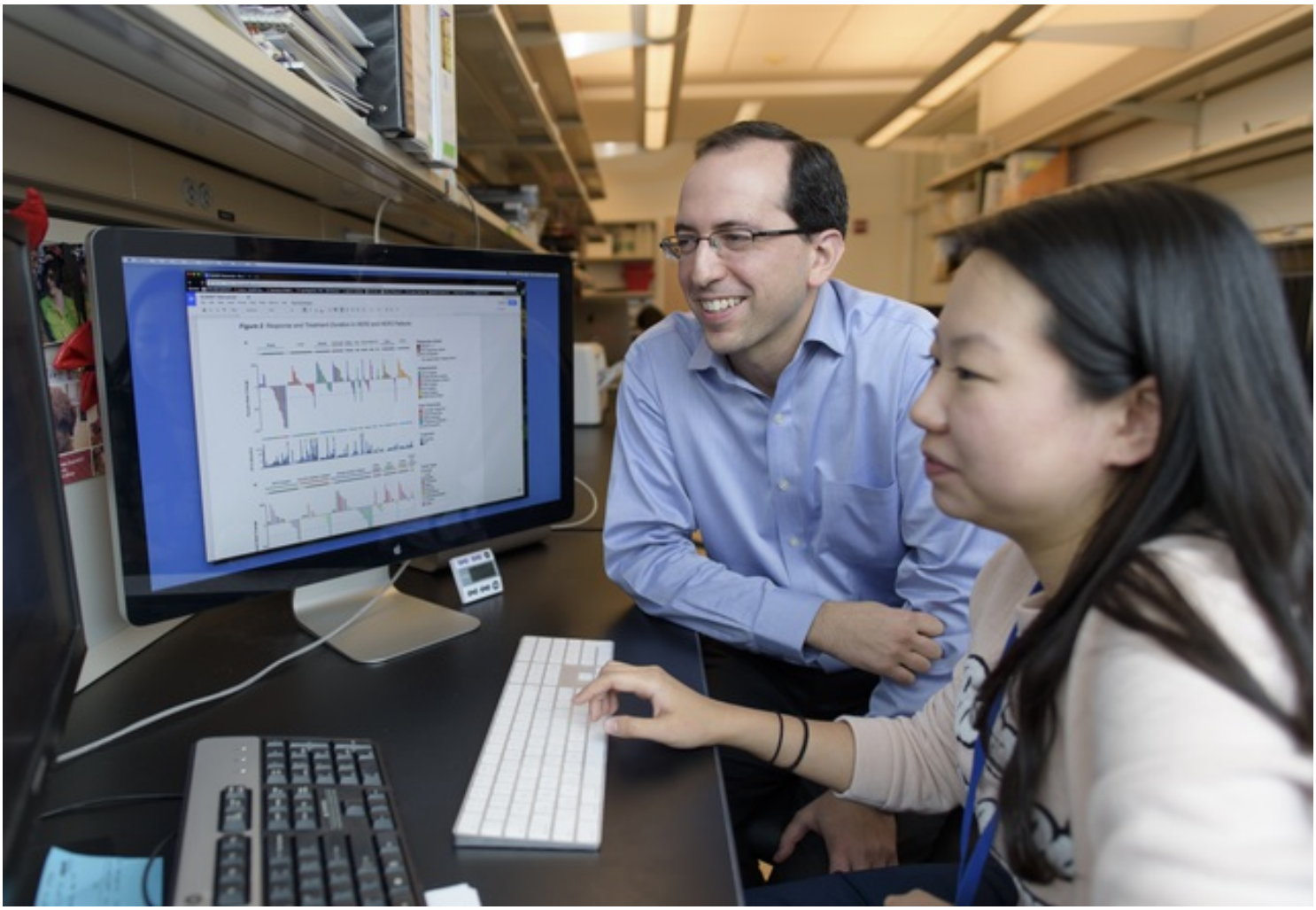
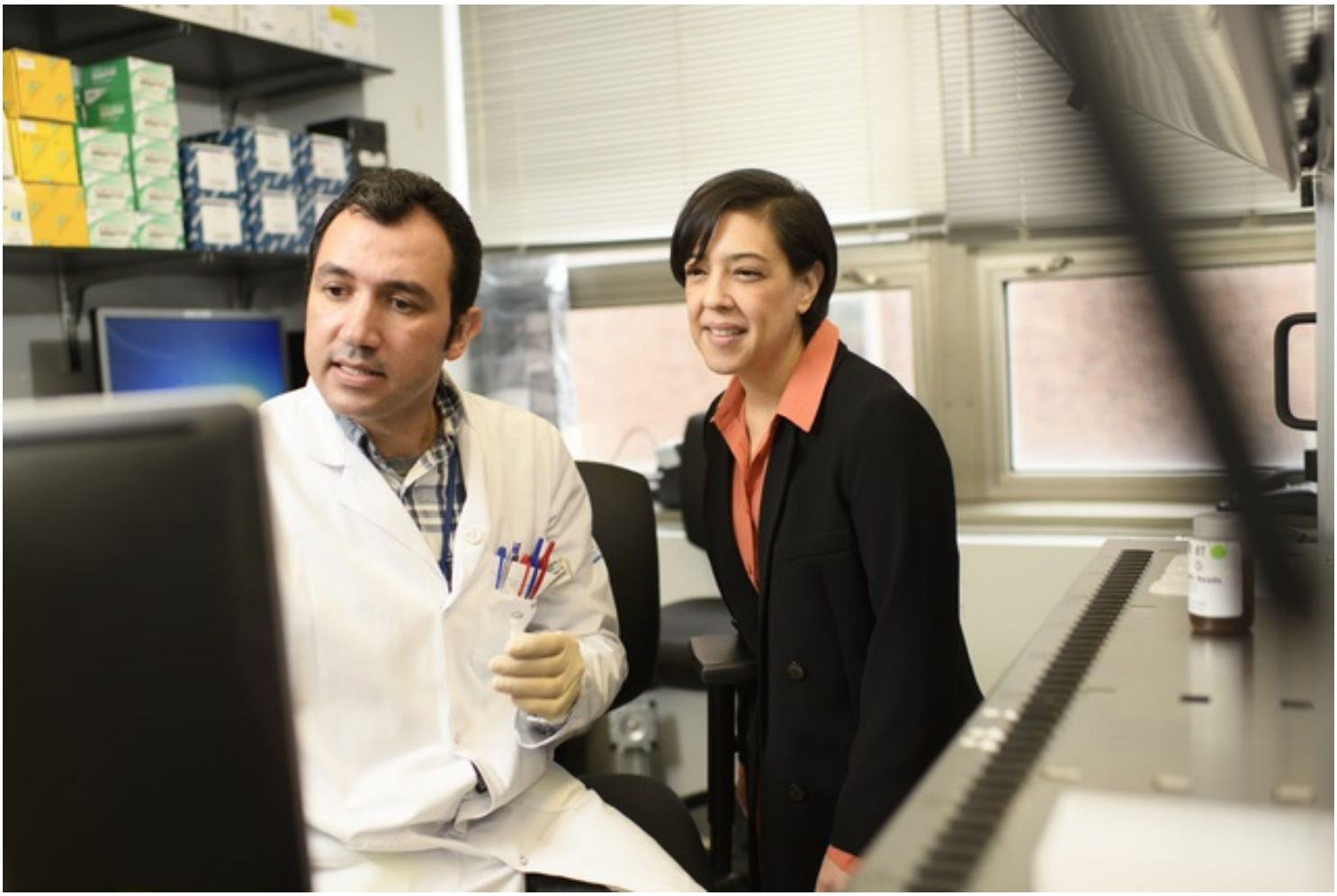
MSK-IMPACT: A Targeted Test for Mutations in Both Rare and Common Cancers

