

ENDURANCE

2008 Progress Report



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Finishing the Race



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The Prostate Cancer Foundation (PCF) was founded in 1993 to find better treatments and cures for prostate cancer. Through its unique model for identifying and selecting promising research programs and rapid deployment of resources, the PCF has funded more than 1,500 programs at nearly 200 research centers in 20 countries around the world.

As the world's leading philanthropic organization for funding prostate cancer research, the PCF is now a foundation without borders. Its advocacy for increased government and private support of prostate cancer research programs has helped build a global research enterprise of nearly \$10 billion.

In 2008, 40 percent fewer men in the U.S. died from prostate cancer compared to what was once projected in 1996. The PCF is a force of **HOPE** for more than 16 million men and their families around the world who are currently facing the disease.

With milestones achieved and challenges ahead, the work of the PCF is enduring. We remain committed to finishing a race that ends when death from prostate cancer is no longer an outcome.

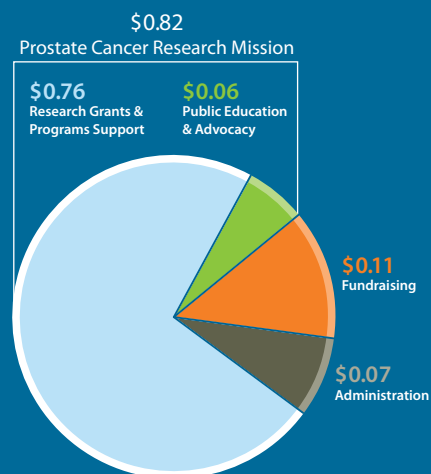
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5-Year Revenue History



2008 Spending



A Tribute to the Vinecki Family

This Progress Report is dedicated to the Vinecki family. Michael Vinecki was diagnosed with prostate cancer on his 40th birthday in May 2008. Since then the family has worked tirelessly in support of prostate cancer awareness. Ten-year-old Winter (see cover photo) participated in the adult *Athletes for a Cure Triathlon* in September. She and Team Winter have helped raise more than \$125,000 for advanced research. Michael lost his battle to cancer in March 2009. He and his family have touched many with their selflessness and caring. We are honored by their support.

FINISHING THE RACE | Endurance for Challenging Times

Dear Friends,

The Prostate Cancer Foundation (PCF) continues to lead the fight against prostate cancer and give hope to more than 16 million men and their families around the world. Thanks to nearly 68,000 donors who contributed in 2008 to support our efforts, we finished the year able to commit more than \$28 million toward specific new research in addition to our existing research allocations. This will bring us closer to our goals of ending suffering from prostate cancer and finding a cure.

Among other highlights in 2008, the PCF provided funding commitments for:

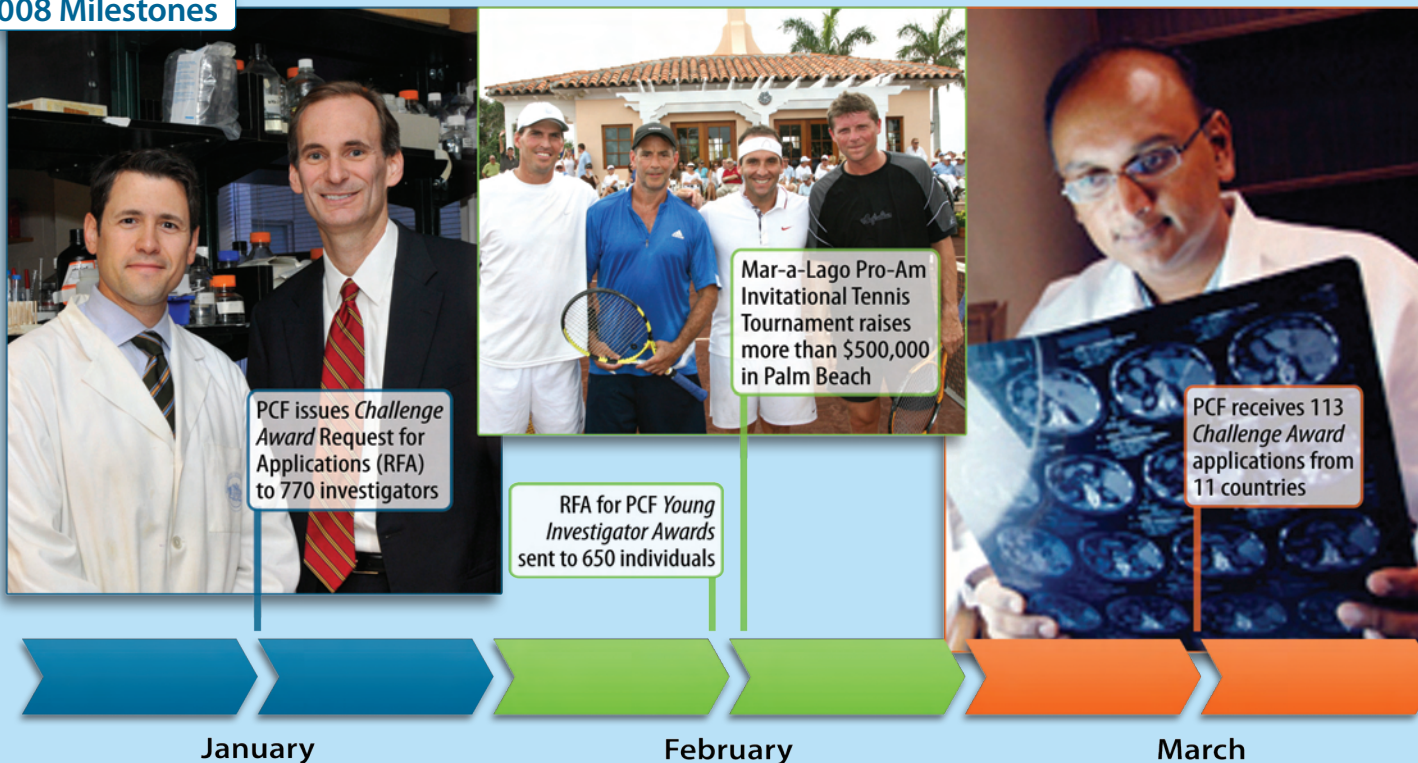
- Nine new multi-year Challenge Awards for scientific teams, totaling \$21.1 million
- Twenty new three-year Young Investigator Awards totaling \$4.3 million

- Studies at ten U.S. sites of the Clinical Trials Consortium, in partnership with the U.S. Department of Defense Congressionally Directed Medical Research Programs (CDMRP). Since 2005, the Clinical Trials Consortium has initiated 44 clinical trials, enabling more than 1,600 patients to participate in the study of new medicines for prostate cancer.

In 2009, the PCF continues to support its existing multi-year commitments and is funding ten new Creativity Awards to support highly innovative ideas that would otherwise be left unfunded.

The PCF's model of venture philanthropy ensures that funds raised for research are distributed swiftly and efficiently to programs showing the most potential to accelerate the discovery and delivery of new therapies for prostate cancer patients.

2008 Milestones



Maintaining the Pace

The number of new prostate cancer cases has risen with aging baby boomers, but the annual number of U.S. deaths has actually declined. This medical feat could not have been accomplished without the work of PCF-supported researchers. But much work remains. Projections indicate there could be an unprecedented number of new cases—300,000—and 42,000 deaths annually by 2015 if the death rate remains unchanged. Fortunately, more progress has been made in the past five years than in the first three decades following President Nixon’s declaration of the nation’s war on cancer in 1971:

- We better understand gene fusions that cause prostate cancer.
- Research in immunotherapy—therapy to alert the body’s immune system to fight cancer—is advancing.

