The sweet spot of the affiliation is translational cancer research, which includes the development of new cancer diagnostics and therapeutics and the training of a new generation of research-capable cancer clinicians. Northwell Health is one of the largest integrated health systems in the nation. Its recently expanded Cancer Institute, with over 200 academic oncologists and clinicians, is part of a system of care encompassing 21 hospitals and 400 outpatient physician practices throughout the New York metropolitan area. Serving more than 8 million people, Northwell treats some 19,000 new cancer cases annually. This makes it one of the most important sites of cancer treatment in the US.

As CEO Michael Dowling has noted, Northwell’s oncologists will make CSHL’s most promising pre-clinical research available to cancer patients in the form of innovative trials. Patients will be receiving advanced treatments and diagnostics they would not otherwise be offered, and benefit from them years before they would be available to patients elsewhere. At the same time, Northwell’s large patient intake provides our scientists with opportunities to perform cancer research using tumor samples from precisely defined subsets of patients. As we move further into the era of targeted therapy, assembling appropriate patient cohorts becomes ever more critical if we want to speed the time it takes to evaluate new treatments.

The urgency of speeding the translation of basic research into clinical advances is captured in this picture of pancreatic cancer patient Gail Poinelli conferring with CSHL’s Dr. David Tuveson (right) and Northwell Health’s Dr. Craig Devoe. The brave Ms. Poinelli, who lost her battle with the illness in 2016, is one of over 40,000 Americans whose lives are claimed by pancreatic cancer annually.

Bruce Stillman, Ph.D.

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The sweet spot of the affiliation is translational cancer research, which includes the development of new cancer diagnostics and therapeutics and the training of a new generation of research-capable cancer clinicians. Northwell Health is one of the largest integrated health systems in the nation. Its recently expanded Cancer Institute, with over 200 academic oncologists and clinicians, is part of a system of care encompassing 21 hospitals and 400 outpatient physician practices throughout the New York metropolitan area. Serving more than 8 million people, Northwell treats some 19,000 new cancer cases annually. This makes it one of the most important sites of cancer treatment in the US.

As CEO Michael Dowling has noted, Northwell’s oncologists will make CSHL’s most promising pre-clinical research available to cancer patients in the form of innovative trials. Patients will be receiving advanced treatments and diagnostics they would not otherwise be offered, and benefit from them years before they would be available to patients elsewhere. At the same time, however, opportunities abound in many areas of science, including cancer, neuroscience, plant biology and quantitative biology—areas of focus at Cold Spring Harbor.

Fortunately, with very strong support from our Board of Trustees and supporters of CSHL, we have seen a dramatic increase in our endowment. But this precious resource should support the core of what makes CSHL one of the leading research institutions in the world of basic discovery science. Having recognized this, it has been increasingly obvious that there are many instances in which we can add value to our science and translate these discoveries they will make an impact in the clinic—and this is particularly the case for cancer.

With this background, we took the initiative in 2015 of entering into a strategic affiliation with Northwell Health, previously known as the North Shore-LIJ Health System. It’s an alliance that I expect to be transformative. It will provide an unprecedented opportunity to add value to certain of our discoveries and multiply the impact of our research.
Christopher Vakoc (above) and colleagues in 2011 discovered a powerful drug target called BRD4 for AML, an often deadly form of leukemia. Translational work has already led to clinical trials testing the effectiveness of a drug called JQ1 (red) that “hits” the target (left).