Members of the team that developed MSK-IMPACT®. (Front row, from left) Ryma Benayed, Maria Arcila, and Khedoudja Nafa. (Back row, from left) Marc Ladanyi, Ahmet Zehir, and Michael Berger.

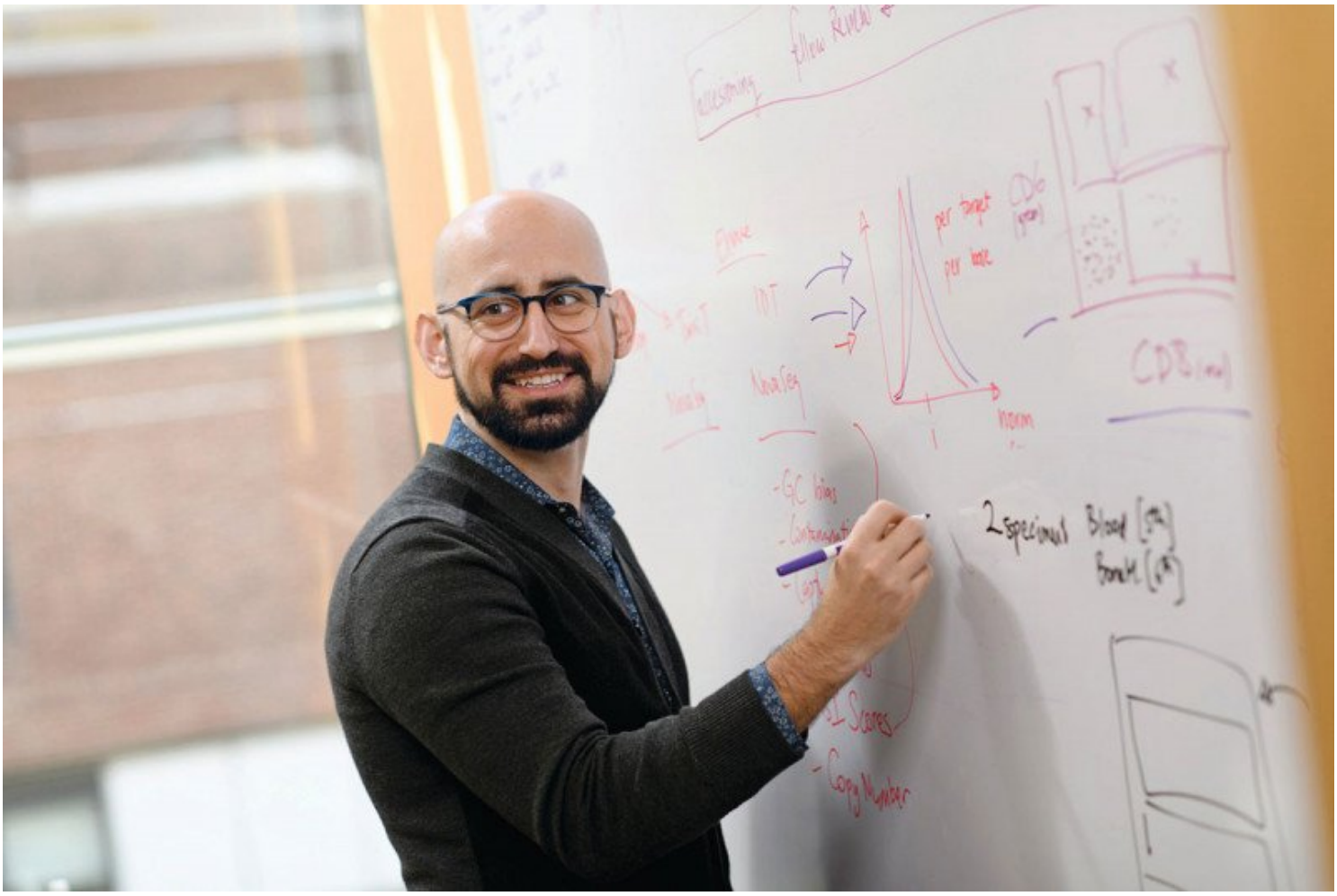
(From left) Molecular geneticist Liying Zhang; pathologist Diana Mandelker; and Marc Ladanyi, Chief of the Molecular Diagnostics Service