- New biomarkers are being identified that can lead to better diagnostics and assessment of patient response.
- Innovative targeted therapies are being developed.
- Growing appreciation of the role of nutrition and exercise is leading to cancer prevention and increased survivorship.

Reaching Beyond the PSA Debate

Since 1980, PSA (prostate-specific antigen) screening, in combination with the digital rectal exam, has helped save many lives. However, because PSA testing can’t discern between highly aggressive, life-threatening and indolent (non-threatening) prostate cancers, controversy continues around its use. While the screening has served us well as a general “smoke detector” for prostate diseases, we’re supporting the development of better, cancer-specific diagnostic tests.

2008 Milestones



Marvin Shanken’s *A Night to Remember* Dinner raises more than \$900,000 in New York for PCF



pcf.org URL is acquired



Annual in-store Safeway campaign raises more than \$12 million for PCF-funded research

PCF receives 76 *Young Investigator Award* applications from 8 countries

PCF commits \$21.1 million for 8 new, multi-year *Challenge Awards*



April

May

June

These include better technologies for collecting and identifying specific circulating tumor cells (CTCs) in blood samples and prostate cancer-specific biomarkers in urine. These are potentially transformational breakthroughs that can save millions of lives while resolving the PSA debate.

Building Public Understanding and Government Support

While the PCF's primary mission is to support research, a portion of our communications effort is focused on providing patients, families and caregivers the latest information on prostate cancer treatment options and lifestyle information. Our website, www.pcf.org, has attracted a growing following of patients, families and donors.

While prostate cancer is the second-most-common cancer in men, it remains one of the least discussed.

Many men simply do not want to talk about medical problems that exist "below the belt." To overcome this problem, the PCF is developing more communication tools directed toward partners and wives, family members, caregivers and younger audiences who are more open to the message of early detection and treatment. In the past year, the foundation has widened its electronic communications by embracing new social media outlets, including Facebook and Twitter.

In our advocacy for increased prostate cancer research funding, the PCF identifies projects and researchers that could benefit from federal funding. We recently joined forces with a coalition of prostate cancer organizations to support continued 2010 appropriations for the Department of Defense's prostate cancer research programs. Members of the PCF leadership team continue to participate on task

July

- 600 home runs and counting
- .289 career batting average
- More than 2,600 hits
- All-Star in the fight against prostate cancer
- Some achievements are truly inspiring
- Major League Baseball® and the Prostate Cancer Foundation are coming up to help the fight against prostate cancer - which strikes 1 in 6 American men. Father's Day, come out to the ballpark or watch the national broadcast games live on FOX at 7PM. Visit mlb.com or go to pcf.org to learn more.
- PCF announces that the June Home Run Challenge with 30 Major League Baseball teams raises \$1.5 million

August

- Skip Ciccarelli, 60, a six-year prostate cancer survivor, finishes a 54-day, 1,700 mile kayak trip from Chicago to New York, raising awareness for prostate cancer
- Dan Fogelberg commemorative pins, designed by his wife Jean, made available at pcf.org, raising \$25,000
- PCF's Hamptons Pro-Am Invitational Tennis Tournament raises more than \$500,000 in New York
- PCF supports 20 Young Investigators with \$4.3 million in grant commitments

September

- RFA for PCF Creativity Awards sent to 1,400 researchers around the world
- Athletes for a Cure Fight Gone Bad III event raises more than \$400,000 for PCF
- Athletes for a Cure Orlando Triathlon raises over \$87,000
- Charles Evans Foundation becomes sponsor of the 2009 PCF Pro-Am Tennis Tournament, making a \$2 million commitment for a PCF Challenge Award

forces and committees that help shape public policy. Since the PCF was founded in 1993, there has been a twenty-fold increase in government funding for prostate cancer programs, and our bipartisan advocacy continues. The PCF represented the entire prostate cancer community—researchers, patients, families and healthcare providers—in the drafting process for the Kennedy-Hutchinson Cancer ALERT Act introduced in the U.S. Senate in early 2009.

One Team, Many Members

One important measure of the PCF's progress is the increased number of men who survived prostate cancer during 2008. This increase is the result, in large part, of the remarkable teamwork of our donors, scientists, patients, caregivers, staffers and others whose lives are affected by this cancer. Together, we are bound to finish what we started in 1993: bringing

human suffering from prostate cancer to an end.

Thank you for your continuing support.

Sincerely,

Mike Milken Jonathan W. Simons



Mike Milken
Founder and Chairman



Jonathan W. Simons, MD
President and Chief Executive Officer
David H. Koch Chair

2008 Milestones



PCF's Annual Scientific Retreat brings nearly 300 of the world's leading prostate cancer researchers together for three days of scientific exchange and discussion



Movember, a global mustache-growing event raises over \$1 million for the PCF in the U.S.



Winter Vinecki (10) named 2008 WebMD Health Hero for raising more than \$125,000 for Athletes for a Cure

PCF's New York Dinner at Daniel raises more than \$850,000 for prostate cancer research

PCF receives 341 Creativity Awards applications from researchers in 15 countries

PCF's Dr. Jonathan Simons is featured at a special ESPN Zone event on prostate cancer in New York

PCF announces 9th multi-year Challenge Award

PCF closes 2008 with total annual revenues of \$37.2 million, coming in 3% over its revenue projections



October

November

December

CONNECTING CANCER AND LIFESTYLE

The PCF has pioneered the field of diet and exercise as it relates to prostate and other cancers. The body of research linking good lifestyle choices to cancer survivorship, and perhaps prevention, continues to grow. Obesity, excess sugars, and cellular oxidation can foster prostate cancer growth. By stressing the importance of approaching prostate cancer through a commitment to lifestyle changes, the PCF's guide on nutrition and exercise provides information that can help a man with (or without) prostate cancer build a stronger mind and body.

In 2008, the PCF updated the latest lifestyle guidelines for prostate cancer patients and recently published an all-new publication: *Nutrition, Exercise and Prostate Cancer*. It is a complete reference for men and their families on the importance of exercise and proper nutrition. The guide was authored by a multidisciplinary team of world experts: David Heber, MD, PhD, UCLA; Stephen J. Freedland, MD, Duke University; Lee W. Jones, PhD, Duke University; William G. Nelson, MD, PhD, Johns Hopkins School of Medicine.

The guide discusses the link between excess body fat and a man's chances of developing prostate cancer by pointing to the fact that body fat secretes hormones and specialized proteins that are growth factors for cancer. As inflammation and oxidation of cells occur, they become damaged, which can contribute to prostate cancer development and progression.

Inflammation and oxidation of fat cells can be changed, however, by pointing one's dietary focus toward eating fruits and vegetables, whole grains, and ocean-caught fish. Cruciferous vegetables, such as broccoli, are especially rich in sulforaphane that acts as a protective sponge against free radicals that cause oxidation.

Multiple studies have reported an increased incidence of obesity and cancer in populations eating a Western diet. Generally, with excess body fat higher levels of sugar are being consumed. This increased intake of sugar has been proven to fuel the growth of cancers, including prostate cancer. Substituting mixed berries and fruits for desserts high in sugar or eliminating soft drinks in favor of water are just some ways to decrease sugar intake.

The guide recommends that by simply eliminating or lowering sugar intake, a man may slow prostate cancer cell growth and progression of the disease. By reducing sugar

levels, one also lowers the body's need to produce insulin, a hormone which is needed to break down sugars. High insulin levels have been linked to an increased risk of diabetes, heart disease, and prostate cancer growth, independent of insulin's interaction with sugar.

Supplementing a balanced diet with multivitamins can be a benefit, however, supplements must be used with caution and do not compensate for a poor diet. Fruits and



vegetables are rich sources of mixed vitamins, minerals, antioxidants and other specialized substances that cannot be replicated in most supplements. Ultimately, individuals should use wise judgment when incorporating supplements into their diet.