role in translating the next wave of fundamental discoveries about cancer into new diagnostics and therapies. It’s reasonable to ask how the new alliance will change the way research is done at CSHL. I want to make clear that it in no way alters our core commitment to basic research, which is unshakable. This collaboration adds to our capabilities in a manner illustrated by two contrasting stories about basic research. One of these stories came to a happy conclusion early in 2015 when the Food and Drug Administration approved palbociclib (Ibrance) for the treatment of metastatic breast cancer. It’s a first-in-class inhibitor of CDK4 and CDK6, enzymes called protein kinases that help regulate the cell division cycle. In 1991, David Beach, then a highly productive CSHL basic scientist who had already published many papers helping to identify the molecular players involved the control of cell division, reported the discovery of yet another factor, which he called Cyclin D. This discovery coincided with the same finding by former CSHL Trustee Charles Scherr of St. Jude’s Children’s Hospital, who went on to discover the protein kinase CDK4, which forms a complex with Cyclin D. It soon became clear from the work of Beach and Scherr that the Cyclin D-CDK4 complex is a critical node in the fundamental decision of whether a cell keeps dividing or rests from proliferation. Importantly, it became apparent that most cancer cells have mutations in this control pathway, thereby pushing tumor cells on the road to unchecked growth and aggressive cancer.

What is poignant about the 2015 approval of Ibrance is the fact that it came a quarter-century after the fundamental discoveries by Beach and Scherr. In the early 1990s, we simply did not know enough about cancer to convert their newly generated knowledge into an effective anticancer drug. Now we do. Another basic research discovery at CSHL, this one quite recent, makes the point about our progress vividly, suggesting why the time is ripe for a clinical alliance that enhances our ability to promptly take our basic insights into the clinic. In 2011, Christopher Vakoc, Scott Lowe and CSHL colleagues performed a screen using RNA interference (RNAi) technology developed at CSHL by Gregory Hannon and his team. The 2011 discovery, which Vakoc has carried forward, revealed a drug target—a protein called BRD4—of unusual potential in the treatment of aggressive forms of leukemia called acute myeloid leukemia (AML). Vakoc discovered that a drug—developed for another purpose by collaborating scientists at the Dana Farber Institute—hit the target, virtually eliminating AML in mouse models. These studies induced a number of pharmaceutical and biotech companies to initiate clinical trials that target AML, some of which are now in Phase II, with positive results already reported from Phase I studies. This is precisely the kind of rapid translation of an important basic scientific result that our new alliance with Northwell Health and its vast clinical system is designed to facilitate. It will enable us to pursue translational science with a vigor we otherwise could not while keeping our basic discovery engine primed.

Two of our faculty are now reaping the rewards of decades of meticulous basic research. Adrian Krainer’s research on RNA splicing—which began in the 1990s and grew out of earlier Nobel Prize-winning work by Louise Chow and Richard Roberts at CSHL and by Sue Berget at MIT—has made possible the development of a drug, now in Phase III trials, for the serious...
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children’s disease, spinal muscular atrophy (SMA). Nicholas Tonks’ fundamental discovery 25 years ago of the first of what proved a large family of enzymes called protein tyrosine phosphatases (PTPs) was the beginning of a scientific odyssey in which Nick has persisted in the face of doubters in the pharmaceutical industry. Tonks’ team has recently demonstrated their ability to target PTP1B—with a drug Nick developed years ago—in cellular signaling pathways that play a key role in HER2-positive breast cancer. Phase I trials will begin at Northwell in the spring of 2016. Other PTP1B-targeting compounds in Tonks’ lab are being evaluated by a major pharmaceutical firm for treatment of diabetes and obesity. It’s another illustration of how basic science can pay off in ways that are not contemplated at the outset. We see similar promise in other fields: for instance, in Zachary Lippman’s basic research on the process of branching morphogenesis in plants, which now points to a way of significantly increasing fruit yields; and in Steven Shea’s fundamental research on social behavior in rodents, which has led to unexpected insights into Rett syndrome, an autism spectrum disorder.

Basic research has made all of these opportunities possible. To keep our discovery science robust, we were pleased this past year to have been asked to join the ranks of select institutions named as beneficiaries of the Scientific Philanthropy Alliance. The SPA serves as an impartial advisor to major philanthropists, promoting basic research as the driver of new ideas, of new economic wealth and for the education of a new generation of talented new scientists. Several benefactors of the Laboratory organized the SPA, which we thank for providing another line of support for the basic research that is the lifeblood of Cold Spring Harbor Laboratory.