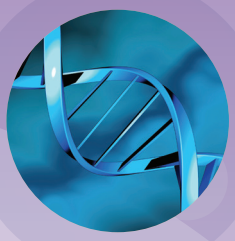
12TH ANNUAL CONFERENCE

Cancer:
A Texas-Sized Problem



JANUARY 22–23, 2015

THE ACADEMY OF
MEDICINE, ENGINEERING & SCIENCE
OF TEXAS

#TAMEST15

THE ACADEMY OF
MEDICINE, ENGINEERING & SCIENCE
OF TEXAS

Welcome to the 12th annual conference of The Academy of Medicine, Engineering & Science of Texas (TAMEST)!

This year's conference focus is on cancer research, encompassing highlights of current problems, new mechanistic information, technology, and therapeutic considerations for a disease that is now the second leading cause of death in the United States.

We have assembled a program of internationally recognized experts who will present their latest research and explore the current status of epidemiology, genetics, initiation, progression, and treatment paradigms for this insidious disease. The program has been designed to be appropriate for both the learned oncologist and scientist, as well as for entering trainees and educated laypeople.

The Edith and Peter O'Donnell Awards program, established in 2005 to recognize the state's most promising young researchers, has honored a total of 40 individuals for their achievements in medicine, engineering, science, and technology innovation. The 2015 Edith and Peter O'Donnell Awards recipients will present their research Thursday afternoon. The evening will conclude with a reception and banquet honoring the O'Donnell Awards recipients.

In the Thursday and Friday luncheon keynotes, we will hear insights from CPRIT Chief Scientific Officer Margaret L. Kripke, Ph.D., and Susan G. Komen® President and CEO Judith Salerno, M.D., M.S.

Thank you for attending TAMEST's Annual Conference and for your continued support of our organization that brings together nationally recognized thought leaders and influential experts from across Texas to promote cross-disciplinary knowledge sharing and discoveries.

Sincerely,

Bert W. O'Malley, M.D.
2015 TAMEST Annual Conference Program Chair

1616 Guadalupe Street, Suite 3.304 | Austin, Texas 78701 | PHONE 512 471 3823 | FAX 512 232 0694 | www.tamest.org | tamest@austin.utexas.edu

AGENDA

THURSDAY, JANUARY 22

8:00 AM – 5:00 PM	**Registration**	Regency Preassembly
8:30 – 9:00 AM	**TAMEST Membership Meeting**	Regency Ballroom ABCD
9:00 – 9:15 AM	BREAK *(Protégés and special guests are invited to join the meeting.)*	

MORNING SESSION

9:15 – 10:00 AM	**Welcome and Remarks**	
10:00 – 10:45 AM	**Keynote Speaker:** ***The ENCODE Project: Interpreting Genomes Using Maps*** **Michael J. Pazin, Ph.D.**, Program Director, Division of Genome Sciences, National Human Genome Research Institute National Institutes of Health	Regency Ballroom ABCD
10:45 – 11:00 AM	BREAK	
11:00 – 11:30 AM	***Epidemiology of Cancer*** **Margaret R. Spitz, M.D.**, Professor, Dan L. Duncan Cancer Center Baylor College of Medicine	
11:30 AM – 12:00 PM	***Obesity, Metabolism and Cancer Prevention: Mechanistic Insights from Transdisciplinary Studies*** **Stephen D. Hursting, Ph.D., M.P.H.**, Professor, Department of Nutrition and the Nutrition Research Institute Director, Nutrition and Cancer Research Program, Lineberger Comprehensive Cancer Center University of North Carolina at Chapel Hill	
12:00 – 1:30 PM	**Luncheon Keynote:** ***CPRIT: Moving Forward*** **Margaret L. Kripke, Ph.D.**, Chief Scientific Officer Cancer Prevention and Research Institute of Texas	Grand Salon