Along with a proper diet, incorporating daily exercise is paramount to preserving one's overall health. Exercising aerobically for approximately a half hour every day (for oxygen intake and to build muscle mass) has a positive impact on burning fat and increasing strength.

As a person ages, the body's metabolism slows down due to a decrease in muscle mass often caused by inactivity. That is why it is vital for men to build and maintain muscle mass throughout their lifetime by eating adequate proteins and doing muscle-building exercises.

Among other new 2008 findings highlighted in the guide, it was shown that exercise not only reduces and helps to maintain weight but also curbs hunger, increases resting metabolism, increases bone density, and improves quality of life. The PCF continues to fund emerging science in the area of nutrition. The guide provides readers with a balanced perspective on making wise choices with regard to lifestyle and nutrition. A free copy of *Nutrition, Exercise and Prostate Cancer* can be ordered or downloaded at www.pcf.org.

ADVANCES IN PROSTATE CANCER RESEARCH: 2008

The complexity of prostate cancer demands investigation of the disease from numerous angles. In the past year, the PCF has witnessed game-changing advances in prostate cancer research accomplished by PCF-funded investigators working around the globe.

Scientific advances in the areas of genetics and genetic testing, immunotherapy, liquid biopsies, and androgen receptor targeting offer hope that the impact prostate cancer has on millions of American men and their families will be diminished. But despite this progress, an American man died every 19 minutes, leaving more than 28,000 families bereaved in 2008. The PCF remains committed to improving diagnostics and treatment for prostate cancer patients, and further reducing the death rate.

New Medicines for Advanced Prostate Cancer

Abiraterone Attracting global media coverage in 2008, Abiraterone was shown to be a promising medication for prostate cancer. It has the potential to treat patients whose disease has relapsed using conventional medical treatment for advanced prostate cancer, including chemotherapy.

PCF-funded researcher Dr. Gerhardt Attard and colleagues at the Institute of Cancer Research and The Royal Marsden Hospital, published findings in the *Journal of Clinical Oncology* detailing how the orally-administered drug works by blocking the pathways that drive prostate cancer. Specifically, Abiraterone blocks the production of androgenic (male) hormones that contribute to the continued growth of prostate cancer.

The PCF Clinical Trials Consortium played an important role by accelerating U.S. clinical testing of Abiraterone in Phase II clinical trials. These evaluations focused on the drug's anti-tumor action and were conducted in 132 patients at five leading prostate cancer centers that are all members of the consortium: Dana-Farber Cancer Institute at Harvard Medical Center, Johns Hopkins Cancer Center, M. D. Anderson Cancer Center, Memorial Sloan-Kettering Cancer Center, and the University of California at San Francisco. The manufacturer of Abiraterone, Cougar Biotechnology, was recently purchased by Johnson & Johnson.

MDV3100 This new therapeutic made headlines for its potential to improve outcomes for patients with hormone-refractory cancer. This drug blocks the androgen receptor for testosterone and other male hormones that help drive tumor growth. One published journal report described "sustained declines" in blood levels of prostate-specific

antigen in patients taking the drug after conventional anti-androgen therapy failed.

Developed by PCF-funded researcher Dr. Charles L. Sawyers at UCLA, a protocol for a large-scale trial of MDV3100 has been submitted to the U.S. Food and Drug Administration by Medivation Inc., a California-based biopharmaceutical company.

The human body possesses defense mechanisms to protect itself against harm, including cancer. The PCF has gone to great lengths to fund research in immunotherapy with the premise that stimulating the immune system's ability to attack prostate cancer cells may be a viable treatment option for patients facing this disease.

Provenge® Investing more than \$2 million to support dendritic cell and immunotherapy research during the past several years, the PCF was encouraged by recent data showing the ability of a new drug, Provenge, to increase patient survival rates. Unlike most vaccines, Provenge is not used to prevent illness but to treat an already existing condition. The vaccine combines an enzyme that is found in most prostate cancer cells with a protein that helps the immune system recognize the cancer as a threat.

PCF-funded researcher Dr. Philip Kantoff, of the Dana-Farber Cancer Institute at Harvard Medical School, was the principal investigator of the Provenge Phase III clinical trial. The PCF provided early funding to Dr. Eric Small at UCSF within the PCF Clinical Trials Consortium to support clinical research focused on measuring immune response in patients treated with Provenge. The findings of Dr. Small and his colleagues were published in the *Journal of Clinical Oncology* in December 2000 and provided important contributions to the initial development of Provenge.

Improved Diagnostics and Prognostics

While the PSA test remains an important tool for detecting the possible presence of prostate cancer, it is not cancer-specific and is used in combination with other diagnostic tools. This shortcoming has led to over-diagnosis and over-treatment of some prostate cancer patients. The PCF is funding research to go beyond the PSA test and make better diagnostics, prognostics and patient response measurements a reality.

Circulating Tumor Cells (CTCs) Dr. Daniel Haber at Massachusetts General Hospital in Boston developed a tool to collect and count rare circulating tumor cells (CTCs) using a microelectromechanical system (MEMS). The microfluidic device (see photo, page 8) is produced using processes similar to those used for manufacturing computer chips. This technology is now being utilized by other PCF-funded researchers to predict survival and disease progression in patients with solid tumors. CTCs from prostate cancer patients have been investigated by Drs. Howard Scher and Johann DeBono of Memorial Sloan-Kettering Cancer Center and The Royal Marsden Hospital, respectively. Laboratory investigations show that more than 5 CTCs in 7.5 ml of whole blood is predictive of an aggressive prostate cancer. Quantifying CTCs is part of a Phase III clinical investigation of Abiraterone. The goal is to determine whether CTC counts are a reliable biomarker for improved survival rates, and if they can be used to shorten the time required to test new medicines.

MicroRNA In Seattle, Dr. Muneesh Tewari, a PCF Arnie's Army Creativity Award recipient, is leading a project at the Fred Hutchinson Cancer Research Center, studying the detection and measurement of microRNA in the blood—a process once thought to be impossible. In the future, microRNA profiling of a patient's blood may be able to predict whether a tumor will respond to a specific treatment. The results could also allow doctors to monitor patient responses during cancer treatment.

Sarcosine Drs. Arul Chinnaiyan and Arun Sreekumar's research on devising new prostate cancer diagnostics may soon lead to a non-invasive urine test for detecting the disease. Their findings at the University of Michigan identified links between prostate cancer and small molecules, termed metabolites. The team profiled more than 1,000 metabolites, and found the metabolite sarcosine to be highly elevated in most metastatic prostate

cancer urine samples. The team's goal is to use metabolites as tools for developing new therapeutic targets and diagnostic biomarkers.

