Message From the Chief Executive Officer, Geoffrey Beene Foundation
October 1, 2014

In 2006, my collaboration with then president Harold Varmus led to the creation of the Geoffrey Beene Cancer Research Center at Memorial Sloan Kettering Cancer Center and gave us the opportunity to focus on accelerated funding for initial-stage research. The remarkable progress that has been made at the Geoffrey Beene Cancer Research Center over the past several years has been a great accomplishment for everyone involved. You are all to be congratulated on your shared research vision made possible by your expertise, passion, and dedication to end suffering across all cancers.

I am pleased to report that as of the date of this letter the total value of combined funding to the Geoffrey Beene Cancer Research Center, from the Geoffrey Beene Foundation and Geoffrey Beene, LLC, now exceeds $138 million since its creation. In addition, I am advised that for every dollar awarded by the Geoffrey Beene Cancer Research Center, grant recipients have received an additional $1.64 in follow-up funding. This equates to a 64% return on the investment on these innovative research initiatives, directly attributed to funding from Geoffrey Beene.

I want to acknowledge the most recent additions to the Geoffrey Beene Cancer Research Center Executive Committee: José Baselga, M.D., Ph.D., Scott Armstrong M.D., Ph.D., and Alexander Rudensky, Ph.D. I thank each of the members of our Executive Committee for overseeing the work of the Geoffrey Beene Cancer Research Center.

As of December 31, 2013, 74 research grants have been awarded and 10 proposals for shared resources have been funded. Each grant funds initial-stage research and is renewed for a second year. As of July 31, 2014, 86 research grants have been awarded and 12 proposals for shared resources have been funded. Check out geoffreybeene.com/cancer-research-center to see some of the remarkable research results.

In 2011 Ping Chi, M.D., Ph.D. was appointed as a Junior Chair and in 2012 Kitai Kim, Ph.D. was appointed as a Junior Chair. In 2013 David Solit, M.D. was appointed as a Senior Chair and in 2014 Joseph Sun was appointed as a Junior Chair. Congratulations to you all!

The annual Geoffrey Beene Cancer Research Center Retreats showcased outstanding presentations which are a tribute to the dedication of our scientists, doctors and lab members who continue to stimulate discussion and collaboration among researchers. The annual Geoffrey Beene Cancer Research Center Symposums are a day of inspiration which invite world-renowned guest speakers.

In 2012 and 2013 the Geoffrey Beene Foundation continued its Rock Stars of Science® campaign by featuring the work of the Geoffrey Beene Cancer Research Center. In helping the Geoffrey Beene Foundation to excite the next generation about careers in science, this nationally recognized campaign continues to draw attention to the problem of scientific illiteracy in the United States and urges increased funding for medical research. “The kind of science we’re talking about isn’t reading the text book, it’s writing the next one” said Scott Lowe, M.D. in the “Rock Stars of Science™” campaign who appeared along with Craig Thompson, M.D., Larry Norton, M.D., Johanna Joyce, Ph.D., Andrea Ventura, M.D., Ph.D., Ping Chi, M.D., Ph.D., along with Ellen Hukkelhoven, Ph.D., Lukas Dow, Ph.D. and Neha Bhagwat, Ph.D., who helped us celebrate the ground breaking revolutionary research across all cancers. Look for the Rock Stars of Science® Public Service Announcements at airports, malls or on the street and take a picture and post it to the Geoffrey Beene and Rock Stars of Science® Facebook pages.

I thank each of you for your continued dedication and for your lifesaving work!

Very truly yours,

G. Thompson Hutton
CEO & Trustee, Geoffrey Beene Foundation
President and CEO, Geoffrey Beene, LLC
Annual Events

Geoffrey Beene Retreat

The Geoffrey Beene Cancer Research Center sponsors a two day retreat every spring. The 2012 and 2013 retreat hosted more than 200 lab trainees, senior leadership, and clinicians from the Sloan Kettering Institute's Cancer Biology and Genetics Program (CBG), Memorial Hospital's Human Oncology and Pathogenesis Program (HOPP), and faculty members across MSKCC. The annual retreat provides a forum for collaboration amongst the various members across the MSKCC community. The poster session is a highlight of the retreat where trainees are given the chance to present their work to faculty members, senior leaders, and their peers. This highly anticipated event focuses on various topics and provides opportunity for participants to share new and innovative activities happening across their MSK community.

During the 2012 retreat William Sellers, Vice President and Global Head of Oncology at the Novartis Institute of Biomedical Research presented on the opportunities and challenges presented when studying the genetic basis of cancer therapy.

During the 2013 retreat Stephen Elledge, Professor in the Department of Genetics at Harvard Medical School gave a presentation, "When half is simply not good enough: Happloinsufficiency in Cancer".

