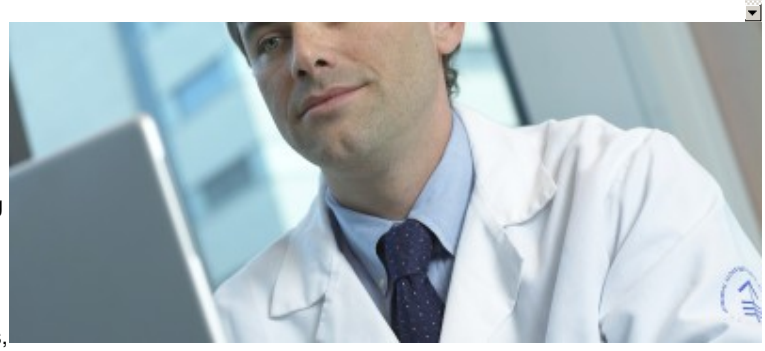
advanced online edition of the journal *Nature.*

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.



David Solit, Laboratory Head in the Human Oncology and Pathogenesis Program

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 Huma 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.