Molecular Cancer Therapeutics Highlights

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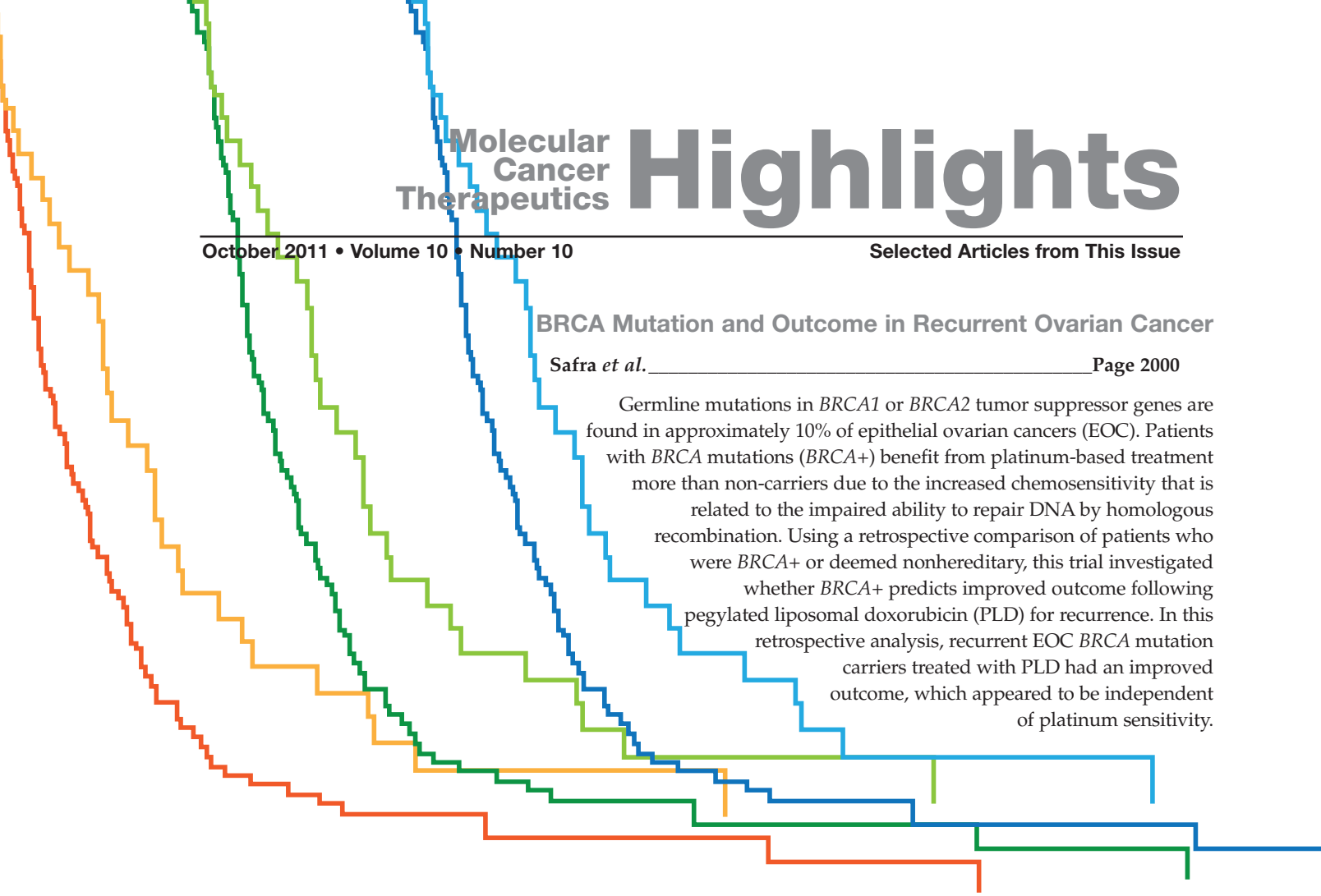
Selected Articles from This Issue



## BRCA Mutation and Outcome in Recurrent Ovarian Cancer

**Safra *et al.*** **Page 2000**

Germline mutations in *BRCA1* or *BRCA2* tumor suppressor genes are found in approximately 10% of epithelial ovarian cancers (EOC). Patients with *BRCA* mutations (*BRCA*+) benefit from platinum-based treatment more than non-carriers due to the increased chemosensitivity that is related to the impaired ability to repair DNA by homologous recombination. Using a retrospective comparison of patients who were *BRCA*+ or deemed nonhereditary, this trial investigated whether *BRCA*+ predicts improved outcome following pegylated liposomal doxorubicin (PLD) for recurrence. In this retrospective analysis, recurrent EOC *BRCA* mutation carriers treated with PLD had an improved outcome, which appeared to be independent of platinum sensitivity.

## Axl and Mer in Cancer

**Verma *et al.*** **Page 1763**

The mammalian TAM receptor tyrosine kinase family (RTK) includes three closely related members: Tyro-3, Axl, and Mer. Abnormal expression and ligand-induced activation of Axl or Mer can provide a survival advantage in a variety of cancers. Inhibition of Axl and Mer may enhance the sensitivity of cancer cells to cytotoxic agents and could potentially be a therapeutic strategy in targeting cancer cells. Verma and colleagues review the role of Axl and Mer in normal cellular function, their role in oncogenesis, and the potential to inhibit these RTKs as therapeutic strategies in treatment of cancer.

## miRNA Target–Dysregulated Network

**Xu *et al.*** **Page 1857**

MicroRNA (miRNA) roles in tumor biology remain largely unknown. Xu and colleagues introduce a systems biology approach based on the miRNA-target dysregulated network (MTDN) in specific tumor phenotypes to prioritize disease miRNAs. The MTDN is constructed by combining miRNA-target interactions with miRNA and mRNA expression profiles in tumor and nontumor tissues. Xu and colleagues' model achieves higher accuracy for classifying prostate cancer from NPC miRNAs in its application to prostate cancer. Predicted prostate cancer miRNAs are closely associated with oncogenesis, and miRNAs within families or from different families show combinatorial dysregulation of target genes. Finally, three miRNA-target regulations are verified to hold in prostate cancer cells by transfection assays.

## ABT-898 Induces Tumor Regression in Ovarian Cancer

**Campbell *et al.*** **Page 1876**

Epithelial ovarian cancer is the most lethal gynecologic malignancy and often is not detected until late stages where current treatment modalities have limited effectiveness. Thrombospondin-1 (TSP-1) is an endogenous inhibitor of angiogenesis and reduced expression is often associated with aggressive tumor growth. In this paper, Campbell and colleagues show that the TSP-1 mimetic peptide ABT-898 was able to induce regression of advanced-stage ovarian tumors, cause destruction of abnormal tumor blood vessels, and significantly prolong survival. TSP-1 shows promise as an important tool in the treatment of advanced stage ovarian cancer.

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