Winter 2017

HIGHLIGHTS

FOR DONORS

LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

someday is today®

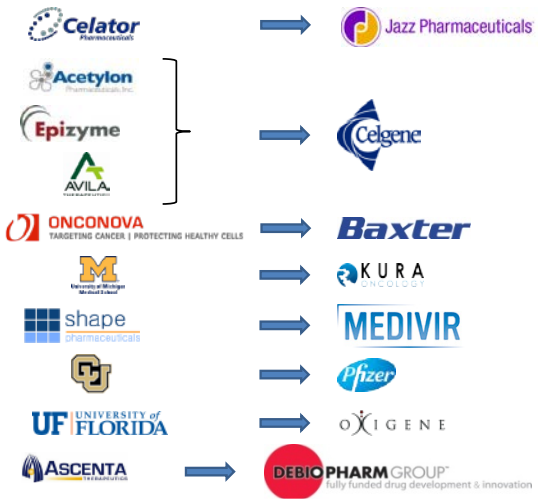
Progress happens when smart money and smart research meet. The Leukemia & Lymphoma Society (LLS) values the generosity of donors who make life-saving advances possible.

TAP Turns Ten

In March 2007, LLS convened the initial committee meeting for the Therapy Acceleration Program. TAP, as it is known, was created to bridge the gap between scientific discovery and product development. It does so by supporting late-stage pre-clinical and early phase clinical trials to determine proof of concept in humans. The goal is to encourage further investment by large pharmaceutical companies and create attractive opportunities for commercial development.

TAP identifies promising projects for near-term development from the extensive pipeline of LLS grants (through the Academic Concierge) and in partnership with commercial enterprises that have diagnostics or treatments with potential application in blood cancers (the Biotechnology Accelerator). Over the past decade, LLS has invested more than $100 million in 50 projects. As a validation of the program's success, eight pharmaceutical companies invested an additional $700 million to push TAP projects closer to the finish line as new therapies to patients.

TAP Bridges the Gap



Starving AML Cells

Researchers at MD Anderson Cancer Center in Houston developed a new drug to interfere with the machinery that supplies energy to cells. They look to use it to starve cells that are cancerous. The new drug, IACS-10759, will be tested in patients with acute myeloid leukemia (AML) who have relapsed or are resistant to therapies. The LLS Therapy Acceleration Program is supporting this first-in-man clinical trial.

At the basis of the investigation is the understanding that all cells rely on two processes to generate energy: glycolysis and oxidative phosphorylation (OXPHOS). Normal cells predominantly use glycolysis for energy; some slow-growing, cancer-initiating cells rely mainly on OXPHOS. If that process is inhibited, normal cells can turn up the glycolysis but cancer cells cannot. Therefore, based on promising preclinical data, inhibiting OXPHOS should selectively kill AML tumors and AML stem cells. This is important because AML stem cells are thought to be the source of disease relapse that are untreatable with today's approved drugs.

The trials will enroll up to 48 patients to determine the drug's safety and tolerability and establish the recommended dose for future trials. They will also evaluate how the drug is absorbed and metabolized (a type of study known as pharmacokinetics); and how it interacts with target tissues (pharmacodynamics); and how it affects patient survival.

This promising drug could warrant further investigation because the team has identified other groups of hematological malignancies and solid cancers that could also be vulnerable to OXPHOS inhibition.

LLS Values Basic Research

In 1960, researchers discovered the first genetic defect proven to cause cancer. They observed an abnormally short chromosome in white blood cells in patients with chronic myeloid leukemia. Decades later, the so-called Philadelphia chromosome led to the development of Gleevec.

"LLS . . . has groomed a remarkable generation of scientists and physician scientists who have led the extraordinary advances in treating hematologic malignancies."

Gary Gilliland, MD, PhD
President, Fred Hutchison Comprehensive Cancer Center

History shows that basic discoveries got us to where we are today. This is why, even with great promise of collaborative, multidisciplinary research, there is always a need for basic molecular research, the open-ended work meant to satisfy scientific curiosity.

Career Development grants are the longest running of LLS programs. First awarded in 1953, these grants attract and retain the highest quality young scientists to blood cancer research by providing salary support to promising postdocs and junior faculty members at a critical time in their career. It has launched careers of many of the most productive clinicians and researchers in cancer, including three Nobel Laureates and nine directors of Comprehensive Cancer Centers.

"LLS is unique in their identification and promotion of the next generation of investigators devoted to increased understanding and better treatment of these diseases. I am extremely grateful for their early support of our work and our continued partnership."