AFTERNOON SESSION

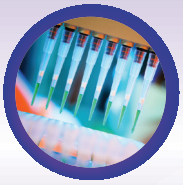
1:45 – 2:30 PM	**Keynote Speaker:** ***Targeting Immune Checkpoints in Cancer Therapy: New Insights and Opportunities*** **James P. Allison, Ph.D. (IOM, NAS)**, Chairman, Department of Immunology; Director, Immunology Platform; Deputy Director, David H. Koch Center for Applied Research of Genitourinary Cancers The University of Texas MD Anderson Cancer Center	Regency Ballroom ABCD
2:30 – 3:00 PM	***Can Theory Help Cancer Biology? The Epithelial-Mesenchymal Transformation as a Test Case*** **Herbert Levine, Ph.D. (NAS)**, Co-director, Center for Theoretical Biological Physics; Hasselmann Professor of Bioengineering Rice University	
3:00 – 3:30 PM	***Advances in Therapy for HER2+ Breast Cancer*** **C. Kent Osborne, M.D.**, Director, Dan L. Duncan Cancer Center; Professor, Medicine and Molecular and Cellular Biology Baylor College of Medicine	
3:30 – 3:45 PM	BREAK	
3:45 – 5:45 PM	**Presentations by the 2015 Recipients of the Edith and Peter O'Donnell Awards**	
6:00 – 7:00 PM	**Reception**	Palm Court
7:00 – 8:30 PM	**Edith and Peter O'Donnell Awards Dinner**	Grand Salon
8:30 – 10:00 PM	**After-dinner Reception**	Palm Court

AGENDA

FRIDAY, JANUARY 23

7:15 – 8:15 AM	**Come and Go Buffet Breakfast**	Regency EFG
8:30 – 9:15 AM	**Keynote Speaker:** ***Targeting the Hedgehog Pathway in Cancer: from Bench to Clinic*** **Frederic de Sauvage, Ph.D.**, Vice President, Molecular Oncology Genentech, Inc.	Regency Ballroom ABCD
9:15 – 9:45 AM	***Prevention and Early Detection of Prostate Cancer*** **Ian M. Thompson, Jr., M.D.**, Director, Cancer Therapy and Research Center, a National Cancer Institute-designated Cancer Center; Glenda and Gary Woods Distinguished Chair in Urologic Oncology, Doctors Hospital at Renaissance; Distinguished Chair in Urologic Oncology; Professor, Department of Urology The University of Texas Health Science Center at San Antonio	
9:45 – 10:15 AM	***Personalizing Medicine for the Kidney Cancer Patient*** **James Brugarolas, M.D., Ph.D.**, Associate Professor of Internal Medicine and Developmental Biology The University of Texas Southwestern Medical Center	
10:15 – 10:35 AM	BREAK	
10:35 – 11:05 AM	***Advanced Imaging of Cancer*** **John D. Hazle, Ph.D.**, Professor and Chairman, Department of Imaging Physics; Bernard W. Biedenharn Chair in Cancer Research The University of Texas MD Anderson Cancer Center	
11:05 – 11:35 AM	***Moving Blood, Removing Boundaries: a Story of Collaboration*** **Stephen H. Little, M.D.**, Associate Professor, Weill Medical College of Cornell University, Cardiovascular Imaging Section, Department of Cardiology Houston Methodist DeBakey Heart & Vascular Center	
11:45 AM – 2:00 PM	**Luncheon Keynote:** ***Blind Alleys and Better Care: Rethinking the War on Cancer*** **Judith A. Salerno, M.D., M.S.**, President and Chief Executive Officer Susan G. Komen®	Grand Salon
2:00 PM	**MEETING CONCLUDES**	

KEYNOTE SPEAKERS



Cancer:
A Texas-Sized Problem

KEYNOTE SPEAKERS

Michael J. Pazin, Ph.D.

Program Director, Division of Genome Sciences, National Human Genome Research Institute
National Institutes of Health

The ENCODE Project: Interpreting Genomes Using Maps

The aspirational goal of the ENCODE Project is to identify all of the functional elements in the human and mouse genomes. Data and derived results are made available through a freely accessible database, ensuring that ENCODE is a community resource for experimental and computational biologists. The functional elements include genes, transcripts, and regulatory sites. Candidate functional elements are identified using genome-wide biochemical assays of RNA production, chromatin structure, protein-DNA occupancy, protein-RNA occupancy, and DNA-DNA interactions. The goal of this presentation is to illustrate how ENCODE is being used to generate or refine hypotheses about the phenotypic consequences of genotypic variation, in the setting of human disease. This presentation will begin with a brief overview of the content and generation of the ENCODE resource. Next, standard use cases for predicting causal variants, target genes, and relevant cell types will be illustrated. Finally, accessing resources from the ENCODE portal will be presented. Ultimately, the mission of the ENCODE Project is to enable the scientific and medical communities to interpret the human genome sequence to understand human biology and to improve health.

