.

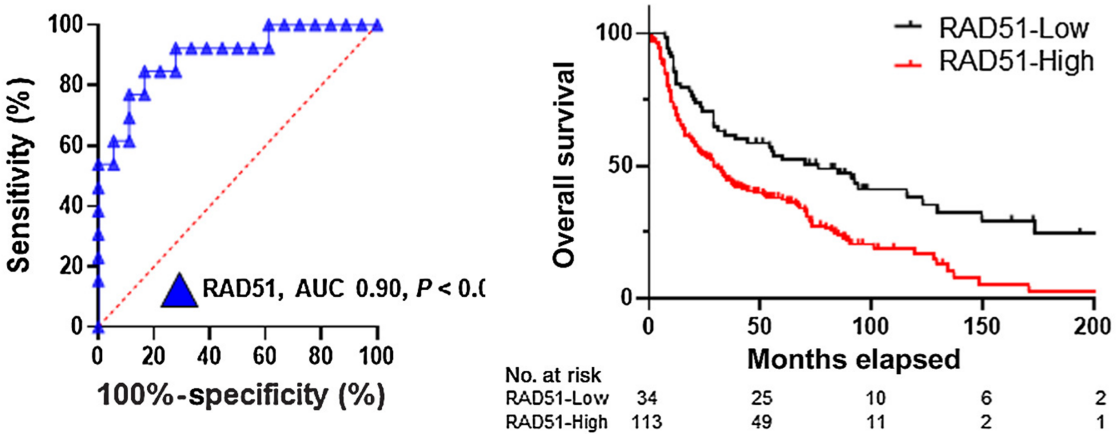

Figure – Detection of platinum resistance using FFPE slides and nuclear foci staining with Rad51. The sensitivity of this assay can be improved upon with additional biomarkers (confidential information available). Scores generated using this assay allow clear stratification of HGSOC patients based on their clinical outcomes.

Stage of Research

Optimized assay on various HGSOC lines as well as patient derived organoids. Final assay validation was carried out using FFPE tumor samples. Assay has been automated using in-house software with robust concordance relative to manual methods.

Publications

Compadre, Amanda J., et al. "RAD51 foci as a biomarker predictive of platinum chemotherapy response in ovarian cancer." Clinical Cancer Research 29.13 (2023): 2466-2479.

Applications

- Characterization of HGSOC before treatment to minimize unnecessary toxicity and rationally triage patients to therapy.

Key Advantages

- Rapid, inexpensive assay with high accuracy to determine platinum and PARP resistance, supplementing existing tests for HR deficiency.

Patents

US-nonprovisional application pending

Related Web Links - Maggie Mullen, MD, MSCI, profile