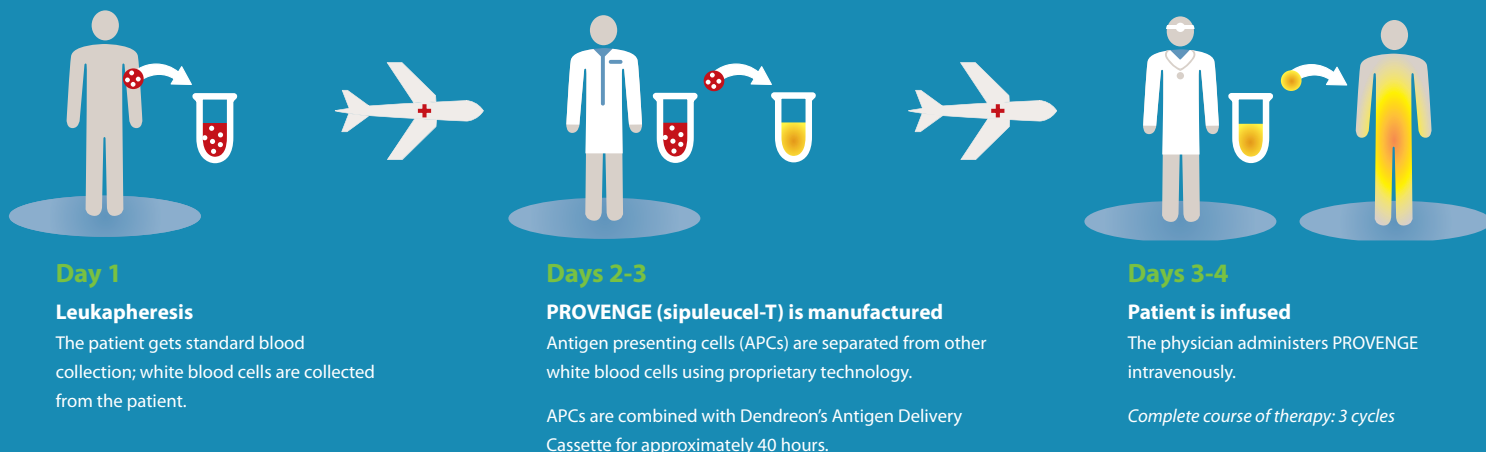
PCA-3 Dr. Jack Schalken from the University of Nijmegen in the Netherlands is also working on developing a molecular diagnostic test of urine for prostate cancer. His research seeks to detect the presence of PCA-3, a prostate cancer-associated gene. Dr. Schalken noted at the PCF's 2008 Scientific Retreat at Lake Tahoe that information on diagnosis and prognosis will likely increase by combining results from these molecular tests with other clinical and laboratory findings.

New Risk Assessment Markers

SNPs In 2008, notable findings out of the U.S. and Sweden were published by PCF-funded scientists who discovered a combination of five gene variants—called single nucleotide polymorphisms (SNPs)—that dramatically raise the lifetime risk of being diagnosed with prostate cancer ten-fold. Identifying disease-associated SNPs is ideal in countries with little ethnic diversity (i.e. genetic diversity), such as Sweden. DNA was collected and studied for potential "hot spots" of differences in genes of men with prostate cancer compared to others. With saliva-based SNP tests now available, the odds of developing prostate cancer can be more readily projected.

SPINK1 PCF Young Investigator Award recipient Dr. Scott Tomlins made headway in genetic research by discovering a gene called SPINK1 (serine peptidase inhibitor, Kazal type 1). It is highly expressed in prostate cancer and plays a role in at least 50 percent of patients. This gene is present in prostate cancers that do not have ETS gene fusions. Although additional investigation is needed, Dr. Tomlins' finding may have identified a new biomarker for a subtype of prostate cancers.

The Provenge (sipuleucel-T) Process



CHALLENGE AWARDS

In 2008, the Prostate Cancer Foundation committed more than \$19 million for eight new Challenge Awards in addition to the Koch-PCF Nanotherapeutics Challenge Award. These multi-year programs with high potential will receive three annual payments, ranging between \$500,000 and \$1.0 million each.

Without PCF funding, these teams would not have the necessary resources to move their work forward. A record 113 teams proposed new hypotheses and approaches in biotechnology that could significantly reduce prostate cancer deaths. They represented 105 cancer programs in 11 countries.

Recipients of PCF Challenge Awards were chosen by an expedited peer review committee of 52 skilled scientific and clinical experts. Specific milestones are outlined by the foundation for yearly review, and research teams are required to share their findings at the PCF's annual Scientific Retreat. A full description of these Challenge Award programs can be found at www.pcf.org.

EPIGENETICS

Michael G. Rosenfeld, MD, University of California, San Diego

Epigenetic Strategies in Androgen Receptor-Dependent Interchromosomal Networking and Translocation Events
Epigenetics is the study of gene control by mechanisms other than changes in gene sequence (genetic changes). This relatively new area of study has generated important discoveries linking gene expression to the development of cancer, and has proven to be vital to prostate cancer research. Dr. Rosenfeld and his expert team propose to apply new genetic biotechnology toward the discovery of genetic and epigenetic changes resulting in prostate cancer. The overall objective of Dr. Rosenfeld's work is to discover new medications that control prostate cancer when all existing treatments have failed.

ETS GENE FUSIONS

Levi A. Garraway, MD, PhD, Dana-Farber Cancer Institute, Broad Institute of MIT and Harvard
Todd R. Golub, MD, Broad Institute of MIT and Harvard
William C. Hahn, MD, PhD, Dana-Farber Cancer Institute, Broad Institute of MIT and Harvard

Discovery of Inhibitors of TMPRSS2/ERG Function in Prostate Cancer

In recent years, scientists have discovered that a specific genetic rearrangement in normal prostate cells leads to the production of cancer promoting factors (ETS factors) in prostate cancer. It is presumed that the discovery of medications that block the activity of ETS factors will arrest the growth of prostate cancer. The team's research applies state-of-the-art genetic biotechnologies in a significant drug discovery effort to target ETS factors produced by prostate cancer cells. Collaborators at the Broad Institute of MIT and Harvard are working with biologists and oncologists at the Dana-Farber Cancer Institute at Harvard Medical School to evaluate ETS factor inhibitors discovered in this work for the goal of developing a life-saving medication for prostate cancer patients.

IMMUNOTHERAPY

James Allison, PhD, Memorial Sloan-Kettering Cancer Center
Padmanee Sharma, MD, PhD, M. D. Anderson Cancer Center

CTLA-4 Blockade in Therapy of Prostate Cancer: Therapeutic Mechanisms and New Directions

Immunotherapy is a form of treatment that involves directing a patient's immune response against their cancer to cause the elimination of tumors. A variety of immunotherapeutic strategies for the treatment of prostate cancer are being developed. There is a significant need for discovery of blood markers that will

A circulating tumor cell (CTC), captured on the nano-sized post of a microfluidic device, is depicted in yellow.

herald an anti-tumor response as well as warn of an impending adverse event due to the therapy. Drs. Sharma and Allison are performing clinical evaluation of advanced immunotherapies and rigorous molecular analysis of patients' response to immunotherapy. The goal is to use these findings to develop more effective and safer immunotherapeutic treatments for prostate cancer.

INTRACRINE ANDROGENS AND ANDROGEN RECEPTOR SIGNALING

Steven P. Balk, MD, PhD, Beth Israel Deaconess Medical Center

Philip W. Kantoff, MD, Dana-Farber Cancer Institute

Peter S. Nelson, MD, Fred Hutchinson Cancer Research Center, University of Washington

Synergistic Targeting of AR and Androgen Metabolism in Prostate Cancer

For advanced prostate cancer patients, the best available treatment is the removal of testosterone hormones (androgens) that drive the growth and progression of prostate cancer. Medications that reduce androgens cause clinical remission invariably followed by disease progression. It is now known that androgens can be produced within tumor tissue, which is one cause for disease progression. Drs. Balk, Kantoff and Nelson are carefully studying androgen reduction in tumor tissue from patients treated with a new generation of androgen production inhibitors to determine the mechanism of inhibition. Since it is likely that patients will ultimately become resistant to the new medications, identification of the mechanisms of resistance will help identify the next generation of prostate cancer treatments.

NUTRITION, METABOLISM AND PATIENT QUALITY OF LIFE

Matthew R. Smith, MD, PhD, Massachusetts General Hospital Cancer Center

Prevention of Treatment and Disease-Related Morbidity During Androgen Deprivation Therapy: A Multi-Center Proposal

As the removal of testosterone and other male hormones (androgens) is currently the best available treatment for advanced prostate cancer patients; the medications used to reduce androgen in patients can cause significant secondary illness. Dr. Smith and his U.S./Canada team of investigators are studying the health consequences of androgen deprivation to determine where medical interventions can be made to prevent these negative consequences. Dr. Smith's expert team is currently investigating how to limit obesity, diabetes, bone fractures and heart disease in patients treated for advanced prostate cancer. Exercise, nutrition and new medications are being employed to enhance the health of these patients with advanced prostate cancer.

