Researchers discover why new melanoma drug stops working

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(Medical Xpress) -- Research led by investigators at Memorial Sloan-Kettering Cancer Center has identified a previously unknown mechanism of resistance to the newly approved melanoma drug, vemurafenib, an oral targeted therapy used to treat advanced melanoma whose tumors contain a mutation in a gene called BRAF. The results of the study are published in the November 23rd advanced online edition of the journal *Nature*.

Vemurafenib, a targeted cancer drug, has been heralded as one of the biggest advances in the treatment of metastatic melanoma in the past 25 years and is now the standard of care for patients with the disease. Until now, however, researchers didn't understand how patients were becoming resistant to the targeted therapy, which was approved by the FDA in August, 2011.

As with most targeted inhibitors, resistance to the drug invariably develops, and pinpointing why this occurs is critical to developing future treatments or combinations of treatments that can overcome the resistance and further extend the lives of patients faced with this deadly disease.

The research was led by senior author David Solit, an Associate Attending Physician on the Genitourinary Oncology Service and member of the Human Oncology and Pathogenesis Program, and included the work of colleagues at Memorial Sloan-Kettering. For the first time, the team isolated a variant splice form of BRAF that causes

resistance to the drug in the lab. Along with physician-scientists at Memorial Sloan-Kettering and collaborating institutions across the country, this variant was proven clinically relevant in patients.

Memorial Sloan-Kettering has been integrally involved in both the pre-clinical and clinical studies of vemurafenib. Investigators at Memorial Sloan-Kettering were the first to define the basis for the drug's selectivity for tumors that express mutant BRAF. The first-in-man and the pivotal phase III clinical trials that led to the FDA approval were also led by principal investigator Paul Chapman of Memorial Sloan-Kettering.

Provided by Memorial Sloan-Kettering Cancer Center