Margaret L. Kripke, Ph.D.

Chief Scientific Officer
Cancer Prevention and Research Institute of Texas

CPRIT: Moving Forward

The Cancer Prevention and Research Institute of Texas (CPRIT) has the potential to transform cancer research in the state of Texas and enable great progress in reducing the burden of cancer throughout the world. At its inception, the strategy of CPRIT's research program was to fund the very best science on any cancer-relevant topic. This was achieved by creating a peer review system of the highest caliber and offering a variety of mechanisms through which research was funded. After CPRIT's restructuring by the state legislature and implementation of new rules during 2013, the research program is now back to its mission of supporting cancer researchers across the state. The basic principles underlying the research program are unchanged, namely, CPRIT will continue to fund the highest quality research that can have an impact on cancer now or in the future. However, as part of the restructuring, CPRIT's Oversight Committee has been charged with developing and adopting priorities within each of its three programs. This presentation will highlight the priorities for research, which are to continue to fund research on a broad range of innovative, investigator-initiated projects; target specific underfunded areas of cancer research; and increase the life science infrastructure by supporting recruitment of outstanding cancer researchers to Texas.

KEYNOTE SPEAKERS

James P. Allison, Ph.D. (IOM, NAS)

Chairman, Department of Immunology
Director, Immunology Platform
Deputy Director, David H. Koch Center for Applied Research of Genitourinary Cancers
The University of Texas MD Anderson Cancer Center

Immune Checkpoint Blockade in Cancer Therapy: New Insights and Opportunities

The existence of multiple non-redundant inhibitory pathways that limit T cell responses offers novel strategies for mobilizing the immune system to attack cancer cells. The best characterized of these immune checkpoints is CTLA-4, which inhibits T cell proliferation by interfering with the interaction of the costimulatory molecule CD28 with its ligands B7-1 and B7-2 on the surface of antigen presenting cells. Antibodies to CTLA-4 have proven effective against multiple tumor types in both pre-clinical and clinical studies. Ipilimumab, an antibody to human CTLA-4, showed long term (>10 years) survival benefit in about 20% of patients in a randomized, placebo-controlled trial in late stage melanoma. In 2011, it was approved by the FDA for treatment of late stage melanoma and is now a standard of care for that disease.

The mechanism(s) of action of anti-CTLA-4 are still being elucidated. We and others have shown that CLTA-4 limits T cell proliferation by a cell intrinsic mechanism. However, there is also evidence that anti-CTLA-4 has to engage the target on both effector (Teff) and regulatory (Treg) T cells. Thus anti-CTLA-4 exerts its anti-tumor effects by multiple mechanisms.

PD-1, another checkpoint, recruits a phosphatase and seems to interfere with T cell antigen receptor mediated signaling. It has two ligands, PD-L1 and PD-L2, which are both expressed on dendritic cells. However, many tumor cells also express PD-L1. Antibodies to PD-1 and PD-L1 have both shown objective responses against several tumor types in clinical trials with response rates of about 25%. A recent phase II trial of a combination of anti-PD-1 and anti-CTLA-4 in melanoma showed objective responses in about 50% of late stage melanoma patients.

These studies and their implications for cancer therapy will be discussed.

KEYNOTE SPEAKERS

Frederic J. de Sauvage, Ph.D.

Vice President, Molecular Oncology
Department of Molecular Biology
Genentech Inc.