PREDICTIVE PRECLINICAL MODELS

Robert L. Vessella, MD, University of Washington

Consortium for the Development and Analysis of Relevant Prostate Cancer Model Systems

Laboratory models that reflect prostate cancer clinical biology are important for investigating new treatments for the disease. Dr. Vessella has organized a national consortium of expert investigators that intend to better characterize existing models of prostate cancer and determine where the gaps are in our understanding of the disease pathology. The deficiencies are being corrected by the creation of a new generation of models suitable for preclinical assessment of new, experimental medications for advanced prostate cancer.

PROGRESSION BIOMARKERS

Daniel Haber, MD, PhD, Massachusetts General Hospital Cancer Center

Clinical and Biological Insights into Prostate Cancer Derived from the Microfluidic Capture of Circulating Tumor Cells (CTCs)

Discovery of biomarkers for predicting disease progression or signaling the effectiveness of an experimental medication for prostate cancer is a priority for the PCF. These markers will increase the pace of drug development and warn physicians earlier when prostate cancer is progressing. Dr. Haber, in collaboration with oncologists, biologists and engineers, is working to refine a system that measures tumor cells in patient blood. Preliminary findings suggest that enumeration of these cells provides an early signal of disease progression. These will be clinically validated.

PROSTATE CANCER STEM CELLS

Owen N. Witte, MD, UCLA

Defining Targets and Biomarkers in Prostate Cancer Stem Cells: New Therapeutic Opportunities

Cancer stem cells are an elusive, small subpopulation of tumor cells that are not only resistant to therapy but also repopulate a solid tumor after most tumor cells are killed by a therapy. Understanding the biology of cancer stem cells and targeting their elimination is a priority in cancer research. Dr. Witte and his team at UCLA and the Salk Institute of Biological Studies are world leading experts in cancer stem cell biology. This team is currently directing their expertise toward studying prostate cancer stem cells. Application of new genetic biotechnologies will better define this critical tumor cell population and reveal new therapeutic targets.

YOUNG INVESTIGATORS

Designed to encourage the most innovative research thinkers to continue their careers in prostate cancer research, the PCF's Young Investigator Award program is for young, early-career scientists. Consistent with our goal to end death and suffering from prostate cancer, these awards focus our efforts on developing human capital and a world-class community of investigators to undertake the next generation of prostate cancer research.

These awards provide \$75,000 per year for three years to support specified research programs. The total \$225,000 award amount is matched by each recipient's institution, providing a total investment of \$450,000 in each innovative research area. Funds may be used flexibly to advance the career and research efforts of the recipients. Mentorship is required for every PCF Young Investigator. Young Investigator awardees and their mentors are invited to participate in the PCF's Annual Scientific Retreat.

Starting with the initial funding cycle in 2008, the PCF intends to fund 100 Young Investigators over the next few years. In 2008, the foundation received 76 applications from eight countries in North America, Europe and Asia, focused on 16 different prostate cancer research areas. Following peer review, the PCF committed a total of \$4.3 million to the first 20 Young Investigator Awards. More detailed information on these Young Investigators is available in the research section of our website at www.pcf.org.

THE GOERGEN FOUNDATION - PCF YOUNG INVESTIGATOR AWARD

Andrew Armstrong, MD, ScM
Duke University

Dr. Armstrong is working to discover biomarkers that will identify patients with prostate cancer who are at higher risk for a more aggressive clinical progression of the disease. Molecular markers to predict metastasis will be studied on circulating tumor cells—the small proportion of prostate cancer cells that “break away” from the primary cancer and enter blood circulation. Patients presenting these markers might be treated aggressively at an earlier stage of disease.

MICHAEL MILKEN SCHOLAR - PCF YOUNG INVESTIGATOR AWARD

Mohamed S. Arredouani, PhD
Beth Israel Deaconess Hospital

Immunization of patients to generate an immune response to eliminate cancer is an increasingly important therapeutic strategy for advanced prostate cancer. Dr. Arredouani hopes to develop a new generation of prostate cancer vaccines with molecules known to be involved in the malignant transformation of prostate cells. Two such molecules have been selected and will be tested.

THE SUSAN AND JAMES BLAIR - PCF YOUNG INVESTIGATOR AWARD

Gerhardt Attard, MD, PhD
The Institute for Cancer Research (London)

Inhibition of CYP17 by Abiraterone has promising anti-tumor activity in advanced prostate cancer. This experimental medication blocks the production of the “gasoline” that fuels cancerous tumor growth. Nonetheless, 50 percent of chemotherapy-treated patients do not respond to Abiraterone from the outset, and the majority of patients eventually develop acquired resistance. Circulating tumor cells are being studied to identify a biomarker profile that predicts which patients might be sensitive to Abiraterone and those that might become resistant.

THE ROBBINS FAMILY - PCF YOUNG INVESTIGATOR AWARD

Tarek Bismar, MD
University of Calgary

A specific gene fusion of pieces from two different chromosomes is present in 50 percent of prostate cancers and is thought to drive the disease. In addition, a normal protein named PTEN suppresses tumor development unless genetically altered as is the case in many advanced prostate cancer cases. Dr. Bismar is studying both of these changes in model systems in an attempt to discover how together they deregulate the control of growth and survival that result in prostate cancer.

THE PETER AND LAURIE GRAUER - PCF YOUNG INVESTIGATOR AWARD

Steve Cho, MD

Johns Hopkins University

New methods to image prostate cancer at the microscopic level are urgently needed. Prostate-specific membrane antigen (PSMA) is expressed on the surface of prostate cancer and represents a promising target for prostate cancer PET imaging. Lower molecular weight, small molecule PET radiotracers should improve solid tumor detection. A small molecule radiotracer PET imaging agent has been developed to target PSMA with higher PET imaging resolution. Dr. Cho is characterizing this PET tracer in prostate cancer clinical trials with the objective of monitoring tumor volume changes during experimental treatment.



THE KOVLER FAMILY FOUNDATION - PCF YOUNG INVESTIGATOR AWARD

Scott M. Dehm, PhD

Masonic Cancer Center, University of Minnesota

In the event that surgery or radiation does not curtail prostate cancer, locally recurrent or metastatic disease may be treated via a systemic blockade of the production or action of androgens. This so-called androgen ablation therapy specifically inhibits the androgen receptor (AR), a receptor that drives the proliferation and survival of prostate cancer. However, androgen ablation is not curative, and prostate cancer can progress. Dr. Dehm is attempting to create models that reflect how the AR continues to cause proliferation and survival of prostate cancer even after androgen synthesis and activity are blocked.



THE GEN-PROBE INCORPORATED - PCF YOUNG INVESTIGATOR AWARD

Eleni Efstathiou, MD, PhD

The University of Texas M. D. Anderson Cancer Center

New experimental drugs that shut off androgen (the fuel for prostate cancer) synthesis will likely become a standard of care for advanced prostate cancer in the next few years. Dr. Efstathiou is measuring androgen levels in the area of prostate cancer bone metastases to determine if androgens are undetectable, as is the case in tumor tissue from other sites, when total androgen suppressive medications are administered. It is thought that these studies will help determine which patients could benefit from or be resistant to these new medications.



MICHAEL MILKEN SCHOLAR - PCF YOUNG INVESTIGATOR AWARD

Adam Feldman, MD

Massachusetts General Hospital Cancer Center

New biomarkers for improved detection and prognosis of prostate cancer are needed. Intracellular, membrane-associated and secreted proteins are differentially expressed by prostate cancer cells compared to benign prostate cells. Dr. Feldman hopes to discover these differentially expressed proteins in urine, delivering a non-invasive practical biological fluid for biomarker discovery. The second goal of this project is to correlate biomarker findings with prostate cancer diagnosis, grade and pathologic stage.



