

The past, present and future of cancer

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Leading cancer researchers reflected on past achievements and prospects for the future of cancer treatment during a special MIT symposium on Wednesday titled "Conquering Cancer through the Convergence of Science and Engineering."

The event, one of six academic symposia taking place as part of MIT's 150th anniversary, focused on the Institute's role in studying the disease over the past 36 years since the founding of MIT's Center for <u>Cancer</u> Research.

During that time, MIT scientists have made critical discoveries that resulted in new cancer drugs such as Gleevec and Herceptin. The center has since become the David H. Koch Institute for Integrative Cancer Research, which now includes a mix of biologists, who are trying to unravel what goes wrong inside cancer cells, and engineers, who are working on turning basic science discoveries into real-world treatments and diagnostics for cancer patients.

That "convergence" of life sciences and engineering is key to making progress in the fight against cancer, said Institute Professor Phillip Sharp, a member of the Koch Institute. "We need that convergence because we are facing a major demographic challenge in cancer as well as a number of other chronic diseases" that typically affect older people, such as Alzheimer's, Sharp said.

In opening the symposium, MIT President Susan Hockfield said that MIT has "the right team, in the right place, at the right moment in



history" to help defeat cancer.

"It's in the DNA of MIT to solve problems," said Tyler Jacks, director of the Koch Institute. "I'm very optimistic and very encouraged about what this generation of cancer researchers at MIT will do to overcome this most challenging problem."

Past and present

In the past few decades, a great deal of progress has been made in understanding cancer, said Nancy Hopkins, the Amgen, Inc. Professor of Biology and Koch Institute member, who spoke as part of the first panel discussion, on major milestones in cancer research.

In the early 1970s, before President Richard Nixon declared the "War on Cancer," "we really knew nothing about human cells and what controls their division," Hopkins recalled. Critical discoveries by molecular biologists, including MIT's Robert Weinberg, revealed that cancer is usually caused by genetic mutations within cells.

The discovery of those potentially cancerous genes, including HER2 (often mutated in breast cancer), has lead to the development of new drugs that cause fewer side effects in healthy cells. While that is a major success story, many other significant discoveries have failed to make an impact in patient treatment, Hopkins said.

"The discoveries we have made are not being exploited as effectively as they could be," Hopkins said. "That's where we need the engineers. They're problem-solvers."

Institute Professor Robert Langer described his experiences as one of the rare engineers to pursue a career in biomedical research during the 1970s. After he finished his doctoral degree in chemical engineering in



1974, "I got four job offers from Exxon alone," plus offers from several other oil companies. But Langer had decided he wanted to do something that would more directly help people, and ended up getting a postdoctoral position in the lab of Judah Folkman, the scientist who pioneered the idea of killing tumors by cutting off their blood supplies.

In Folkman's lab, Langer started working on drug-delivering particles made from polymers, which are now widely used to deliver drugs in a controlled fashion.

Langer and other engineers in the Koch Institute are now working on ways to create even better drug-delivery particles. Sangeeta Bhatia, the Wilson Professor of Health Sciences and Technology and Electrical Engineering and Computer Science, described an ongoing project in her lab to create iron oxide nanoparticles that can be tagged with small protein fragments that bind specifically to tumor cells. Such particles could help overcome one major drawback to most chemotherapy: Only about 1 percent of the drug administered reaches the tumor.

"If we could simply take these poisonous drugs more directly to the tumors, it would increase their effectiveness and decrease side effects," Bhatia said.

Other Koch engineers are working on new imaging agents, tiny implantable sensors, cancer vaccines and computational modeling of cancer cells, among other projects.

Personalized medicine

Many of the targeted drugs now in use came about through serendipitous discoveries, said Daniel Haber, director of the Massachusetts General Hospital Cancer Center, during a panel on personalized cancer care. Now, he said, a more systematic approach is needed. He described a new



effort underway at MGH to test potential drugs on 1,000 different tumor cell lines, to find out which tumor types respond best to each drug.

At MIT, Koch Institute members Michael Hemann and Michael Yaffe have shown that patient response to cancer drugs that damage DNA can be predicted by testing for the status of two genes — p53, a tumor suppressor, and ATM, a gene that helps regulate p53.

Their research suggests that such drugs should be used only in patients whose tumors have mutations in both genes or neither gene — a finding that underscores the importance of understanding the genetic makeup of patients' tumors before beginning treatment. It also suggests that current drugs could be made much more effective by combining them in the right ways.

"The therapies of the future may not be new therapies," Hemann said.
"They may be existing therapies used significantly better."

The sequencing of the human genome should also help achieve the goal of personalized <u>cancer treatment</u>, said Eric Lander, director of the Broad Institute and co-chair of the President's Council of Advisors on Science and Technology, who spoke during a panel on biology, technology and medical applications. Already, the sequencing of the human genome has allowed researchers to discover far more cancer-causing genes. In 2000, before the sequence was completed, scientists knew of about 80 genes that could cause solid tumors, but by 2010, 240 were known.

Building on the human genome project, the National Cancer Institute has launched the Cancer Genome Atlas Project, which is sequencing the genomes of thousands of human tumors, comparing them to each other and to non-cancerous genomes. "By looking at many tumors at one time, you can begin to pick out common patterns," Lander said.



He envisions that once cancer scientists have a more complete understanding of which genes can cause cancer, and the functions of those genes, patient treatment will become much more effective. "Doctors of the future will be able to pick out drugs based on that information," he said.

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