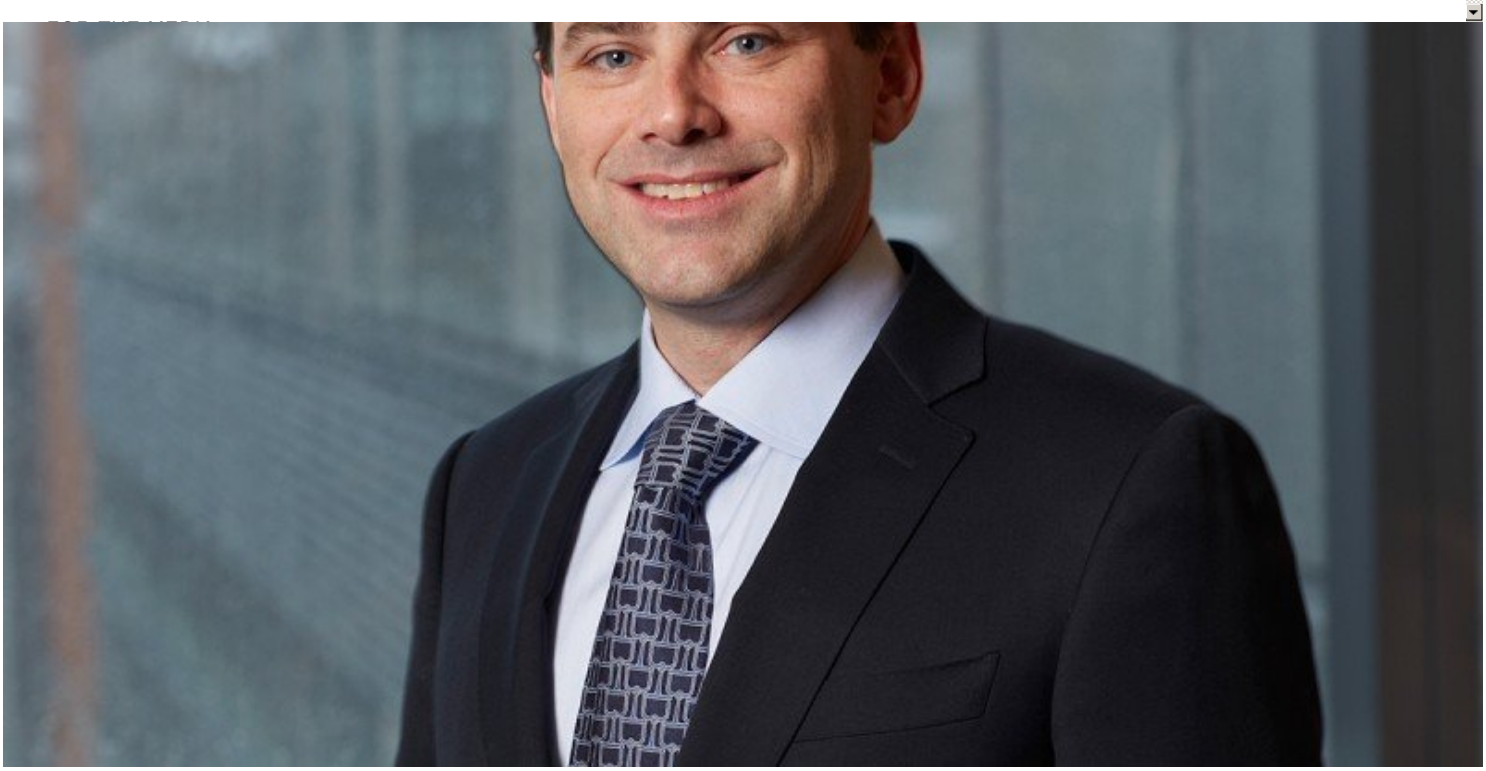

David Solit, Director of the Marie-Josée and Henry R. Kravis Center for Molecular Oncology

## Summary

David Solit, Director of the Marie-Josée and Henry R. Kravis Center for Molecular Oncology, discusses how working with cancer patients drives him to develop more-effective, personalized cancer treatments.

David Solit became a doctor because he wanted to care for patients. But after he decided to specialize in oncology, a lack of good treatment options for many of them convinced him to enter the laboratory to discover new ways to treat advanced cancers.

The drive to develop better therapies inspires not only Dr. Solit's work but also his free time: He is an active participant in Cycle for Survival, Memorial

Sloan Kettering's indoor team cycling event that raises money for rare cancer research, and also recently ran in the New York City Marathon as a member of Fred's Team, the Memorial Sloan Kettering fund-raising program that enables athletes to raise money by competing in endurance events such as marathons.

Dr. Solit is the Director of the Marie-Josée and Henry R. Kravis Center for Molecular Oncology (CMO), Memorial Sloan Kettering's new collaborative center that is undertaking a wide-ranging effort to correlate tumor genetics with clinical outcomes and responses to therapy. He is also a member of the Human Oncology and Pathogenesis Program, where his laboratory team works to identify novel drug targets.

In a recent interview, we talked to him about how research in cancer genetics can lead to more-effective, personalized therapies.

## What are your clinical specialties?

I am a medical oncologist who specializes in the treatment of genitourinary cancers using chemotherapy and other drugs such as hormonal agents. I primarily care for patients with prostate and bladder cancers, but our service sees patients with kidney and testicular cancers as well. I also lead clinical trials to evaluate experimental targeted therapies.

