SU2C TOP SCIENCE ACCOMPLISHMENTS

INTRODUCTION

Since our founding in 2008, Stand Up To Cancer has funded 101 team science projects, with budgets of up to $22 million to support large networks of researchers focusing on determining if new treatments or drug combinations are useful against different types of cancer. We've also provided research grants to 48 individual researchers to test cutting-edge approaches that might not get funded under traditional mechanisms. All of the funded projects are expected to bring new and better treatments to people with cancer as fast as possible. We do this through intense competitions for funding, innovative collaborations with industry when appropriate, and vigorous ongoing scientific review over the life of each grant.

Over 1,600 scientists have been engaged in all forms of translational research on behalf of new treatments for cancer, and over 12,000 patients have participated in SU2C-funded clinical trials. Over $603 million has been pledged to support this work. And the results have been exceptional.

SU2C research has contributed to the FDA approval of six new cancer therapies, including treatments for breast, ovarian and pancreatic cancers and difficult-to-treat leukemia. Additionally, SU2C-supported research has led to FDA Breakthrough Designation Status being awarded for combination treatments in colon and prostate cancers. Promising trial results have been submitted to the FDA or are nearing completion for colon, lung, and ovarian cancers and for metastatic melanoma. We've provided significant funding for the science of immunotherapy, in which the body's own immune system is engaged to fight cancers. And technologies using blood tests to identify cancers early, imaging cancers to understand tumor progression, and new laboratory tools to target drug discovery and precision medicine have been advanced. Below are short descriptions of many of these accomplishments.

There will be more advances to come as our current research projects continue their work and new teams are launched. In the coming years, Stand Up To Cancer will continue to bring new hope, and better approaches to the prevention, diagnosis, and treatment of cancer, to people everywhere.

ACCOMPLISHMENT #1 - PANCREATIC CANCER: FIRST NEW FIRST-LINE TREATMENT APPROVED IN 15 YEARS

Gemcitabine Plus Abraxane for Pancreatic Cancer

Based on work by the SU2C Pancreatic Cancer Dream Team, the FDA in September 2013 approved a new combination of drugs that enables longer survival in patients with advanced pancreatic cancer. This was the first approval for a first-line pancreatic cancer treatment in 15 years. The researchers also developed a new method of identifying pancreatic tumors that have spread to the brain and liver, which could significantly aid in diagnosis. Finally, after many long years, we are beginning to be able to provide the nearly 56,700 people diagnosed each year with pancreatic cancer with a menu of treatment options and promise.

ACCOMPLISHMENT #2 - BREAST CANCER: IBRANCE TARGETS A NEW MOLECULAR PATHWAY TO THWART DISEASE

Ibrance for Breast Cancer

In February 2015 the FDA granted accelerated approval to Ibrance (aka palbociclib from Pfizer) to treat advanced breast cancer after the SU2C Breast Cancer Dream Team showed dramatically increased survival in women taking it. This approval is intended for postmenopausal women with estrogen receptor (ER)–positive, human epidermal growth factor receptor 2 (HER2)–negative metastatic breast cancer who have not yet received an endocrine-based therapy. It is to be used in combination with letrozole, another FDA-approved product used to treat certain kinds of breast cancer in postmenopausal women. This approval was a first-in-class CDK4/6 inhibitor approval by the FDA. It improved treatment options for women with metastatic disease, as Ibrance is approved in the first-line setting when combined with letrozole. Of the over 271,000 people, mostly women, diagnosed with breast cancer each year, at least 187,000 are expected to have the kind of cancer that will be helped by this discovery.

ACCOMPLISHMENT #3 - OVARIAN CANCER: NEW DRUG PROVIDES ONE-TWO PUNCH, TARGETS TWO PATHWAYS BY WHICH CANCER GROWS

Rucaparib for Ovarian Cancer

In December 2016, the FDA granted accelerated approval to a new drug, rucaparib (or Rubraca from Clovis Oncology) to treat women with BRCA1/2 mutated ovarian cancer, making it only the second PARP inhibitor to gain approval. The approval was based in part on data from a study conducted by the SU2C Ovarian Cancer Research Fund Alliance–National Ovarian Cancer Coalition Ovarian Cancer Dream Team, among others. This treatment is for Ovarian Cancer patients with mutated BRCA1/2 who may or may not be resistant to chemotherapy, approximately 4,000 of the over 22,500 cases of ovarian cancer diagnosed annually in the United States.