Margret Shipp, MD
Professor of Medicine, Harvard & Director of Lymphoma, Dana-Farber Cancer Institute

Broad Questions Can Have Profound Consequences

Recipients of LLS Career Development grants address broad scientific questions. Benjamin Ebert, MD, PhD, at Brigham and Women's Hospital in Boston, is studying gene mutations that cause malignancies such as myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). His basic research could lead to clinical significance because it could potentially predict whether a patient is likely to have a good outcome with a stem cell transplant, an option that has a high rate of subsequent therapy-related tumors.

Hematologic malignancies have been presumed to be a consequence of aggregate DNA damage. As cells divide, they pass along small mutations that have no obvious function. The lifetime accumulation of such mutations are associated with increased risks of blood cancer. This age-related condition is known as clonal hematopoiesis of indeterminate potential (CHIP).

Dr. Ebert hypothesized that in patients undergoing autologous stem cell transplantation, CHIP would be associated with an increased risk of MDS and AML. He sequenced all the genes in a small sample of lymphoma patients who developed secondary malignancies following transplant and found that CHIP was common at the time of transplant. Then he performed targeted sequencing in samples from hundreds of lymphoma patients who had undergone transplants and learned that certain mutations were found at low levels years before the subsequent malignancy developed. Patients with more than one mutation had a particularly elevated risk.

In studying five- and ten-year overall survival, Dr. Ebert determined that patients with CHIP at the time of transplant had significantly inferior survival compared with those without the mutations (59.9% vs. 72.4% at five years; 30.4% vs. 60.9% at ten years).

As a result of this research, what began as a larger question of scientific curiosity could potentially lead to a test to stratify newly diagnosed lymphoma patients so that alternatives to autologous transplant can be explored.

The PATh to Improved Therapies

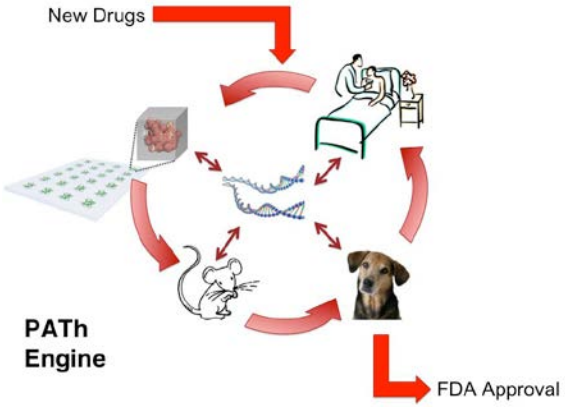
New drugs are supposed to hit specific targets but evaluating their activity is daunting. There are many possible dose schedules and combinations of agents with different pharmacological properties. Mouse models do not always correlate with human studies and mutations often fail to accurately identify which patients to treat with a given drug.

To identify patients most likely to respond to therapy, develop new therapies and understand the pathways that govern the growth of B-cell lymphomas, LLS committed $2 million to a new partnership with Weil Cornell Medical College in collaboration with Cornell University College of Veterinary Medicine and the Methodist Hospital of Houston. A team of scientists and clinicians led by Ari Melnick, MD, and John Leonard, MD, will use new, superior models of human lymphomas.

Cornell scientists and engineers developed an innovative modeling platform called "Progressive Assessment of Therapeutics" (PATh). Its three-dimensional tissue culture systems better mimic the environment in which cancer cells grow and allow hundreds of tests to be done simultaneously to leverage automation to quickly assess the activity of thousands of treatments.

From these assays, the best therapies will be tested in mice and in pet dogs that have already been diagnosed with lymphomas, which are the most frequent tumors found in dogs and similar to their human counterparts. These canine co-clinical trials will increase the number of trial participants and the robustness of findings if a drug is effective in more than one species.

This project has the potential to improve the efficiency of the experimental therapeutics pipeline and develop easily monitored markers to predict treatment outcomes. Such a precision medicine approach will improve treatment outcomes for lymphoma patients.



Collaborators Seek New Immunotherapies for Lymphoma

Nearly half of all patients with diffuse large B cell lymphoma (DLBCL) who are treated with the current standard of care stop responding and experience disease progression or relapse. Spurred by the finding that activating a patient's immune cells can induce clinical responses, even in refractory DLBCL patients, LLS is investing $5 million to develop advanced immunotherapies for these patients.