Back to top ^

## Tell us more about the trials you're involved in.

Before becoming Director of the Marie-Josée and Henry R. Kravis Center for Molecular Oncology, I served as the Director of the Developmental Therapeutics Group. The focus of this multidisease team of doctors, nurses, and researchers is the development of targeted inhibitors for patients with all types of cancer.

Targeted therapies are drugs aimed at blocking the molecular changes inside cancer cells that make tumors grow and spread. Many of the studies we conduct are first-in-human trials of experimental drugs or drug combinations that have shown promise in laboratory studies.

Back to top ^

## How do these clinical studies with patients relate to what you're doing in the laboratory?

I began my laboratory studies working with [Memorial Sloan Kettering physician-scientist] Neal Rosen. Dr. Rosen leads a cell biology and molecular pharmacology research laboratory in which one focus is to determine how drugs work and the mechanisms by which they are able to kill cancer cells.

Upon establishing my own independent research laboratory, I was interested in developing genetic methods whereby we could determine why some cancer cells were more sensitive to certain treatments than others. The past several years have seen dramatic advances in the technology available for analyzing tumor DNA. My laboratory has sought to apply these new methods to our studies of drug sensitivity and resistance.

Back to top ^

## Is this the idea behind the exceptional responder initiative?

Yes, the exceptional responder initiative is a classic example of translational research. In translational research studies, we use insights from the laboratory to guide clinical research. Similarly, we also use clinical results to guide new laboratory studies.

We choose to focus on patients who have dramatic and durable responses to experimental cancer drugs in trials that are disappointing overall. Statistically, these are negative studies: The drugs did not work for most patients in the study.

But in some of these statistically negative clinical trials, there are a few patients who have dramatic and durable responses to the treatment, sometimes lasting for years. For these responding patients, the experimental agent was the "correct" therapy. By analyzing these patients using next-generation sequencing methods, we have been able to identify genetic signatures that explain their dramatic drug sensitivity.

We then seek to identify other patients whose tumors have a similar genetic profile to these exceptional responders. Excitingly, many of these patients are similarly responsive to the same therapy that was so effective in the outlier patients. This approach has enabled us to resurrect therapies whose development was previously halted because the treatment had little benefit in most patients.

Since our initial example, which we published in 2012 in *Science*, we have performed a series of similar outlier studies. In almost every case, we've beer

successful in identifying the mutation that explained biologically why the drug was so effective in the exceptional responder. In many cases, this approach has also identified new drug targets or areas of research that we are now pursing in the laboratory.

Back to top

## What does this mean for patients?

These findings have led to a new type of clinical trial in which patients are enrolled not on the basis of the tumor's location in the body, but rather on the basis of its specific mutational profile. This is very different from how oncology studies have been performed historically, which was cancer-type specific: Lung cancer patients were all treated in a similar fashion, as were bladder cancer patients, and so on.

Recent efforts to define the genetic basis of cancer have shown that cancer subtypes as defined by site of origin are a heterogeneous collection of many different diseases. At Memorial Sloan Kettering, we are moving away from the paradigm of treating cancer as if it were one disease. Rather, the goal is to treat *individual* cancers based upon their specific mutational profile. We call this precision or personalized medicine. The expectation is that these personalized therapies will be more effective and have fewer side effects.

The goal of the Marie-Josée and Henry R. Kravis Center for Molecular Oncology is to make this individualized treatment approach widely available, as opposed to only offering these tailored therapies to patients enrolled in clinical trials.

Back to top

## What technology has made this research possible?

In order to successfully perform these mutation-focused clinical trials, we need a method in the clinic to be able to screen patients for the mutations of interest. We've thus worked very closely with our colleagues in the Diagnostic Molecular Pathology Laboratory, especially Marc Ladanyi and Maria Arcila , to make universal screening of cancer patients a reality at Memorial Sloan Kettering.

We also work closely with [genomics researcher and CMO Co-Associate Director] Michael Berger to develop genomic tests that can rapidly and at low cost look for mutations in hundreds of genes at the same time. This type of technology development will be a major focus of the CMO.

Back to top

## How has the way that cancer patients are treated changed over the past decade?

We've seen a number of examples over the past ten years where by defining the molecular cause of a disease, we have been able to successfully develop a targeted drug that has unprecedented antitumor effects in patients whose tumor harbors the targeted mutation or gene.

For diseases such as chronic myelogenous leukemia, these newer targeted approaches have resulted in significant improvements in both survival and quality of life. However, for many common cancers such as lung cancer, these newer targeted drugs are effective only in small, genetically defined subsets of patients — and for many cancers, effective targeted therapies do not currently exist.

From a scientific perspective, it is incredibly exciting and rewarding to have played a role in the clinical development of several of these newer therapies. Like most people, a diagnosis of cancer has impacted many of my own family members and friends.

As a practicing medical oncologist, I am also reminded weekly that we still lack effective treatments for many patients. I am optimistic, however, that recent advances in cancer genetics will lead to the identification of new drug targets and combinatorial therapies that will expand the benefits of personalized therapy to all cancer patients.

Back to top

PREVIOUS
In the News

NEXT
Bold Initiative to Transform Cancer Care Established with a $100 Million Gift

## Connect

Contact us

Locations

APPOINTMENTS
800-525-2225

## About MSK

About us

Careers

Giving

## Cancer Care

Adult cancer types

Child & teen cancer types

Integrative medicine

Nutrition & cancer

Find a doctor

## Research & Education

Sloan Kettering Institute

Gerstner Sloan Kettering Graduate School

Graduate medical education

MSK Library

---