ACCOMPLISHMENT #4 - ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN AND YOUNG ADULTS: FIRST-OF-ITS-KIND THERAPY THAT TRAINS PATIENT'S IMMUNE CELLS TO ELIMINATE CANCER

CAR-T and CRS for Pediatric Cancer

Two related FDA approvals are helping cancer patients with acute lymphoblastic leukemia. First, the chimeric antigen receptor T-cell (CAR-T) therapy Kymriah™ (tisagenlecleucel), from Novartis, was approved by the FDA in September 2017 for the treatment of relapsed or refractory leukemia in children and young adults. SU2C–St. Baldrick's Foundation Pediatric Cancer Dream Team scientists helped carry out the preliminary clinical work that led to the conclusive trial for this first-of-its-kind therapy that trains a patient's immune cells to eliminate cancer. The FDA also approved a new treatment to manage severe cytokine release syndrome (CRS), the "cytokine storm" that affects some patients. SU2C-supported scientists identified biomarkers that can help predict which patients receiving T-cell therapy will encounter CRS. The biomarkers will help guide management of the patient and mitigate the effects of CRS. In the United States, this new therapy should help about 400 relapsed or refractory (R/R) B-cell acute lymphoblastic leukemia patients per year.

ACCOMPLISHMENT #5 - PROSTATE CANCER: PERSONALIZED MEDICINE REVEALS STRATEGIES TO REPAIR DAMAGED DNA IN SOME MEN WITH METASTATIC CANCER

DNA Repair for BRCA1/BRCA2 Prostate Cancer

In 2016, an FDA Breakthrough Therapy Designation was granted for use of the monotherapy PARP inhibitor olaparib in metastatic castration resistant prostate cancer. The drug had been approved two years earlier for treating certain types of ovarian cancer, and research by the SU2C–Prostate Cancer Foundation Prostate Cancer Dream Team had uncovered similar genetic mutations might be used to treat their target disease. The FDA decision was based on the TOPARP-A clinical trial results obtained by the Dream Team. As a result of the Team's findings that men with BRCA mutant prostate cancer responded to olaparib, men with metastatic prostate cancer are recommended to have their DNA sequenced as they could be candidates for this targeted therapy. Since this finding, additional clinical trials have been opened to explore the use of PARP inhibitors in cancer types exhibiting DNA repair deficiencies. Over 176,600 men are diagnosed with prostate cancer each year in the United States, and up to one-third may be eligible for this treatment.

ACCOMPLISHMENT #6 - BREAST, OVARIAN CANCERS: TREATMENT STRATEGY SEEKS TO INCREASE EFFECTIVENESS OF TARGETED THERAPIES FOR WOMEN WITH "TRIPLE NEGATIVE" CANCERS

Olaparib Plus PI3K Inhibitor for Breast and Ovarian Cancers

Currently, doctors lack effective treatment options for the subtype of breast cancers known as "triple negative" breast cancer, which accounts for about 20% of new breast cancer diagnoses each year. Starting in 2015, SU2C-funded scientists have tested a new combination of experimental treatments for these cancers. The combination involves a PARP inhibitor which turns off one of the cell's DNA-repair mechanisms and helps halt future growth of the cancerous cell. The second agent is PI3K inhibitor, which shuts down a kinase that broadly stimulates cell growth. Together, a dramatic synergistic response has been observed, and scientists are working to understand why. It seems that the PI3K inhibitor makes the cells more sensitive to the PARP inhibitor. Clinical trials to further refine this discovery are underway, and by 2019 we will know if a new treatment can be widely tested for triple-negative breast cancer.

ACCOMPLISHMENT #7 - METASTATIC MELANOMA: DOUBLE-TRACK THERAPY WORKS TO BOLSTER THE IMMUNE SYSTEM TO FORTIFY CANCER-FIGHTING CELLS AND PREVENT RECURRENCE

Checkpoint Inhibitor Plus Adoptive Cell Therapy

Melanoma cells, like most cancer cells, are able to impersonate normal cells and therefore are not identified by the body's immune system. Melanoma cells with a BRAF gene mutation are also able to turn off the immune system's response and keep growing. Once it starts spreading, melanoma acts aggressively and can often move to the brain. Science does not yet have treatments for many mutations that drive melanoma. To get around this lack of treatments, SU2C researchers are focused on both helping the immune system recognize melanoma cancer cells and stopping those cells from turning off the immune system. In doing so, they have developed a treatment that, for the first time, administers two types of immunotherapy simultaneously to control cancer. First, adoptive cell therapy teaches the immune system to recognize the cancer cells as a foreign invader, but the cancer can quickly adapt itself to avoid detection. The addition of a second immunotherapy, called IPI (for ipilimumab), uses antibodies to block the action of protein receptors that can stop the immune system's work. The combined effects of the two therapies seem to be enough to eliminate the cancer. Further testing of the concept is being supported by SU2C.

