DUKE INSTITUTE FOR GENOME SCIENCES & POLICY

An Integrated Genomic-Based Approach to Personalized Treatment of Patients with Advanced-Stage Ovarian Cancer

Journal of Clinical Oncology 25:517-525 (2007)

Abstract Purpose. The purpose of this study is to develop an integrated genomic-based approach to personalized treatment of patients with advanced-stage ovarian cancer. We have utilized gene expression profiles to identify patients likely to be resistant to primary platinum-based chemotherapy and also to identify alternate targeted therapeutic options for patients with de-novo platinum resistant disease. Patients and Methods. A gene expression model that predicts response to platinum-based therapy was developed using a training set of 83 advanced stage serous ovarian cancers, and tested on a 36-sample external validation set. In parallel, expression signatures that define the status of oncogenic signaling pathways were evaluated in 119 primary ovarian cancers and 12 ovarian cancer cell lines. In an effort to increase chemo-sensitivity, pathways shown to be activated in platinum-resistant cancers were subject to targeted therapy in ovarian cell lines. Results. Gene expression profiles identified patients with ovarian cancer likely to be resistant to primary platinum-based chemotherapy, with greater than 80% accuracy. In patients with platinum-resistant disease, we identified expression signatures consistent with activation of Src and Rb/E2F pathways, components of which were successfully targeted to increase response in ovarian cancer cell lines. Conclusions. We have defined a strategy for treatment of patients with advanced stage ovarian cancer that utilizes therapeutic stratification based on predictions of response to chemotherapy, coupled with prediction of oncogenic pathway deregulation as a method to direct the use of targeted agents.

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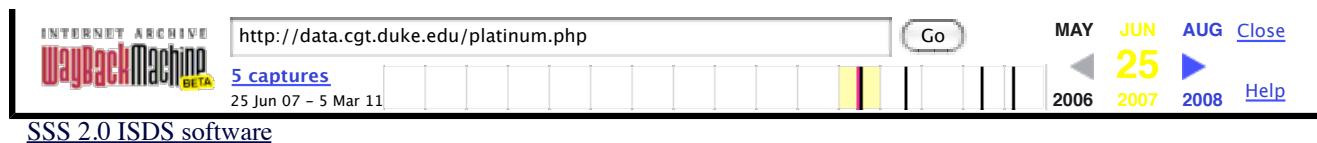
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Datasets

PlatinumJCO.zip
correctedplatinum_RMA.xls

Supplemental Information

Parameters for SSS software.txt

INTERNET ARCHIVE
WayBackMachine BETA

http://data.cgt.duke.edu/platinum.php | Go | MAY **JUN** **AUG** Close

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SSS 2.0 ISDS software

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