SYMPOSIUM PROGRAM

22nd Annual International Symposium of the Hunter College Center for Study of Gene Structure & Function

sponsors:

Weill Cornell Medical College, Clinical & Translational Science Center (CTSC)

Hunter College of the City University of New York

This symposium is dedicated to the memory of Erwin Fleissner PhD, former Hunter Gene Center Director (1987-1998), who made important contributions to cancer research throughout his career.

Additional CTSC member institutions: Memorial Sloan-Kettering Cancer Center, Hospital for Special Surgery, Hunter College School of Nursing, Cornell University Cooperative Extension.
Collaborator: New York Academy of Sciences.

The Weill Cornell Medical College designates this educational activity for a maximum of 5 AMA PRA Category 1 Credits™.

Physicians should only claim credit commensurate with the extent of their participation in the activity.

http://cancersymposium.hunter.cuny.edu

Center for Study of Gene Structure and Function

The Gene Center is a consortium of researchers within Hunter College of The City University of New York — one of the largest public universities in the nation. At the heart of the Gene Center's mission is an imperative to build unique collaborations among biologists, chemists, biopsychologists, biophysicists, and bioanthropologists; to recruit and equip outstanding faculty; to develop and share core research facilities; and to implement strategies for scientific networking.

Since the Center's inception in 1985, the growing number of papers published in peer-reviewed journals and the number and amount of grants obtained by the faculty have been the most visible hallmarks of the Center's success. The Gene Center provides a vibrant research environment marked by workshops on cutting-edge research techniques; frequent research colloquia by guest scientists; and an annual international symposium, which is a major event on the New York scientific calendar.

The Gene Center encourages bright undergraduates to make a career of scientific research by hosting a Summer Program for Undergraduate Research (SPUR). Established in 1994, SPUR was formed to prepare and mentor qualified American undergraduate students who would like to pursue graduate biomedical research. SPUR was especially developed to recruit and nurture minority talent. Hunter College is a leader in academic diversity, with an undergraduate student population that reflects the demographics of New York City. Dr. Robert Dottin, Director of the Gene Center, along with the Hunter College community has successfully diversified the faculty and graduate student bodies, providing role models for excellence in Science.

Visit the Gene Center website: http://genecenter.hunter.cuny.edu

This activity has been planned and implemented in accordance with the Essentials and Standards of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Weill Cornell Medical College and Hunter College of the City University of New York. Weill Cornell Medical College is accredited by the ACCME to provide continuing medical education for physicians.

The RCMI Program enhances the research capacity and infrastructure at minority colleges and universities that offer doctorates in health sciences. http://www.ncrr.nih.gov/resinfra/ri_rcmi.asp

National Center for Research Resources

The NCRR provides laboratory scientists and clinical researchers with the environments and tools they need to understand, detect, treat, and prevent a wide range of diseases. This support enables discoveries that begin at a molecular and cellular level, move to animal-based studies, and then are translated to patient-oriented clinical research, resulting in cures and treatments for both common and rare diseases. NCRR connects researchers with one another, as well as with patients and communities across the Nation, to harness the power of shared resources and research. http://www.ncrr.nih.gov

NATIONAL INSTITUTES OF HEALTH

The NIH, a part of the U.S. Department of Health and Human Services, is the primary Federal agency for conducting and supporting medical research. Composed of 27 Institutes and Centers, the NIH provides leadership and financial support to researchers in every state and throughout the world. Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability. http://www.nih.gov

Clinical and Translational Science Center

The Clinical and Translational Science Center (CTSC) is a unique collaboration between renowned biomedical and community organizations centered on Manhattan's east side. Weill Cornell Medical College and Graduate School of Medical Sciences is home to the administrative core of the CTSC, led by CTSC Program Director Julianne Imperato-McGinley, MD, Associate Dean of Translational Research and Education at Weill Cornell Medical College (WCMC).

In addition to WCMC, the CTSC partner institutions include:

- Hunter College, Center for Gene Structure and Function
- Hunter College, School of Nursing
- Hospital for Special Surgery
- Memorial Sloan-Kettering Cancer Center
- Cornell University Co-operative Extension in New York City

Affiliated hospitals include New York-Presbyterian Hospital, Lincoln Medical Center, Methodist Hospital, New York Downtown Hospital, New York Queens Hospital, Wyckoff Heights Medical Center, and Brooklyn Hospital.

