the Karolinska Institute in Stockholm, Sweden; The Netherlands Cancer Institute in Amsterdam; the Vall d’Hebron Institute of Oncology in Barcelona, Spain; and the German Cancer Research Center in Heidelberg.

The centers aren’t merging their daily operations, but they are creating what Eggermont terms an “e-hospital,” in which researchers at the six institutions will have access to patient data from the other partners. To ensure that information is compatible, the centers plan to adopt uniform protocols for obtaining biopsies and storing the results, performing molecular diagnostics, monitoring patients’ immune function, and carrying out other key procedures.

“We will have a common standard of material that we can trust that will allow us to share our data,” says Eggermont. A collaborative effort with this degree of interconnection “has never been done before,” he says.

One of the benefits of Cancer Core Europe, organizers say, will be more potential participants for clinical trials. Each year, the hospitals enroll 60,000 new cancer patients and treat between 250,000 and 300,000 people. Given these numbers, the project “has already attracted quite a bit of interest from the pharmaceutical industry,” says Carlos Caldas, MD, of the Cambridge Cancer Centre, who is also one of the consortium’s organizers. A larger pool of patients, for example, might help researchers test targeted therapies.

By combining forces, researchers might also be able to determine which cancer treatments are most effective. Health care funders increasingly demand this information, but definitive answers are hard to come by, Eggermont says, because cancer treatment is so complex, involving multiple approaches such as chemotherapy, surgery, radiation, and immunotherapy. By prospectively creating annotated databases of patient information, the project meets the requirements for this kind of outcome research, he says.

The centers are providing the initial funding for the collaboration, but the group intends to seek European Union grants. Within the next few months they plan to choose a scientific director to supervise the integration of their data and procedures. Cancer Core Europe should be up and running within 3 years, Eggermont says. After that, the partners may look to add new members and perhaps create a Europe-wide virtual cancer institute, he says.

Scientists Share Nobel Prize for “Nanoscopy”

Three scientists from the United States and Germany were awarded the 2014 Nobel Prize in Chemistry for their contributions to developing super-resolved fluorescence microscopy, a giant step forward in biomedical imaging that has given biologists a window into the inner workings of cells on a nanometer scale.

For most of the 20th century, scientists believed that it was not possible to resolve images smaller than half the wavelength of light (approximately 0.2 µm), a principle known as Abbe’s diffraction limit. Nobel Laureates Eric Betzig, PhD, of Howard Hughes Medical Institute in Ashburn, VA; Stefan Hell, PhD, of the Max Planck Institute for Biophysical Chemistry in Gottingen, Germany; and William E. Moerner, PhD, of Stanford University in Palo Alto, CA, circumvented that principle by using fluorescence to map the position of molecules within a cell.

“Because of the methods they developed, we can now use a microscope with 10 times more resolution than what we had in the past,” says Carlos J. Bustamante, PhD, professor of chemistry, physics, and molecular and cellular biology at the University of California, Berkeley. “Scientists can now visualize how things are organized and function within cells, which has had, and continues to have, a profound impact on all of biological research.”

The award recognizes two revolutionary approaches that underlie what has become known as “nanoscopy”: stimulated emission depletion (STED) microscopy and Photo-Activatable Light Microscopy (PALM).

In the STED microscope, developed by Hell, one light pulse excites all the fluorescent molecules while another deactivates fluorescence almost everywhere except in a nanometer-sized volume in the middle. By sweeping along a cell sample and continuously measuring light in those small volumes, researchers can create a complete image of a cell at a much higher resolution than with a regular optical microscope.

Moerner was the first to measure fluorescence in a single molecule. He discovered that one variant of green fluorescent protein could be turned on and off at will by varying the wavelength of light, enabling scientists to isolate specific molecules within a cell.

Building on Moerner’s work, Betzig developed PALM, a technique that uses weak light pulses to activate small subgroups of fluorescent proteins at different times, with a new subgroup activated each time the fluorescence dies out. The positions of the glowing proteins can be registered with a regular microscope because they are almost always more than 0.2 µm apart. The process produces multiple images that are then superimposed to create one extremely high-resolution image.