Development of a Hedgehog Pathway Inhibitor for the Treatment of Basal Cell Carcinoma

The Hedgehog (Hh) pathway is an ancient signalling cascade that directs patterning in most animals and is crucial for proper development. While Hh signalling is very active during embryogenesis, it remains relatively quiet in adult life. However, aberrant reactivation of the pathway in adult tissue can lead to the development of cancer. This presentation will cover examples of how the Hh pathway activation in tumors such as basal cell carcinoma (BCC) and medulloblastoma is the result of inactivating mutations in PATCHED (PTCH) or activating SMOOTHENED (SMO) mutations. Targeting the Hh pathway with small molecule antagonists therefore provides a new therapeutic opportunity for the treatment of these tumor types. Vismodegib (GDC-0449), an oral Hedgehog (Hh) pathway inhibitor, was tested in a first-in-human, first-in-class, phase I study of BCC patients. Strong anti-tumor activity was observed in patients with locally advanced and metastatic BCC, thereby highlighting the potential benefit of inhibiting aberrant Hh signalling in tumors where the pathway is mutated. These results were confirmed in a pivotal study, leading to the approval of vismodegib by the FDA for that indication. While most BCC tumors display Hh pathway activity, only a subset of medulloblastoma tumors are caused by mutations in the Hh pathway. Early evidence of clinical benefit of vismodegib in a medulloblastoma patient selected for Hh pathway activity was demonstrated. However, as is the case for most targeted therapies used in cancer, acquired resistance can develop in man and in mouse models. Mechanisms of resistance appear to always lead to reactivation of Hh signalling, highlighting the profound dependence of these tumors on this pathway.

Judith A. Salerno, M.D., M.S.

President and Chief Executive Officer
Susan G. Komen®

Blind Alleys and Better Care: Rethinking the War on Cancer

The nation has been engaged in the "war on cancer" since the mid-1970s, with Texas researchers and institutions leading the way. But translating research findings into better care for all has been challenging on many fronts. The "war" metaphor may have raised unrealistic public expectations about how science works and created new and unfair burdens for cancer patients. As scientists, clinicians, and philanthropic institutions, it is our new challenge to promote a better, more nuanced understanding among patients and the public about advancing science for improved care.

O'DONNELL AWARDS RECIPIENTS

MEDICINE

Thomas F. Westbrook, Ph.D.

Associate Professor of Molecular and Human Genetics and Biochemistry and Molecular Biology
Baylor College of Medicine

New Addictions in Cancer: from Discovery to Therapeutics

One of the most impactful advances in cancer treatment has been the development of drugs that inhibit cancer-causing genes, or oncogenes. Based on the success of such oncogene-targeting therapies, the cancer community has largely focused on searching for new oncogene targets by massive genetic and epigenetic characterization of cancer genomes. However, the ability to translate this waterfall of genomic knowledge into clinically-beneficial therapeutic strategies is impeded by major obstacles. For instance, the function of approximately 90% of human genes are unknown, thus making it difficult to predict how any individual genetic change in a cancer contributes to disease pathogenesis or treatment opportunities. To address such challenges, Dr. Westbrook's laboratory has spent the past decade developing transformative genetic technologies that enable scientists to rapidly search for gene function. In particular, the Westbrook team has leveraged these technologies to uncover genetic circuits driving human malignancy and new entry points for cancer therapy. Among the most impactful discoveries is the Westbrook team's elucidation of gene networks driving triple-negative breast cancer (TNBC), an aggressive cancer diagnosed in more than 200,000 women annually. Through multi-disciplinary studies, Dr. Westbrook's group has illuminated how these newfound cancer genes that drive TNBC may also confer unique vulnerabilities within breast cancer cells. These studies have culminated in new therapeutic opportunities for breast cancer patients. The implications of these discoveries for the mechanisms and therapeutics of cancer will be discussed.

ENGINEERING

Haiyan Wang, Ph.D.

Professor, Department of Electrical and Computer Engineering
Texas A&M University

Emerging Opportunities in Oxide Nanocomposite Heterostructures: Novel Functionalities by Materials Design

Vertically aligned nanocomposite (VAN) thin films have recently attracted significant research interests for exploring fundamental physics and novel functionalities. In this talk, microstructure evolution in various VAN systems will be reviewed and discussed, ranging from highly-ordered nanocheckerboard, nanopillars embedded in matrix to nanomaze structure. The unique vertically alignment of VAN phases gives rise to more effective strain-, phase- and interface- coupling, resulting in enhanced physical properties. Representative examples include tunable magnetotrasport property, magnetic anisotropy, fuel cells, and energy-related materials. The concept of "novel functionalities by materials design" will be discussed.