ACCOMPLISHMENT #8 - COLON CANCER: STRATEGY TO DELAY TREATMENT RESISTANCE PROVIDES MORE OPTIONS FOR PATIENTS

Colon Cancer

By analyzing the DNA and biological makeup of patients' tumors, the SU2C–Dutch Cancer Society Personalized Treatment Translational Team discovered a new multi-drug combination that is effective in clinical trials in KRAS-mutated cancer, a type of colon cancer which is found in up to 15% of colon cancer patients. It may become a new standard of care for this disease. In this hard-to-treat cancer, the tumor uses several mechanisms to replicate, and the combination of mechanisms also gives the cancer the ability to generate resistance to treatment. Now, a new combination of drugs has been devised that first targets a mutant BRAF kinase within the tumor cell, turning it off and preventing replication and growth. Another drug in the combination therapy turns off tumor replication occurring via PI3K, a pathway that regulates the growth of the cell, allowing the drug to remain effective in the body longer. The FDA awarded a Breakthrough Therapy Designation in June 2018, an expedited process for drug development, for the Braftovi-Mektovi-Cetuximab combination to be used for the treatment of BRAF V600E-Mutant Metastatic Colorectal Cancer.

ACCOMPLISHMENT #9 - IDENTIFYING CANCER EARLY: BLOOD TESTS FOR CANCER DNA OPEN UP NOVEL TREATMENT AVENUES

Using Blood Tests to Find Cancer

Because cancer treatments work best on newer cancers, medical science is continually seeking ways to detect cancers early so they can be treated most effectively. A key investigative strategy has been pushed forward based on the fact that evidence of many cancers can be found in the blood. A 2009 Dream Team successfully designed a physical chip to identify tumor cells that had left the tumor and were circulating in the blood. A 2015 Dream Team took advantage of the fact that cancers shed DNA as they proliferate to show that it is possible to detect "circulating DNA" earlier than cancer can be identified using CT scans, the current preferred therapeutic tool. Preliminary work, variously using blood and stool samples, has been published in major journals, and the teams are extending and refining the approaches. Once ready for widespread use, such an approach will be helpful in three scenarios: First, it will be used as a test when cancer is suspected but not diagnosed. Second, it will be a noninvasive screening tool for people with a genetic or familial history of cancer. And third, circulating DNA assays should be very helpful in watching for the recurrence of cancer in people who have already received treatment. Detecting those returning cancers earlier will likely vastly improve treatment options. Finally, our Interception projects are looking to extend this concept.

ACCOMPLISHMENT #10 - ORGANOIDS: A NEW RESEARCH TOOL IS DEVELOPED FOR TARGETED DRUG DISCOVERY AND PERSONALIZED MEDICINE IN CANCERS

Organoids

Scientists and medical doctors both, for different reasons, need to be able to grow cancers in laboratory settings to test new therapies and determine which drugs might work best for a particular patient. Recent breakthroughs in isolating diseased cells and growing them in the lab is making this possible, and SU2C has been at the forefront of bringing the new technology to the study and treatment of cancer. Organoids are miniature cellular systems, created from a person's own tissues, that allow scientists to understand and study disease progression in a realistic setting. This allows scientists to quickly observe how new treatments affect not only the tumor cells, but also the surrounding tissue that supports cancer growth. This powerful system more closely mimics the real-life situation, avoiding the false positives and other pitfalls associated with animal tissue samples or other laboratory techniques. Organoids can be used to test targeted therapies, combinations of drugs, and methods for detecting cancers in humans. SU2C grantees are working to make this possible in breast, colon, pancreatic, and esophageal cancers.

ACCOMPLISHMENT #11 - IMAGING CANCER: HOW CELLS "EAT" SUGAR SHEDS LIGHT ON TUMOR PROGRESSION AND CANCER DETECTION

^{18}Fluoroglutamine Imaging Technique

In order to perform their work and to replicate, most cells in the body rely on glucose as their primary energy source, but there are a number of other sugars and amino acids that circulate in the bloodstream for cells to ingest for fuel. Some tumors use glutamine as their energy source, which offers scientists an intriguing new way to see and measure the progress of cancer cells once they have been located. SU2C-supported researchers have created a "tagged" dye version of glutamine that can be seen on scanners after a cell absorbs it. This provides for better imaging of tumors. As a result, some cancers that are notoriously difficult to measure can receive a detailed confirmatory diagnostic, for instance when a patient is being investigated for possible pancreatic cancer after an MRI shows a shadow on the pancreas. Originally developed for better imaging of pancreatic cancers, the technique also shows promise in measuring and monitoring the progress of some brain cancers. If the technology can be developed for widespread use, it will allow doctors to detect the spread of cancers in the body, measure responses to treatment, determine when new medicines are needed, and reduce the reliance on expensive and complicated PET scanning for patients with cancer.