The CTSC is designed to bring together the resources of all partner and affiliate institutions to facilitate novel translational research. Separately, these institutions include superb academic centers of excellence, a diverse patient base, and a unique community-engagement program designed to foster collaboration between community groups and translational research scientists. Each partner and affiliate has an unmistakable character that enhances multi-disciplinary interaction. Integration of these unique resources and intellectual assets will facilitate translation of research findings in the laboratory to clinical research at the bedside and ultimately to best practices within underserved communities.

For more information about the CTSC, please visit http://www.med.cornell.edu/ctsc. A Translational Research Support Team and a wide range of services, including core laboratories and professionally staffed patient care inpatient and outpatient units, are available to support clinical and basic science investigators who are interested in translational research. Contact a CTSC Research Facilitator to find out more: hks2001@med.cornell.edu.

The CTSC is funded through the Clinical and Translational Science Awards, a national consortium that is transforming how clinical and translational research is conducted.

The 22nd Annual International Symposium of the Center for Study of Gene Structure & Function at Hunter College, with the Weill Cornell Medical College Clinical and Translational Science Center, is supported by the National Institutes of Health, National Center for Research Resources, Research Centers in Minority Institutions - G12-RR-003037 and Clinical Translational Science Award - UL1RR024996

9:00am **Opening and Welcoming Remarks**
Robert Dottin, Director of the Center for Study of Gene Structure & Function and Professor of Biology at Hunter College, CUNY
Jennifer J. Raab, President, Hunter College, CUNY

9:15am **Tribute to Erwin Fleissner**
David Foster, Rosalyn Yalow Professor of Biology at Hunter College, CUNY

9:20am **Remarks by Sidney A. McNairy, Jr.,** Director, Division of Research Infrastructure, National Center for Research Resources, National Institutes of Health and **Julianne Imperato-McGinley,** Associate Dean of Translational Research, Weill Cornell Medical College

MORNING SESSION

Interfacing with Patients: Prevention to Treatment

Kenneth Offit, Memorial Sloan-Kettering Cancer Center, Moderator.

9:30am **Olufunmilayo Olopade,** Keynote Speaker
Center for Clinical Cancer Genetics, University of Chicago Medical Center
Nature, Nurture and Breast Cancer

10:05am **Otis Brawley**
American Cancer Society
A Historical Perspective of Breast Cancer Health Statistics

10:30am **Break**

10:45am **Larry Norton**
Memorial Sloan-Kettering Cancer Center
Cancer as a Disease of Cell Mobility

11:10am **Franco Cavalli**
Oncology Institute of Southern Switzerland, Bellinzona
The Worldwide Fight Against Cancer: Problems and Hopes

11:30am **Panel discussion with Q&A**

12:00pm Lunch & Science Poster Session

AFTERNOON SESSION

Molecular Targeted Pathways for Better Cancer Treatments

Clifford Hudis, Memorial Sloan Kettering Cancer Center, Moderator.

1:30pm **Robert Weinberg,** Keynote Speaker
Massachusetts Institute of Technology and Whitehead Institute
Mechanisms of Malignant Progression

2:05pm **Michael F. Clarke**
Stanford Institute for Stem Cell and Regenerative Medicine
Consequences of Utilization of Stem Cell Pathways by Cancer Cells

2:25pm **Break**

2:40pm **Poster Awards Ceremony**

3:00pm **Jill Bargonetti**
Hunter College City, University of New York
Pharmacogenomics for Cancers with Compromised p53

3:20pm **Neil Bander, MD**
Weill Cornell Medical College, New York-Presbyterian Hospital
Targeted Treatment of Metastatic Prostate Cancer with a Radiolabeled Antibody

3:40pm **Panel discussion with Q&A**

4:10pm **Summary of the Day**
John Leonard, Weill Cornell Medical College, New York-Presbyterian Hospital

4:20pm **Closing Remarks**
Robert P Dottin, Director, Hunter College, Gene Center

Olufunmilayo Olopade, MD

Center for Clinical Cancer Genetics,
University of Chicago Medical Center

Nature, Nurture and Breast Cancer

Abstract:

- Inherited mutations in the BRCA1 and BRCA2 tumor suppressor genes are the strongest indicators of breast and/or ovarian cancer risk.
- Understanding the limitations of the various mutation ascertainment methods is critical when assessing of the literature reporting BRCA1/2 mutation frequencies in different populations.
- Prevalence of BRCA1/2 mutations among high-risk cancer patients may vary by ethnicity, study inclusion criteria, and mutation detection techniques.
- Many studies focus on the prevalence of BRCA1/2 mutations in different ethnic populations. However, the cancer risks associated with these mutations are a function of mutation penetrance.
- Founder mutations in some populations may affect the prevalence of inherited BRCA1/2 mutations. The limited genetic variability in members of founder populations can help reduce the variability in penetrance of BRCA1/2 mutations, providing a more reproducible assessment of true BRCA1/2-associated cancer risk in these populations.
- Clinicians interested in providing personalized cancer-risk counseling for patients should understand the contributions of BRCA1/2 mutations in diverse populations, BRCA1/2 mutation penetrance, and potential modifying factors particular to patients'

Bio: The Walter L Palmer Distinguished Service Professor of Medicine and Human Genetics at the University of Chicago and Associate Dean for Global Health, Dr. Olufunmilayo (Funmi) Olopade epitomizes the "bench to bedside" philosophy of research in her application of scientific discoveries to clinical medicine and has seamlessly integrated her findings into clinical applications. As a Hematologist/Oncologist, Dr. Olopade specializes in cancer risk assessment and treatment of aggressive breast cancers that disproportionately affect young women. A member of many professional societies, including the Association of American Physicians, Dr Olopade has national and international recognition as a cancer geneticist. A speaker in much demand, she effectively communicates the benefits of advanced cancer research, inspires students and colleagues, and provides a role model for women scientists worldwide.

Dr. Olopade received her medical degree with distinction from the University of Ibadan in Nigeria. She came to the United States as a resident in internal medicine at Cook County Hospital, Chicago where she was named Chief Medical Resident. Dr. Olopade completed her postdoctoral fellowship training in the section of Hematology/Oncology at the University of Chicago and was appointed to the faculty in 1991. Dr Olopade is Founding Director of the Cancer Risk Clinic in the Department of Medicine and holds many other faculty, hospital, and administrative posts.

Dr. Olopade is the recipient of numerous honors and awards including the James S. McDonnell Foundation Scholar award, the Doris Duke Distinguished Clinical Scientist award and a 2005 MacArthur Fellowship "genius" grant.

Otis Brawley, MD

American Cancer Society

A Historical Perspective of Breast Cancer Health Statistics

Abstract: A major theme of this talk is that disparities by race, area of geographic origin or socioeconomic status do exist. Many of the disparities are related to disparities or inequities in pattern of care among the poor and especially among Black Americans. There are differences in preventive services as well as differences in treatment once diagnosed. It is an unsettling truth that we as a society have made meager efforts to solve this problem. While healthcare disparities are a civil rights issue, adequate healthcare is a human right.

In landmark papers, Bach and colleagues(1) have catalogued the literature, disease by disease, to show that almost always the literature supports the concept that " equal treatment yields equal outcome in the treatment of cancer" and Shavers and Brown(2) detailed the data demonstrating that a larger proportion of minority and poor patients receive less than optimal care when compared to non-minority patients. In plain language "there is not equal treatment."

In Scotland and in the U.S., the poorest Americans tend to present with higher stage disease at diagnosis. Studies of Scots and Americans show that wealthier women with breast cancer are more likely to present with estrogen receptor positive disease when compared to poorer women even within the same stage. A higher portion of the poorer women are overweight or obese (3;4). In a large study of Americans, breast cancer mortality rates were higher among women with less education than among women with more education. This finding was true irregardless of race (5).

An important question deserving more scientific resources includes: "What is it about poverty that influences breast cancer tumor biology and the molecular markers of breast tumors?" What are the environmental influences on tumor biology? The word "environmental" has broad meaning and includes dietary influences and other chemical pollutants as well as reproductive habits.

We in medicine often do a sort of medical racial profiling to identify persons at higher risk for a disease. A Black American with breast cancer is more likely to have a triple negative tumor meaning the tumor is less likely to express estrogen receptors, progesterone receptors, and her 2 neu (6). Most studies suggest that equal treatment yields equal outcome among equal patients and there is not equal treatment for many in the U.S., meaning that a black woman is less likely to get optimal care in the U.S. compared to a white woman with the same disease.