THE EARLE I. MACK - PCF YOUNG INVESTIGATOR AWARD

Steven Frank, MD

The University of Texas M. D. Anderson Cancer Center

Following prostate cancer treatment, men are often embarrassed if they become incontinent. Recent data reveals that up to 33 percent of men or approximately 73,000 men annually will be wearing diapers or pads for up to two years following their treatment. Dr. Frank's goal is to eliminate incontinence in men treated with brachytherapy by using MRI image-guided radiation therapy. With accurate dose determination, cancer cure rates will increase and side effects will decrease translating into an improvement in quality of life following treatment.



THE JOY AND JERRY MONKARSH FAMILY FOUNDATION - PCF YOUNG INVESTIGATOR AWARD

Isil Guney, PhD

Dana-Farber Cancer Institute

Prostate cancers are initially dependent on androgens for survival and androgen-ablation therapies comprise the only effective treatment for metastatic disease. Eventually, however, prostate tumor cells acquire the capacity to survive and proliferate at exceedingly low levels of circulating androgens. Such hormone therapy-resistant prostate cancers are incurable. A thorough understanding of the molecular events that promote the development of hormone resistance in prostate cancer is necessary for the design of effective therapies for patients with hormone-resistant disease. Dr. Guney is working to identify molecules that are suitable for development as therapeutic targets in advanced prostate cancers.

THE NEUBAUER FAMILY FOUNDATION - PCF YOUNG INVESTIGATOR AWARD

Thomas Guzzo, MD

University of Pennsylvania

Dr. Guzzo is creating a prostate cancer translational research unit within the urology division at the University of Pennsylvania. Dr. Guzzo is focusing on clinical outcomes to improve surgical results for men diagnosed with early prostate cancer that include novel approaches to reducing morbidity from surgery.

THE DEFEO FAMILY - PCF YOUNG INVESTIGATOR AWARD

Andrea Harzstark, MD

University of California at San Francisco

Immunotherapy offers the potential to stimulate a prostate cancer patient's immune response to kill a growing tumor. Unfortunately, cancer cells are very weak vaccine agents alone, and require other co-therapeutic strategies to be effective. Dr. Harzstark is working to enhance the immune response to prostate cancer with a variety of approaches that might result in elimination of tumors.

PCF YOUNG INVESTIGATOR AWARD

Sarah Holt, PhD

Fred Hutchinson Cancer Research Center

Carcinogenic effects of estrogen on the prostate have been demonstrated in laboratory models. There is a current resurgence of interest in using synthetic estrogens to treat patients with advanced prostate cancer. Dr. Holt is studying genetic alterations in genes responsible for estrogen sensitivity and metabolism in the prostate of 1,457 prostate cancer patients compared to 1,351 control subjects without prostate cancer. Results should help identify patients with increased risk for primary prostate cancer and those who might develop a more aggressive form of the disease.

MICHAEL MILKEN SCHOLAR - PCF YOUNG INVESTIGATOR AWARD

Lorelei A. Mucci, ScD, MPH

Harvard School of Public Health

A recent finding in prostate cancer biology is the existence of specific gene fusions of chromosomes in disparate regions of a patient's genome. These gene fusions give rise to expression of molecules with strong cancer-causing properties. Emerging data suggest men with tumors that lack the fusion have an improved prognosis compared to men with fusion-positive prostate cancer. Dr. Mucci is studying 1,500 prostate cancer patients to understand the relationship of the gene fusions to hormonal balance, energy balance, and healthy weight. The impact of these physiological properties on patient survival will be determined.

THE WILLIAM L. EDWARDS - PCF YOUNG INVESTIGATOR AWARD

Mark Pomerantz, MD

Dana-Farber Cancer Institute

During the past two years, genomic scans have identified the genetic basis of prostate cancer risk. Dr. Pomerantz is looking to determine the molecular basis of increased prostate cancer risk in individuals that possess the genomic alterations. Understanding these mechanisms of risk may lead to new targets to inhibit the progression of prostate cancer.

THE DURDEN FOUNDATION - PCF YOUNG INVESTIGATOR AWARD

Ganesh Raj, MD
UT Southwestern Medical Center

The androgen receptor (AR) system plays a central role in prostate cancer and represents a critical target for innovative drugs for the treatment of this disease. Targeting specific genes is now possible, but the delivery of these new inhibitors to their targets is difficult. Dr. Raj's goal is to refine a system that will combine an MR imaging agent and a drug delivery vehicle for gene-targeted inhibitors. Specific gene targets are the AR and AR-associated molecules.

THE THOMAS H. LEE - PCF YOUNG INVESTIGATOR AWARD

William L. Redmond, PhD
Earle A. Chiles Research Institute, Robert W. Franz Cancer Research Center
Providence Portland Medical Center

Recent clinical trials have demonstrated that immunotherapy-based treatments hold promise for prostate cancer therapy, including tumor-specific vaccines and immuno-enhancing agents. Dr. Redmond hopes to further enhance cancer vaccine therapy by the discovery and development of new classes of immunostimulators.

PCF YOUNG INVESTIGATOR AWARD - ANONYMOUS DONOR

Nima Sharifi, MD
UT Southwestern Medical Center

Metastatic prostate cancer is treated with androgen deprivation therapy that reduces testosterone, the "gasoline" that fuels the growth and progression of prostate cancer. Despite frequent responses, tumors almost always recur with subsequent activation of the androgen receptor (AR), the target for testosterone. Therapies that down-regulate ARs using novel mechanisms, have a tremendous potential to introduce new treatments and improve the outlook for prostate cancer patients. Dr. Sharifi is working to determine if the down regulation of certain antioxidants will over activate AR function. Her second objective is to develop a new method for finding better tumor markers that herald prostate cancer progression in a state of high oxidation.

THE LEFRAK FAMILY - PCF YOUNG INVESTIGATOR AWARD

Scott Tagawa, MD
Weill Cornell Medical College

J591 is a monoclonal antibody against prostate-specific membrane antigen (PSMA), a molecule on the surface of prostate cancer cells. Studies using J591 linked to radioisotopes (radioimmunotherapy, RIT) have demonstrated safety and efficacy as well as the ability to target known sites of disease in metastatic prostate cancer. Dr. Tagawa is furthering clinical investigations of J591 in patients with advanced prostate cancer to determine the dosage and optimal administration schedule required to effectively treat the disease.