O'DONNELL AWARDS RECIPIENTS

SCIENCE

Yuh Min Chook, Ph.D.

Professor of Pharmacology, Biophysics
Eugene McDermott Scholar in Biomedical Research
The University of Texas Southwestern Medical Center

Signals and Blockers in Nuclear-Cytoplasmic Transport

Our research focuses on nuclear-cytoplasmic transport by Karyopherinβ proteins. Using structural/biochemical/bioinformatics approaches, we discovered the first new class of nuclear-localization-signal (named PY-NLS) in 25 years, and showed that physical characteristics, rather than sequence motifs alone, describe PY-NLS recognition. We designed the first nuclear-import inhibitor and revealed properties that govern Karyopherin-PY-NLS affinities. Our discoveries allowed neuroscientists to determine that defective nuclear import can cause familial-ALS disease. We have since determined the structural/energetic basis of ALS mutations in a PY-NLS and correlated them to disease severity. We also showed for the first time how the exportin CRM1 recognizes nuclear-export-signals, both through crystallographic and bioinformatics analyses. Our discoveries in nuclear export were critical for the design of new CRM1 inhibitors that are in clinical trials for cancers. We have revealed unexpectedly different chemical mechanisms for diverse inhibitors that were originally thought to act similarly, possibly explaining greatly improved tolerance of these new drugs.

TECHNOLOGY INNOVATION

Charles J. Collins, Ph.D.

Vice President of Systems Research and Development
Luminex Corporation

MAGPIX: The Power of Multiplexed Detection

Using differentially dyed, functionalized microspheres, Luminex xMAP Technology and platforms allow users to quickly detect and quantify many different analytes (multiplex) from the same sample, at lower cost than single analyte testing and with excellent assay performance. The latest generation of analyzer, the MAGPIX, uses common LEDs as a light source and a CCD camera to capture images of the microspheres. These images, which can contain up to 50,000 beads, are processed through highly sophisticated and adaptive algorithms to translate light into an actionable biological result which is often the diagnosis of a patient's condition. The FDA clearance of the MAGPIX instrument with the multiplexed xTAG Gastrointestinal Pathogen Panel, has brought lifesaving testing to U.S. hospitals. The compact and robust MAGPIX technology has also enabled new testing across the globe, from gastrointestinal disease in Haiti, to malaria testing in Papua New Guinea, to Ebola testing in Africa.

EDITH AND PETER O'DONNELL AWARDS

SPEAKERS

Margaret R. Spitz, M.D.

Professor, Dan L. Duncan Cancer Center
Baylor College of Medicine

Epidemiology of Cancer

Classical epidemiologic studies have made seminal contributions to identifying the etiology of most common cancers. Overall cancer death rates continue to decline in the U.S. among both men and women, among all major racial and ethnic groups, and for most common cancer sites, including lung, colo-rectum, female breast, and prostate. The challenge we now face is how to continue those gains in the face of new obstacles, like obesity and HPV infection. The field of epidemiology has matured dramatically since molecular epidemiology emerged as a defined discipline in the late 1980s as an extension of traditional epidemiologic research to incorporate biomarkers with questionnaire data to further our understanding of the mechanisms of carcinogenesis. Now, the discipline of cancer epidemiology is experiencing a further paradigm shift with the need for rapid and efficient integration of the emerging wealth of genomic, epigenomic, metabolomic, and transcriptomic information for prediction of both cancer risk and of outcome. During this presentation, examples from the lung cancer literature will be used to illustrate these themes. This research requires thoughtful team science initiatives across a growing list of disciplines (e.g. epidemiology, clinical medicine, statistics, environmental health, genomics, behavioral and social science). Finally we emphasize the need to accelerate the pace of translating scientific discoveries to have broader public health impact.

Stephen D. Hursting, Ph.D., M.P.H.