“By finding a way to determine where all the molecules are located in a sample, they solved the problem of how to distinguish between individual molecules that are closer together than the wavelength of light,” says Bustamante. “They separated in time what could not be separated in space.”

The Laureates will share the $1.1 million prize, which will be awarded on December 10 in Stockholm, Sweden.

TKIs May Be Option for Ph-Like ALL

Researchers may have found a new way to treat a common subtype of acute lymphoblastic leukemia (ALL) that was identified just 5 years ago.
Children and young adults with Philadelphia chromosome-like (Ph-like) ALL have genetic alterations that may be vulnerable to tyrosine kinase inhibitors (TKI). Researchers reported in September at the American Association for Cancer Research conference Hematologic Malignancies: Translating Discoveries to Novel Therapies.

ALL is the most common childhood cancer. In 2009, scientists first identified Ph-like ALL, a precursor B-cell ALL subtype with a poor prognosis that has emerged Ph-like ALL, a precursor B-cell ALL subtype, increased with age, from 10% in older patients to 27% among young adults. Older patients also had a much higher risk for relapse and death within 5 years.

Next-generation sequencing on 154 patients with Ph-like ALL identified kinase-activating alterations in 91% of patients. Researchers found 35 distinct alterations of 13 kinase and cytokine receptor genes, with ABL1, CRLF2, JAK2, and EPOR among the most common.

Using the first mouse models of Ph-like ALL, researchers found that treating mice with dasatinib reduced the tumor burden of leukemia cells harboring ABL1, ABL2, or CSF1R fusions. In vitro analyses suggest that cells expressing EPOR and JAK2 rearrangements are sensitive to ruxolitinib (Jakafi; Incyte) and those with the ETV6–NTRK3 fusion are sensitive to crizotinib (Xalkori; Pfizer).

Researchers also treated 12 patients with Ph-like ALL with dasatinib, imatinib (Gleevec; Novartis), or ruxolitinib on a compassionate-use basis. Eleven continue to respond, with one in remission for nearly 3 years, Roberts says.

The Children’s Oncology Group plans to launch a clinical trial in July 2015 to screen all B-cell ALL patients for Ph-like ALL. Those with Ph-like ALL who test positive for a kinase alteration will receive a TKI in combination with chemotherapy.

For now, Roberts says, some children receive TKIs off-label. “If a B-ALL patient comes through Children’s Oncology Group with high-risk clinical features and an assay that indicates they have a kinase alteration, clinicians are advised to add a logical TKI to chemotherapy,” she says.

**Radiation Boosts Immunotherapy**

New research reveals that radiation increases the power of immunotherapy to combat cancer, and provides a possible explanation for this effect.

Researchers have long thought that radiation impairs the immune system, but many of the studies supporting that conclusion exposed subjects to extensive radiation fields or even full-body radiation. For example, when the researchers irradiated one side of the animals, tumors on both sides shrank, suggesting that radiation produces this systemic effect.

The results suggest that radiation boosts immunotherapy through a variety of mechanisms by which radiation could augment immunotherapy isn’t clear.

To address these questions, a team led by Sharabi and medical oncologist Charles Drake, MD, PhD, of the Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, implanted mice with melanoma and breast cancer cells. The researchers then injected the animals with antibodies that block CTLA-4 or PD-1, two immune checkpoint proteins. Some mice also received stereotactic radiation therapy that hits only the tumor and a few millimeters of neighboring tissue.

Radiation and immunotherapy increased the animals’ survival and shrank their tumors more than either treatment alone, the researchers revealed last month at the American Society of Radiation Oncology meeting in San Francisco, CA. For example, breast tumors in mice that received both kinds of therapy were less than one sixth the size of tumors in animals that received only immunotherapy.

The researchers also found that the combination of radiation and immunotherapy increased the number of CD8+ T cells targeted against tumor antigens in the animals’ draining lymph nodes. “The study establishes that tumor-specific immune responses can be induced by combined treatment in this model system,” says Sharabi.

“The ultimate goal is to treat with local radiation and get a systemic effect that works against metastases,” adds Drake. An experiment in which the researchers implanted cancer cells on both sides of the mice and then gave them immunotherapy had little impact on the tumors on either side. However, when the researchers irradiated one side of the animals, tumors on both sides shrank, suggesting that radiation produces this systemic effect.

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