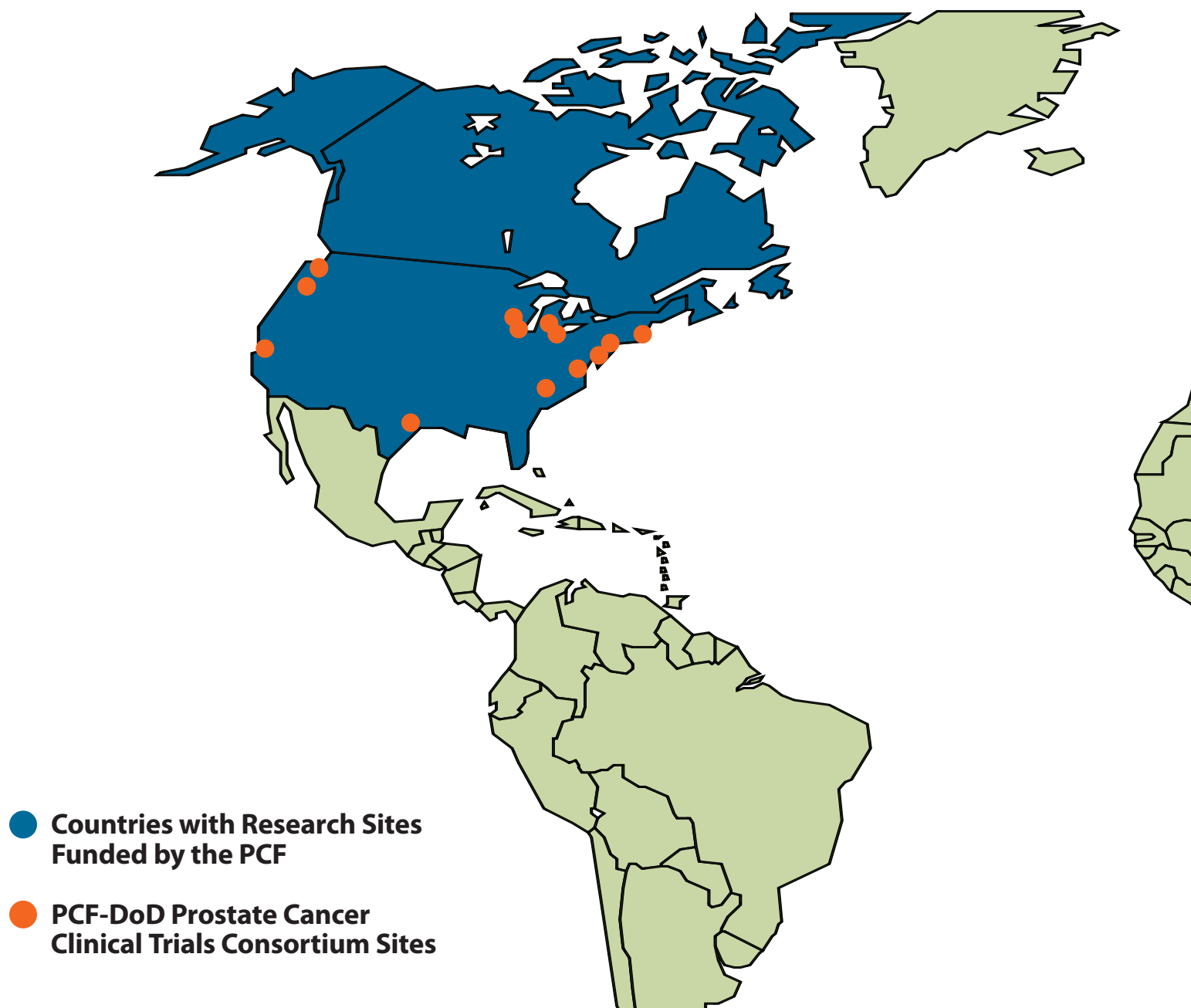
PCF YOUNG INVESTIGATOR AWARD

Scott Tomlins, PhD
University of Michigan

Specific chromosomal rearrangements in more than half of prostate cancers, using a unique analysis of DNA microarray data, were identified in 2005. These rearrangements result in the fusion of two genes that are normally located on separate chromosomes. These gene fusions become rational targets for prostate cancer therapy and also can be used for diagnosis. Dr. Tomlins is focusing on developing tests for the early diagnosis of prostate cancer using these gene fusions as well as characterizing additional dysregulated genes in prostate cancer.

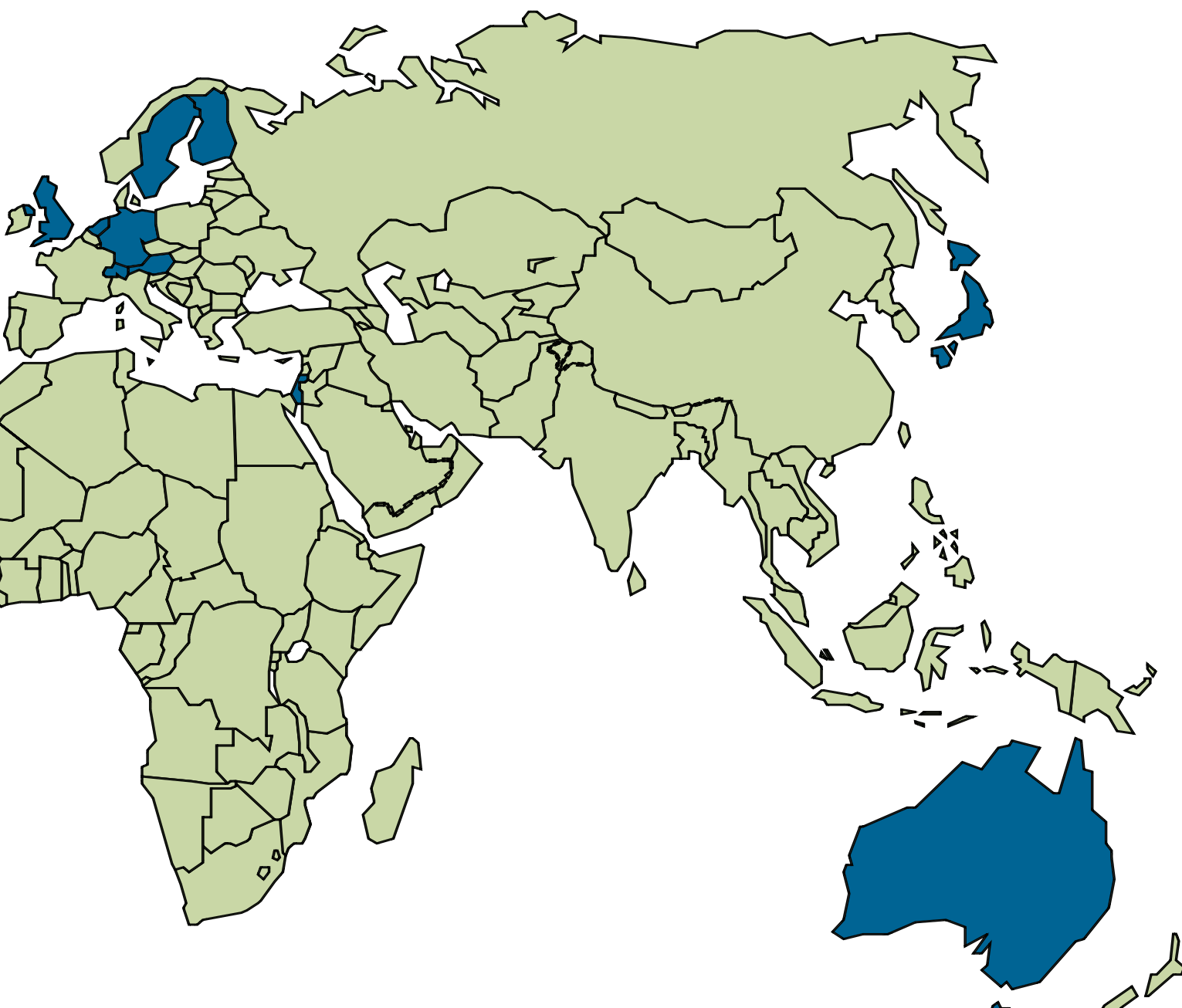


A GLOBAL RESEARCH ENTERPRISE



Many Countries, One Goal

Although based in the U.S., the Prostate Cancer Foundation's research enterprise has a far-reaching global presence, making it an organization without borders. It has solidified a global commitment to the end of prostate cancer. Receiving a research grant from the PCF has grown to become a prestigious milestone for both researchers and their institutions. Having raised more than \$370 million to find a cure, the PCF has funded more than 1,500 projects at nearly 200 institutions in twelve countries: Australia, Austria, Canada, Finland, Germany, Israel, Japan, the Netherlands, Sweden, Switzerland, United Kingdom and the United States.