(From left) Michael Berger, Associate Director of the Marie-Josée and Henry R. Kravis Center for Molecular Oncology, and computational biologist Helen Won



(From left) Laboratory technologist Nelio Chavez and Maria Arcila, Director of the Diagnostic Molecular Pathology Laboratory



Computational biologist Ahmet Zehir

MSK-IMPACT® stands for Integrated Mutation Profiling of Actionable Cancer Targets. It is a targeted tumor-sequencing test available to MSK patients. MSK-IMPACT can detect mutations and other critical changes in the genes of both rare and common cancers. With the MSK-IMPACT test, doctors can quickly find out whether a tumor has changes that make the cancer vulnerable to particular drugs. MSK patients can then be matched to the available therapies or clinical trials that will most benefit them.

Expanding Genomic Testing to More Patients

Until recently, the genomic testing of tumors was routine practiced only for people with certain solid tumors, such as melanoma, lung cancer, and colon cancer. MSK-IMPACT is much more inclusive. It can be used on any tumor, no matter where in the body the cancer started. MSK-IMPACT potentially offers thousands of people better treatment options through precision oncology.

MSK-IMPACT was developed and shown to be clinically useful by scientists in the Department of Pathology's Molecular Diagnostics Service and the Marie-Josée and Henry R. Kravis Center for Molecular Oncology (CMO). The test uses cutting-edge next-generation DNA-sequencing technology. It is capable of detecting many classes of genomic changes. These include mutations, gene amplifications and deletions, and genomic rearrangements and signatures such as microsatellite instability and tumor mutation burden. MSK-IMPACT provides a comprehensive picture of the full spectrum of genetic changes in a tumor.

Back to top

Looking for Changes That Can Be Targeted With Drugs

MSK-IMPACT analyzes 505 genes. These genes were nominated by researchers and experts from across MSK. The genes were chosen because they

play a critical role in the development and behavior of tumors. All actionable targets (genes that provide important information about the disease and possibly can be targeted with drugs) are included. MSK-IMPACT will be updated regularly as new targets are discovered. A companion test for people with blood cancer, MSK-IMPACT Heme, has also been validated and is in use. That test evaluates 400 genes, many of them the same genes that are included for solid tumors.

In November 2017, MSK-IMPACT was authorized by the U.S. Food and Drug Administration. It was the first academic or commercial tumor-profiling test to earn this distinction. MSK-IMPACT test results from the Molecular Diagnostics Service are reported in each patient's electronic medical record. Patients and their families can discuss additional details about the MSK-IMPACT test with their doctors, such as its potential use and whether it is appropriate to have this testing. MSK-IMPACT is also used as a research test in the CMO to look at samples collected for research purposes. These results may not be returned to patients but are informing research advances and discoveries made by MSK investigators.

To take full advantage of MSK-IMPACT, MSK doctors and researchers developed a knowledge base called OncoKB®. This system includes information about the clinical and biological effects of more than 4,000 genomic changes. That information is based on public databases, scientific literature, and clinical guidelines.

OncoKB® can help doctors find the best therapies based on a tumor's genomic profile. People with an actionable mutation that has not yet been studied in their tumor type may be eligible for treatment in a type of clinical study called a basket trial. Traditional clinical trials focus on a particular cancer type, which is typically defined based on where in the body the cancer started. (In the breast, lung, or prostate, for example.)

Basket trials, however, focus on specific genetic changes in tumors regardless of where those tumors are located. Patients with many different types of cancer may enroll in basket trials if their tumors all carry similar mutations. Basket studies may include many more people than disease-specific trials. This allows for faster enrollment in clinical trials and faster analysis of the results, potentially leading to new therapies more quickly.