Professor, Department of Nutrition and the Nutrition Research Institute
Director, Nutrition and Cancer Research Program, Lineberger Comprehensive Cancer Center
University of North Carolina at Chapel Hill

Obesity, Metabolism and Cancer Prevention: Mechanistic Insights from Transdisciplinary Studies

The prevalence of obesity, an established risk and progression factor for many cancers, has tripled over the past five decades in the U.S., with ~36% of adults currently obese (BMI>30 kg/m^2). The mechanisms underlying the obesity and cancer connection are becoming increasingly clear and reveal several potential targets and strategies for breaking the obesity-cancer link. We have established in multiple genetically engineered mouse models of mammary, pancreatic, colon, and other epithelial cancers that diet-induced obesity (DIO) enhances tumor development and progression, while calorie restriction (CR), which prevents or reverses obesity, inhibits cancer in these same models. Molecular characterization of tumors from DIO- or CR-treated mice indicate the mammalian target of rapamycin (mTOR) pathway, in collaboration with inflammatory pathways, is central to many of the anticancer effects of CR and procancer effects of obesity. Genetic and pharmacologic approaches in mice further suggest the mTOR and nuclear factor kappa (NFK)-B pathways provide important targets for disrupting the obesity-cancer link. Translational studies involving weight loss interventions in obese women show good concordance between mouse and human serum and tissue markers of energy balance-related hormones and cytokines, and provide further evidence of a central role of mTOR and inflammatory pathways in preventing obesity-related cancers.

SPEAKERS

Herbert Levine, Ph.D. (NAS)

Co-director, Center for Theoretical Biological Physics
Hasselmann Professor of Bioengineering
Rice University

Can Theory Help Cancer Biology? The Epithelial-Mesenchymal Transformation as a Test Case

One of the hallmarks of cancer is the ability of malignant cells to invade tissues, eventually leading to the establishment of secondary tumors far removed from the initial site. As is well-known, death is usually associated with this metastatic spread. In this talk, we describe an analysis of a specific microRNA circuit involved in the epithelial-mesenchymal transition (EMT), which creates motile cells of importance for both embryonic development and cancer metastasis. Our results imply that the form of the regulation allows in general for a hybrid intermediate state of the network, which we identify with cells undergoing collective motility and simultaneously exhibiting partial epithelial properties such as cell-cell adhesion; these cells may also be more likely to exhibit "stemness" properties and concomitant drug resistance. These ideas are quite consistent with recent reports that circulating clusters of tumor cells are the most likely pathway towards establishment of growing metastatic lesions.

C. Kent Osborne, M.D.

Director, Dan L. Duncan Cancer Center
Professor, Medicine and Molecular and Cellular Biology
Baylor College of Medicine

Advances in the Treatment of Breast Cancer

The focus of this presentation will cover how the diagnosis and treatment of breast cancer have changed dramatically over the past 40 years. Tumors have become smaller due to screening, surgery is much less aggressive, and the use of systemic therapy to kill micro-metastases frequently present but undetectable at diagnosis has led to marked reductions in mortality. The recognition that breast cancer is a group of different diseases based on the genomic profile of tumors that gives rise to disparate behavior and treatment response is now further improving outcome. Therapeutically breast cancer is subdivided into luminal (estrogen receptor +) A or B, HER2+ (amplified for the HER2 gene), and triple negative (absence of receptors) based on its gene profile. Luminal A and B tumors are treated effectively with therapies that block estrogen while Luminal B tumors are more aggressive and also need chemotherapy. HER2+ tumors are treated by therapies that target and block HER2 in addition to chemotherapy and endocrine therapy, while triple negative tumors are treated with chemotherapy due to the lack of a clear treatment target. Genomic profiling of tumors is likely to identify other treatment targets that permit further personalization of treatment.

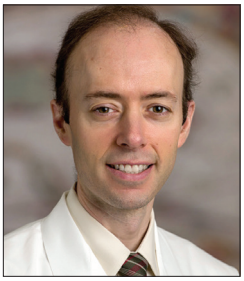
SPEAKERS

Ian M. Thompson, Jr., M.D.