2008 Challenge Awards

- 9 programs funded with a three-year \$21.1 million commitment
- 113 applications received from 105 institutions in 11 countries
- 5 multinational collaborations submitted applications

2008 Young Investigator Awards

- 20 investigators funded with a three-year \$4.3 million commitment
- 76 applications received from 14 institutions in 8 countries

2009 Creativity Awards

- 10 one-year programs funded with a \$1.0 million commitment
- 70 percent of past programs have gone on to earn additional funding
- 341 applications received (Q4 2008) from 151 institutions in 15 countries

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Bob McKnight
Ryan Nelson
Casey Nelson
Joseph Nuzzarello
Nick O'Kane
Ian Parmiter
Andy Petranek
Propane Industry Pros4Care
Steve Rakow
Pete Ridge
Will Rutledge
Kelly Slater
Karen Smyers
Neal Thompson
Steven Trussell
John M. White
Team Winter
Matt Woehnker
John Yodzis
Pam Zam

*Every effort has been made to ensure completeness and accuracy of this list.
If errors or omissions exist, please accept our apologies and call 800.757.CURE (2873). Thank you.*

APPEAL FOR SUPPORT

Dear Friend:

In the past sixteen years, deaths from prostate cancer have been reduced by nearly 40 percent compared to what was once projected, game-changing research programs have delivered promising results, and hope has continued to soar. On behalf of patients, families, caretakers and our PCF research scientists that serve them, *thank you*. This progress would be unsustainable without your ongoing support.

Your investment in the Prostate Cancer Foundation (PCF) is wisely deployed. Since 1993, virtually every important discovery in the battle against this disease has been facilitated by PCF funding or coordination. Moreover, every dollar you contribute to the PCF is multiplied 20 to 30 times; our activities set into motion a ripple that spurs research at government, private and charitable institutions and, in effect, leverages the millions of dollars we raise into billions.

You also help us build a dynamic, collaborative community. Sixteen years ago, prostate cancer researchers had no vantage point to comprehend the full scope of others' efforts. Today, no other organization has a more comprehensive and real-time view of the full prostate cancer landscape and its most promising research than the PCF. Our approach has galvanized the prostate cancer research community and has been a catalyst for accelerating scientific discovery.

Your continued generosity is more important than ever. The need is especially urgent now, with continued pressures on federal budgets and years of flattened research funding from the National Institutes of Health. This challenge to research funding is a serious threat to the momentum we've built.

Your donation is vital for us to reach our goal of ending prostate cancer. We appreciate your support and ask that you give now.

With deepest gratitude,



Jonathan W. Simons, MD

President and Chief Executive Officer

David H. Koch Chair

DONATION OPPORTUNITIES

The Prostate Cancer Foundation welcomes gifts of cash, securities, non-cash assets and gifts by will or living trust. We also welcome contributions made in memory, in tribute or in honor of friends or loved ones.

Donations

Please mail your check to:

Prostate Cancer Foundation
1250 Fourth Street
Santa Monica, CA 90401

To make an online contribution, please visit our website: www.pcf.org

If you prefer, you can make a donation by phone by calling toll-free (800) 757-CURE (2873).

Memorial or Tribute Gifts

- Honor the memory of a loved one or celebrate the accomplishments of a friend or family member by helping others
- Make a memorial or tribute gift and the PCF will send an acknowledgement card to the family or honoree

Monthly Giving

Set up recurring donations for a convenient and manageable gift process that fits your monthly budget.

Other Gift Suggestions

- Assets or property including appreciated stock and real estate
- Bequest – include a gift to the PCF in your will
- Name the PCF as the primary or contingent beneficiary on a life insurance policy
- Rollover funds from your IRA as a gift to the PCF and avoid all tax on the rollover (valid through December 31, 2009 and applies to those 70-1/2 years and older)

More information: www.pcf.org

STATEMENTS OF FINANCIAL POSITION

Years Ended December 31	2008	2007
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 27,894,591	\$ 21,275,262
Pledges receivable	4,043,333	6,442,212
Marketable securities	25,312	52,868
Prepaid expenses	80,497	59,216
Other receivables	—	50,564
Total current assets	32,043,733	27,880,122
Fixed assets:		
Furniture and fixtures	37,180	37,180
Office equipment	110,574	110,574
Leasehold improvements	246,891	246,891
Computer Software	344,384	325,280
Total fixed assets	739,029	719,925
Less accumulated depreciation	(606,244)	(542,457)
	132,785	177,468
Investments	960,000	—
Long-term pledges receivable	2,772,772	1,236,542
Total assets	\$ 35,909,290	\$ 29,294,132
LIABILITIES AND NET ASSETS		
Accounts payable	\$ 76,830	\$ 366,535
Accrued liabilities	1,377,160	1,546,860
Research awards payable	18,462,755	8,650,000
Total liabilities	19,916,745	10,563,395
Unrestricted net assets	15,992,545	18,730,737
Total liabilities and net assets	\$ 35,909,290	\$ 29,294,132

STATEMENTS OF ACTIVITIES

Years Ended December 31	2008	2007
Support and revenues:		
Donations	\$ 36,720,708	\$ 34,773,813
Net realized and unrealized loss on investments	(3,805)	(1,578)
Interest and other income	520,254	624,047
Total support and revenues	37,237,157	35,396,282
Program services:		
Research grants, association awards and donations	28,069,538	14,274,150
Scientific conferences	2,086,024	2,420,640
Public awareness and advocacy expense	2,529,047	1,560,191
Total program services	32,684,609	18,254,981
General and administrative expenses	2,887,230	2,420,921
Fund-raising expenses	4,403,510	4,729,126
Total expenditures	39,975,349	25,405,028
Change in net assets	(2,738,192)	9,991,254
Net assets at beginning of year	18,730,737	8,739,483
Net assets at end of year	\$ 15,992,545	\$ 18,730,737

STATEMENTS OF CASH FLOWS

Years Ended December 31	2008	2007
OPERATING ACTIVITIES		
Change in net assets	\$ (2,738,192)	\$ 9,991,254
Adjustments to reconcile change in net assets to net cash provided by operating activities:		
Depreciation and amortization	63,787	63,082
Donation of marketable securities	(116,462)	(227,158)
Net realized and unrealized gain (loss) on investments	3,805	1,578
Proceeds from sales of marketable securities	237,758	225,580
Changes in operating assets and liabilities:		
Pledges receivable	862,649	3,052,251
Marketable securities	(1,057,545)	(23,484)
Prepaid expenses	(21,281)	3,185
Other receivables	50,564	60,034
Accounts payable	(289,705)	179,704
Accrued liabilities	(169,700)	175,196
Research awards payable	9,812,755	(4,881,870)
Net cash provided by operating activities	6,638,433	8,619,352
INVESTING ACTIVITIES		
Purchase of furniture, equipment and improvements	(19,104)	(146,282)
Net cash used in investing activities	(19,104)	(146,282)
Net increase in cash and cash equivalents	6,619,329	8,473,070
Cash and cash equivalents at beginning of year	21,275,262	12,802,192
Cash and cash equivalents at end of year	\$ 27,894,591	\$ 21,275,262

REPORT OF INDEPENDENT AUDITORS

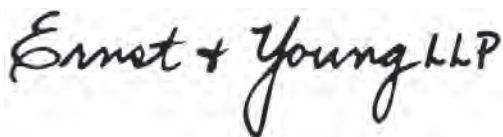
Board of Directors

Prostate Cancer Foundation

We have audited the statements of financial position of the Prostate Cancer Foundation (the Foundation) as of December 31, 2008 and 2007, and the related statements of activities and cash flows for the years then ended. These financial statements are the responsibility of the Foundation's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States and the standards applicable to financial audits contained in *Government Auditing Standards*, issued by the Comptroller General of the United States. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Foundation's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Foundation's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Foundation at December 31, 2008 and 2007, and the changes in its net assets and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States.



September 23, 2009

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