A notable feature of MSK-IMPACT is that two DNA samples from each person are sequenced and compared: DNA from tumor tissue and from normal tissue. The normal tissue is usually a blood sample. Directly comparing the tumor's genome to the genome in normal blood ensures that the mutations detected by MSK-IMPACT are specific to the cancer cells.

VIDEO | 05:30

Learn More About the Molecular Diagnostics Service at MSK

Go inside the molecular pathology lab, located on the fourth floor of the Arnold and Maria Schwartz Cancer Research Building at MSK. This is where tumor-sequencing tests MSK-IMPACT® and MSK-ACCESS® take place. These tests can help doctors learn important information about individual people's cancers and help guide their treatment.

Video Details →

What's more, looking at normal genomes can show whether there are any inherited genetic mutations associated with an increased risk of cancer. When these mutations are found, patients and their families are referred to the Clinical Genetics Service. The service provides both screening and counseling. Research into the function of inherited mutations is being done through the Robert and Kate Niehaus Center for Inherited Cancer Genomics.

MSK-IMPACT may also reveal mutations in blood cells associated with clonal hematopoiesis. These mutations are more common in older people. They may lead to an increased risk of a secondary blood cancer or cardiovascular disease. To monitor people with clonal hematopoiesis for early detection of these adverse health effects, MSK established the first clonal hematopoiesis clinic in 2018.

Back to top ^

A Focus on Data Sharing

An important goal of MSK-IMPACT is to gather data and share analyses within MSK and with the public. The data gathered are being used to develop smarter cancer therapies. MSK-IMPACT results that have been stripped of all patient-identifying information are available for scientific use by everyone at MSK through the cBioPortal. This important resource facilitates critical scientific and clinical advances at MSK. MSK-IMPACT results are also shared more broadly with the wider scientific community through AACR GENIE. Through this American Association for Cancer Research consortium, MSK-IMPACT data can be used along with tumor-sequencing data from other institutions.

As of the end of 2018, more than 100 scientific publications by MSK authors have included results from MSK-IMPACT testing. A partial list of selected key papers is shown below.

Multiple Cancer Types

- Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients
- Mutation detection in patients with advanced cancer by universal sequencing of cancer-related genes in tumor and normal DNA vs. guideline-based germline testing
- Therapy-related clonal hematopoiesis in patients with nonhematologic cancers is common and associated with adverse clinical outcomes
- Reliable pan-cancer microsatellite instability assessment by using targeted next-generation sequencing data
- Genome doubling shapes the evolution and prognosis of advanced cancers
- Widespread selection for oncogenic mutant allele imbalance in cancer
- Microsatellite instability is associated with the presence of Lynch syndrome pan-cancer
- AACR Project GENIE: powering precision medicine through an international consortium

Individual Cancer Types

- Prospective comprehensive molecular characterization of lung adenocarcinomas for efficient patient matching to approved and emerging therapies
- The genomic landscape of endocrine-resistant advanced breast cancers
- Clinical sequencing defines the genomic landscape of metastatic colorectal cancer
- Genetic predictors of response to systemic therapy in esophagogastric cancer
- Clinical and molecular characterization of patients with cancer of unknown primary in the modern era
- Prospective genomic profiling of prostate cancer across disease states reveals germline and somatic alterations that may affect clinical decision-making
- Real-time genomic profiling of pancreatic ductal adenocarcinoma: potential actionability and correlation with clinical phenotype
- Next-generation sequencing of nonmuscle invasive bladder cancer reveals potential biomarkers and rational therapeutic targets
- The molecular landscape of recurrent and metastatic head and neck cancers: insights from a precision oncology sequencing platform
- Clinical utility of prospective molecular characterization in advanced endometrial cancer
- Prospective genotyping of hepatocellular carcinoma: clinical implications of next generation sequencing for matching patients to targeted and immune therapies
- Comprehensive molecular profiling of intrahepatic and extrahepatic cholangiocarcinomas: potential targets for intervention

Back to top