Director, Cancer Therapy and Research Center, a National Cancer Institute-designated Cancer Center
Glenda and Gary Woods Distinguished Chair in Urologic Oncology, Doctors Hospital at Renaissance
Distinguished Chair in Urologic Oncology
Professor, Department of Urology
The University of Texas Health Science Center at San Antonio

Early Detection and Prevention of Prostate Cancer

Prostate cancer is ubiquitous in aging men; although lifetime prevalence exceeds 70%, lifetime risk of death is 2-4%. These data illustrate that most tumors are indolent and diagnosis and/or treatment will not benefit the patient nor society. Prostate carcinogenesis, despite intensive investigations, is complex and multifactorial. Despite a host of putative preventive interventions, only one has proven effective yet complex: finasteride, a five alpha reductase inhibitor, reduces the overall risk of prostate cancer by 30% and treated symptoms associated with age-related prostate hyperplasia. The benefit is only seen for low-risk tumors—those that are found 'by accident' during biopsies whose purpose is to detect life-threatening tumors for which treatment interrupts the natural history of progression and death. Prevention of low-risk tumors, however, reduces the burden of overdetection and overtreatment with cancer screening. Prostate cancer detection has improved dramatically through the integration of multiple biomarkers and biomeasures (e.g., age, family history, race/ethnicity). This presentation will focus on how optimal current prevention and early detection involves identification of patients at risk of disease, and also how offering prevention followed by monitoring with multivariable tools designed to preferentially detect high risk disease, allows treatment and cure.



James Brugarolas, M.D., Ph.D.

Associate Professor of Internal Medicine and Developmental Biology
The University of Texas Southwestern Medical Center

Personalizing Medicine for the Kidney Cancer Patient

Kidney cancer is diagnosed in over 60,000 Americans yearly and is particularly prevalent in Texas. The most common type, clear-cell renal cell carcinoma (ccRCC), is characterized by loss of the *VHL* gene. We discovered that the *BAP1* gene is somatically inactivated in 15% of ccRCC. Mutations in *BAP1* tend to anti-correlate with mutations in a second gene, *PBRM1* (mutated in 50% of ccRCC), whereas BAP1-deficient tumors are of high grade, PBRM1-deficient tumors are of low grade. Interestingly, *VHL*, *BAP1* and *PBRM1* are all located in the same chromosome arm (3p), and one allele is frequently co-deleted in ccRCC. We propose that ccRCC begins with an intragenic *VHL* mutation, followed by loss of 3p and that subsequent mutation in either *PBRM1* or *BAP1* results in tumors with different aggressiveness. Notably, *Vhl* is on a different chromosome than *Bap1* (and *Pbrm1*) in the mouse, which may explain why *Vhl*-heterozygous mice, unlike humans, are not predisposed to ccRCC. However, simultaneous inactivation of both *Vhl* and *Bap1* causes ccRCC in mice. This presentation will provide examples of how our work establishes the foundation for the first molecular genetic classification of sporadic ccRCC, identifies subtypes of ccRCC with different outcomes in patients, and presents a unified model for ccRCC development.

SPEAKERS

John D. Hazle, Ph.D.

Professor and Chairman
Department of Imaging Physics
Bernard W. Biedenharn Chair in Cancer Research
The University of Texas MD Anderson Cancer Center

Advanced Imaging of Cancer

The role of imaging in the management of the cancer patient continues to increase. Imaging is used for early detection, diagnosis, staging, and estimating response to therapy. Traditionally, advances in imaging have largely been in instrumentation—better scanners that are more sensitive, faster, or higher resolution. More recently, interest in imaging function at the molecular level has resulted in advances in the tracers available for detecting more fundamental changes in tissue. Most recently, the computational aspects of signal and image-processing are being recognized as important for the quantification of imaging data as biomarkers for inclusion in *big data* approaches to understanding cancer and response to therapy. This presentation will include an overview of recent trends in instrumentation, tracers, and data processing that are having significant impact on cancer care and research.

Stephen H. Little, M.D.

Associate Professor, Weill Medical College of Cornell University
Cardiovascular Imaging Section
Department of Cardiology
Houston Methodist DeBakey Heart & Vascular Center

