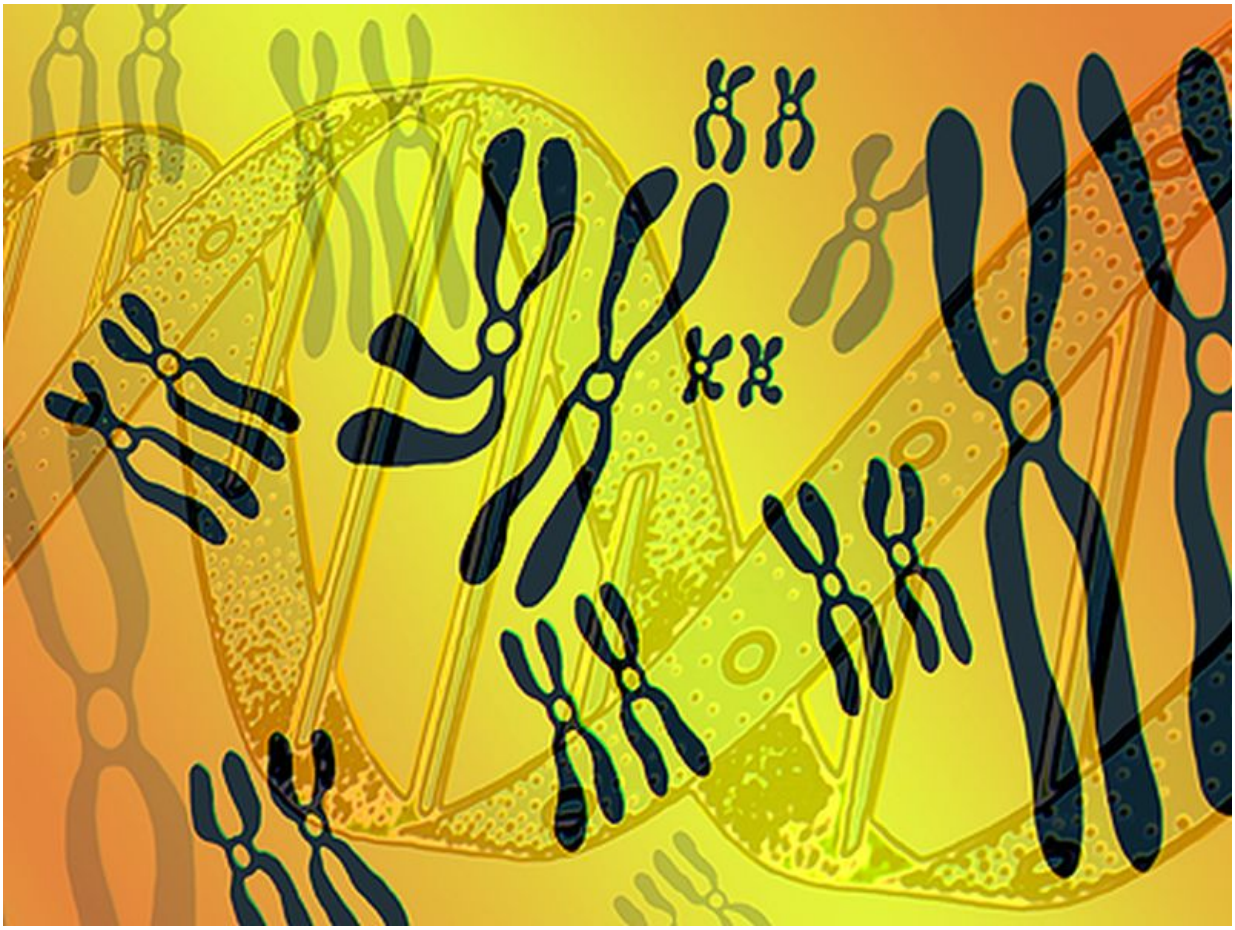
MedicalXpress

TP53, MDM2 alterations linked to cisplatin resistance in GCT

September 23 2016



(HealthDay)—In germ cell tumors (GCTs), *TP53* and *MDM2* alterations

correlate with cisplatin resistance and are associated with inferior outcome, according to a study published online Sept. 19 in the *Journal of Clinical Oncology*.

Aditya Bagrodia, M.D., from the Memorial Sloan Kettering Cancer Center in New York City, and colleagues identified a genetic basis for cisplatin resistance among men with GCT who received a cisplatin-containing chemotherapy regimen and had available tumor tissue. The investigators performed whole-exome sequencing or targeted exon-capture-based sequencing on 180 tumors. Using a combination of post-chemotherapy parameters, patients were classified as cisplatin sensitive or resistant.

The researchers found that *TP53* alterations were only seen in cisplatin-resistant tumors, and were especially common among primary mediastinal nonseminomas (72 percent). Patients with adverse clinical features, categorized as poor risk according to the International Germ Cell Cancer Collaborative Group (IGCCCG) model more often had *TP53* pathway alterations, including *MDM2* amplifications. Independent of the IGCCCG model, *TP53* and *MDM2* alterations predicted adverse prognosis. Fifty-five percent of cisplatin-resistant GCTs had actionable alterations, including novel *RAC1* mutations.

"A substantial portion of cisplatin-resistant GCTs harbor actionable alterations, which might respond to targeted therapies," the authors write. "Genomic profiling of patients with advanced GCT could improve current risk stratification and identify novel therapeutic approaches for patients with cisplatin-resistant disease."

Several authors disclosed financial ties to the pharmaceutical industry.

More information: Abstract
Full Text (subscription or payment may be required)