A collaborative team led by Anas Younes, MD, at Memorial Sloan Kettering Cancer Center, is working on a second generation of chimeric antigen receptors (CAR-T), an approach in which immune T cells are extracted from a patient and engineered to sharpen their ability to spot cancer. The modified cells target CD19, a protein found on many B cell cancers, proliferate and kill the tumor. This shows great promise for patients with acute lymphoblastic leukemia but results in DLBCL patients have been more modest.

One hypothesis is that the DLBCL microenvironment inhibits T cell receptors. The researchers are exploring how to design cells that secrete antibodies to modulate the microenvironment and reactivate the tumor response. They also look to enhance T cell effectiveness by adding a co-stimulator to the current stimulation mechanism.

The role of a certain receptor is also being studied. The researchers speculate that tumor differences contribute to the effectiveness of immune activation and they will use a genetic screen to determine what regulates interactions between T cells and tumors.

They will also follow up on a recent observation that DLBCL frequently lacks a set of cell surface proteins (known as MHC) that help T cells to recognize a tumor. This investigation will determine why natural killer immune cells, which can target cells that lack MHC proteins, fail to eliminate tumors.

It is highly likely that these integrated projects will lead to clinical trials.

Taking it to Church: Enhancing Access to Myeloma Treatments

Myeloma is a relatively rare blood cancer that is twice as likely to be found in black people as in white people. Survival rates for white myeloma patients have improved much more than for black patients, in part due to delays in treatment and unequal access to therapies and stem cell transplantation. Lower-income people are particularly vulnerable to these disparities.

The Leukemia & Lymphoma Society (LLS) is collaborating with the National Black Church Initiative (NBCI) to improve survival rates in African Americans. The partnership will receive support from a 2016 Celgene Innovation Impact Award.

NBCI is a faith-based coalition of 34,000 churches comprised of 15 denominations and 15.7 million African Americans that works with major organizations to reduce healthcare disparities. Because families often turn to their pastors for information, support, and advice, health promotion efforts through churches offer great potential to improve health outcomes in black communities.

This program aims to heighten awareness of myeloma, provide resources and educate the community on treatments and the value of participating in clinical trials, and offer patients and caregivers a sustainable support system. The 18-month initiative will be piloted in two markets, Atlanta, GA and Washington, D.C. and will launch in March, which is Myeloma Awareness Month.

Together, LLS and NBCI will implement six intervention components in both cities.

1. Networks of Myeloma Ambassadors—myeloma patients or caregivers trained to reach out with support and information;
2. Myeloma Sundays during Sunday worship at select key churches. These will include myeloma-focused "health sermons" given collaboratively by a pastor and a local healthcare provider. The church's Fellowship Hour will feature LLS staff and Ambassadors to provide information about medical, psychosocial and financial resources;
3. In-depth education programs led by healthcare providers;
4. Church-based myeloma support groups facilitated by trained professionals;
5. A directory of resources and cancer centers for each area;
6. Connections to LLS Information Specialists who will assist with understanding treatment options, financial resources and clinical trial enrollment.

The measures of effectiveness will include post-Myeloma Sunday surveys, attendance at education programs, the number of support groups formed, tracking the use of Ambassadors and calls for LLS Co-Payment Assistance and Information Specialists. LLS will hire local staff in metro Atlanta and the District of Columbia to collaborate with pastors and community members, specifically with churches and residents in lower-income neighborhoods.

This program is the first collaboration in the country between churches and a major health advocacy organization that systematically works through churches to heighten awareness of myeloma and create ongoing, personalized connections with myeloma patients and caregivers. It will increase access to specialized care and improve quality of life.

I support LLS because...

. . . I like to write stories about hope.

Merging onto the highway this morning on my way to the office, a familiar door-bell ring on my phone signaled an incoming text message. I resisted the urge to fetch the phone from my pocket and waited 20 minutes until I arrived at the office. The message was short: "Sad news. Alan died."

What began as a day "at work" became something more. A day with purpose. Alan's mother-in-law is a neighbor and friend who has shared with me the lows of his 10-year blood cancer struggle and the high of his becoming a father last month. Tales of woe and of wonder are not uncommon to me. I've worked at LLS for 11 years and write the newsletter of amazing science and hopeful individuals that you are reading now. The stories never stop amazing me. Sadly, some end like Alan's. Others, perhaps yours, are still being written. And that's why I give. - *Rich Schneyer, New York*

To support research in the area of greatest concern to you, contact us at 1-888-773-9958.