Moving Blood, Removing Boundaries: a Story of Collaboration

In health or disease, the cardiovascular system must ensure a continuous flow of blood to all metabolically active human tissues. However, the determinants of efficient blood flow are more complex than the simple necessity of a pump and patent blood vessels. Emerging concepts at the forefront of contemporary cardiovascular science include the coupled mechanics of heart valve function; the prediction of fluid-structure interactions; the non-invasive recognition of abnormal flow and its consequences; and the pursuit of long-lasting repair and restoration of cardiovascular function. This presentation will highlight the collaboration among Houston's medical, academic, and engineering communities that has brought innovation in visualization, physical simulation, and mathematical modeling to the objective of improving outcomes for patients with heart valve dysfunction. Our research team coalesced around the vision that heart function can be characterized according to engineering principles of materials and fluids, and reproduced both physically and via dynamically coupled fluid-mechanical simulation. A flow system for functional imaging of normal and prosthetic heart valves has significantly advanced progress toward patient-specific treatment options. By forming this multi-disciplinary collaboration we have begun to develop computational and physical models to simulate the complex multi-physics problems which characterize the human cardiovascular system.

PROTÉGÉS

Protégés are invited to attend the conference as special guests of TAMEST Members.

Erez Lieberman Aiden, Ph.D.
Assistant Professor, Molecular and Human Genetics
Baylor College of Medicine
Brendan Lee, Ph.D.

Regina C. Almeida, Ph.D.
Researcher, Computational Mechanics
LNCC - Brazil / ICES - The University of Texas at Austin
J. Tinsley Oden, Ph.D.

Todd Alan Anderson, Ph.D.
Professor and Chair, Department of Environmental Toxicology
Texas Tech University
Danny Reible, Ph.D.

Umesh Bageshwar, Ph.D.
Assistant Professor, Department of Molecular and Cellular Medicine
Texas A&M Health Science Center
Akhil Datta-Gupta, Ph.D.

Bonnie Bartel, Ph.D.
Ralph and Dorothy Looney Professor, Department of Biosciences
Rice University
The Late James L. Kinsey, Ph.D.

Oguzhan Bayrak, Ph.D.
Professor, Department of Civil, Architectural and Environmental Engineering
The University of Texas at Austin
James O. Jirsa, Ph.D.

Abdeldjelil Belarbi, Ph.D.
Hugh Roy and Lillie Cranz Cullen Distinguished Professor, Department of Civil and Environmental Engineering
University of Houston
Kaspar William, Ph.D.

Kapil N. Bhalla, M.D.
Medical and Scientific Director, Cockrell Center for Advanced Therapeutics
Houston Methodist Research Institute
Neal Copeland, Ph.D.

Sibani Lisa Biswal, Ph.D.
Associate Professor, CHBE
Rice University
George J. Hirasaki, Ph.D.

Roger T. Bonnecaze, Ph.D.
Co-Director, William and Bettye Nowlin Chair in Engineering, NASCENT Engineering Research Center
The University of Texas at Austin
Donald R. Paul, Ph.D.

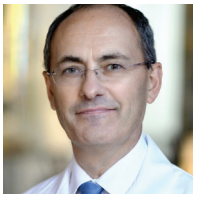
Luis H. Camacho, M.D.
Director
Center for Oncology and Blood Disorders
George L. Stegemeier, Ph.D.

Jenny C. Chang, M.D.
Director
Houston Methodist Cancer Center
Nancy A. Jenkins, Ph.D.

Sharon Y.R. Dent, Ph.D.
Chair, Department of Epigenetics and Molecular Carcinogenesis
The University of Texas MD Anderson Cancer Center
Guillermina "Gigi" Lozano, Ph.D.

Ethan Dmitrovsky, M.D.
Provost and Executive Vice President
The University of Texas MD Anderson Cancer Center
Helen Piwnica-Worms, Ph.D.

PROTÉGÉS



Matthew J. Ellis, Ph.D.
Director, Lester and Sue Smith Breast Center
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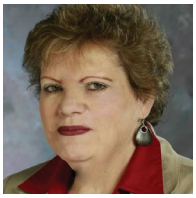

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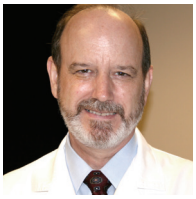

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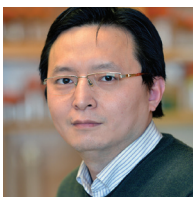

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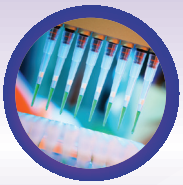

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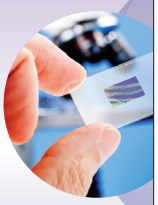

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