Symposium

The Geoffrey Beene Cancer Research Center sponsors a cancer symposium that is open to the cancer research community and the public. The annual symposium invites guest speakers centered around topics chosen by the GBGRC Executive Committee.

2012 GBCRC Symposium topic was "Cancer Heterogeneity". Invited speakers were Sean Morrison, PhD, Charles Swanton, MD, PhD, Jeffrey Settleman, PhD.

2013 GBCRC Symposium topic was "New Approaches to Targeted Therapy". Invited speakers were Martin Nowak, PhD, Robert Schlegel, PhD, and Louis Staudt, MD, PhD. The Geoffrey Beene Cancer Research Center sponsors a cancer symposium that is open to the cancer research community and the public. The annual symposium invites guest speakers centered around topics chosen by the GBGRC Executive Committee.
Investigator Grant Recipients

2012

Timothy Chan, MD, PhD
The Mutational Landscapes underlying Tumor Aggres-
siveness in Adenoid Cystic Carcinoma

James Hsieh, MD, PhD
Genetic Basis of mTOR Treatment Response and Its Impli-
cation in Kidney Cancer

Alexandra Joyner, PhD
Role of Reciprocal Epithelial-
Stromal Signaling Elicited by Hedgehog-GLI Signaling in Prostate Cancer

Mithat Gönen, PhD
Integrated Genetic Profil-
ing to Predict Response to Therapy in Acute Myeloid Leukemia

Christopher Park, MD, PhD
Targeting CD99 in Leukemic Stem Cells in Acute Myeloid Leukemia

2013

Omar Abdel-Wahab, MD
Somatic genetic alterations in the pathogenesis and therapy of histiocytic disorders

Yu Chen, MD, PhD
Generation of personalized models of prostate cancer for correlates of disease response and progression

Nai-Kong Cheung, MD, PhD
Bispecific antibody to engage T cells for cancer therapy

Ping Chi, MD, PhD
Clinically targeting ETV1 in advanced gastrointestinal stromal tumor (GIST)

Filippo Giancotti, MD, PhD
Inactivation of neogenin in castration-resistant prostate cancer

Morgan Huse, PhD
Quantitative approaches for the mechanistic analysis of tumor cell killing by cytotoxic lymphocytes

Raajit Rampal, MD, PhD
Combined JAK2/HSP90 inhibition in primary myelofibrosis, post-essential thrombocytopenia myelofibrosis, and post-polycy-
themia vera myelofibrosis

Joseph Sun, PhD
Investigating the role of transcription factor Zbtb32 in the NK cell response against tumor establishment and metastasis

Wolfgang Weber, MD
Theranostics of neuroendocrine tumors with somatostatin antagonists
Special Highlights

Jason Lewis, PhD

Of the 1 million people each year who develop metastatic esophagogastri
cric (EG) cancer worldwide, an estimated 200,000 will have tumors that
harbor ERBB2 (HER2) gene amplification and/or oncoprotein overex-
pression. Trastuzumab, an FDA approved monoclonal antibody that
binds to the extracellular domain of HER2, is the standard of care for pa-
tients. However, after an initial response secondary resistance invari-
brably ensues. The molecular basis of trastuzumab resistance in esophagogastric
cancer remains unknown and until now, no other HER2-directed therapy
has shown clinical efficacy in these patients. Drs. Jason Lewis, Yelena
Janjigian and Jorge Carrasquillo are developing functional PET imaging
techniques to help understand mechanisms of trastuzumab resistance,
to help stage and monitor treatment response in esophagogastric cancer.
Heterogeneity of HER2 expression within primary tumors and metas-
tasis is a particular challenge and may contribute to trastuzumab resistance.
Moreover, the biodistribution of trastuzumab varies in each patient and is
heavily impacted by the extent of tumor load, which may contribute to
variations in patient responses. 89Zr-trastuzumab PET may thus help elucidate
the molecular basis of resistance to trastuzumab in esophagogastric cancer.

Dr. Lewis was awarded a Beene grant in 2008 “Zirconium-89 labeled antibodies for immunoPET” to establish
Zr-89 as a PET radionuclide at MSK. This grant established the technology that has now advanced into 4 clini-
cal trials at MSKCC including a Phase I clinical study of 89Zr-trastuzumab PET in patients with HER2-positive
esophagogastric cancer. In preliminary studies at MSKCC, 89Zr-trastuzumab PET provided excellent tumor
visualization in patients with HER2-positive esophagogastric cancer. In light of the promising preclinical
and clinical activity of afatinib, a pan-HER kinase inhibitor, a phase 2 study of afatinib in trastuzumab-refractory
ERBB2-amplified EG cancer is accruing patients at MSKCC. In preliminary studies at MSKCC, 89Zr-trastuzumab PET
provided excellent tumor visualization in patients with HER2-positive esophagogastric cancer. In light of the promising preclinical
and clinical activity of afatinib, a pan-HER kinase inhibitor, a phase 2 study of afatinib in trastuzumab-refractory
ERBB2-amplified EG cancer is accruing patients at MSKCC. In preliminary studies at MSKCC, 89Zr-trastuzumab PET
data demonstrate that 89Zr-trastuzumab but not FGDG-PET can accurately and non-invasively quantitate changes in HER2 expression and tumor size in
HER2-positive esophagogastric cancer treated with afatinib. This work spurred a second Beene grant funded to
Dr. Lewis in 2011 on the “Development of 89Zr-5A10 for the measurement of AR signaling in advanced prostate
cancer with positron emission tomography.”

Tim Chan, MD, PhD

Dr. Chan is a physician scientist and the principal investigator of a cancer genetics
laboratory at the Memorial Sloan-Kettering Cancer Center. He is also Vice Chair
of the Dept. of Radiation Oncology. Dr. Chan’s laboratory focuses on utilizing
genome-wide strategies to elucidate the molecular details of oncogenesis. The goal
of this work is to use this information to understand the underpinnings of these
tumors and to develop new therapeutic modalities.

Can you please provide a summary of your Geoffrey Beene Cancer Research
Center sponsored project?
Title: The mutational landscapes underlying aggressiveness in adenoid cystic carci-
noma
Adenoid cystic carcinoma (ACC) is an epithelial malignancy that commonly arises from major and minor salivary
glands. This malignancy is associated with very significant morbidity and mortality. It is remarkable for its high rate
of perineural invasion, a high tendency for recurrence, and ultimately, low rates of survival. Ten year survival rates are
approximately 40%. ACC is an understudied malignancy for which the molecular alterations underlying tumoigenesis
are obscure. Through a systematic approach employing global, large-scale analysis of primary tumors with diverse clini-
cal outcomes, state-of-the art next generation sequencing and analysis, and validation of genetic alterations prognostic
for recurrence, we proposed to elucidate the mutational landscape underlying ACC aggressiveness. Our work elucidat-
ed the genetic changes underlying ACC, uncovered the mutations that drive tumor aggressiveness, and helped identify
potential novel targets for therapy.

How has the Beene Center enabled you to further your research endeavors? How do you think the Beene Center
RFA is essential for scientists at MSKCC?
The Beene Center provides critical resources for investigators at MSKCC to pursue high risk/high reward research. In
a time when federal funding is shrinking and increasingly concentrated on funding conservative, risk adverse science,
the Beene Center provides the means to swing for the fences. This type of research is critical for achieving the discover-
ies needed to provide tomorrows breakthrough cancer treatments.

Has your Beene Center project allowed for any gains in the patient care?
This work provided the first genetic blueprint of ACC. It was also the first large-scale cancer mutation discovery study
for any cancer type to have originated from MSKCC. This work identified over a dozen new potential targets for ACC
and provided much needed biomarkers for particularly aggressive tumors. The work will form the basis of clinical trials
for ACC for the next decade.
The Geoffrey Beene Cancer Research Center (GBCRC) operates with the continued support from the Geoffrey Beene Foundation and Geoffrey Beene, LCC. The GBCRC supports new an innovative initiatives, operational expenses, and cutting edge technology. GBCRC funding has become essential to the MSK community by providing competitive funding for research proposals each year. These research grants have become a great source of support for innovative projects as well as seed money for pilot projects. These proposals support the mission of the Geoffrey Beene Cancer Research Center by taking bold and transformative steps to achieve major advances in making cancer a more manageable disease.
Dave Solit, MD
Geoffrey Beene Sr. Chair

Dr. Solit is a Medical Oncologist and a Laboratory Scientist. As a member of the Genitourinary Oncology Service, he specializes in treating cancers of the prostate, bladder, kidneys, testes, and other related cancers.

Dr. Solit is very involved in clinical trials, particularly trials of targeted drugs known as kinase inhibitors. These drugs block pathways inside cancer cells that cause the cells to grow or spread. One area of focus in his research is studying patients who are known as extraordinary responders. These are people with difficult-to-treat cancers who are found to respond exceptionally well to a new drug, even though that drug does not work in most people with the same disease. His laboratory in the Human Oncology and Pathogenesis Program at Memorial Sloan Kettering completed the first whole-genome analysis of a patient with bladder cancer. This patient had a complete and durable response to a novel targeted drug that was only effective in a small minority of patients. By performing this analysis, he was able to determine what was genetically unique about this patient’s tumor. Dr. Solit is now testing the same drug in other patients whose tumors have a similar genetic profile.

As the Director of the Center for Molecular Oncology at Memorial Sloan Kettering Cancer Center, Dr. Solit also leads a multidisciplinary team of clinicians, geneticists, bioinformaticians and laboratory scientists. The mission of the Center for Molecular Oncology is to integrate molecular and clinical information to develop therapies that are individualized to each patient’s cancer.