The study of Lund et al (7) is eye opening. She assessed care received by black and white women in a population based SEER registry. Black women experienced longer treatment delays after a diagnosis, regardless of stage at diagnosis. Black women were 4 to 5 fold more likely to experience delays in treatment of greater than sixty days after diagnosis. For local-regional disease, significantly more black women did not receive cancer directed surgery (7.5% vs 1.5% of white women). Among patients meriting breast conserving surgery, only 61% of blacks vs 72% of whites received radiation. Among women who should have received hormonal therapy, black women were less likely to receive it (7). Griggs et al (8) found evidence that some chemotherapy drugs are given in lower than recommended doses due to obesity. In the U.S., blacks have a higher prevalence of obesity than whites.

Access to care is a real problem in the U.S. It is only one element in the problem of disparities in health. Of 285 million Americans, 35 million (12%) are poor, more than 50 million have no health insurance. The number of Americans who have inadequate health insurance is even larger than the number of uninsured. Of Americans living without health insurance, they include 20% of all blacks, 32% of all Hispanics, 11% of all whites. The absolute number of whites without health insurance is larger than the black and Hispanic number combined. We might be able to persuade more Americans to support efforts to eliminate health disparities if it was defined in socioeconomic terms versus racial terms.

Rational health promotion and advocacy of behavioral change is imperative if we are to reduce disparities. Beyond race, we as health care providers must realize that poverty and unfortunate circumstance drive many in the human race to receive less than optimal care and incorporate unhealthy habits. So often, scientists have obsessed about biologic differences among racial groups and not focused on the question "how do we provide adequate care to include preventive care and education to those who so often do not receive it?" These are academic issues for nurse and physician health care providers as well as social workers, economists, and others.

1. Schrag D, Panageas KS, Riedel E, Cramer LD, Guillem JG, Bach PB et al. Hospital and surgeon procedure volume as predictors of outcome following rectal cancer resection. *Ann.Surg.* 2002;236:583-92.
2. Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. *J.Natl.Cancer Inst.* 2002;94:334-57.
3. Gordon NH. Socioeconomic factors and breast cancer in black and white Americans. *Cancer Metastasis Rev.* 2003;22:55-65.
4. Thomson CS, Hole DJ, Twelves CJ, Brewster DH, Black RJ. Prognostic factors in women with breast cancer: distribution by socioeconomic status and effect on differences in survival. *J.Epidemiol.Community Health* 2001;55:308-15.
5. Albano JD, Ward E, Jemal A, Anderson R, Cokkinides VE, Murray T et al. Cancer mortality in the United States by education level and race. *J.Natl.Cancer Inst.* 2007;99:1384-94.
6. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. *JAMA* 2006;295:2492-502.
7. Lund MJ, Brawley OP, Ward KC, Young JL, Gabram SS, Eley JW. Parity and disparity in first course treatment of invasive breast cancer. *Breast Cancer Res.Treat.* 2008;109:545-57.
8. Griggs JJ, Culakova E, Sorbero ME, van RM, Poniewierski MS, Wolff DA et al. Effect of patient socioeconomic status and body mass index on the quality of breast cancer adjuvant chemotherapy. *J.Clin.Oncol.* 2007;25:277-84.

Bio: As the chief medical officer and executive vice president of the American Cancer Society, Otis Webb Brawley, MD, is responsible for promoting the goals of cancer prevention, early detection, and quality treatment through cancer research and education. He champions efforts to decrease smoking, improve diet, detect cancer at the earliest stage, and provide the critical support cancer patients need. He also guides efforts to enhance and focus the research program, upgrade the Society's advocacy capacity, and concentrate community cancer control efforts in areas where they will be most effective. Further, as an acknowledged global leader in the field of health disparities research, Dr. Brawley is a key leader in the Society's work to eliminate disparities in access to quality cancer care.

Dr. Brawley currently serves as professor of hematology, oncology, medicine and epidemiology at Emory University. From April of 2001 to November of 2007, he was medical director of the Georgia Cancer Center for Excellence at Grady Memorial Hospital in Atlanta, and deputy director for cancer control at Winship Cancer Institute at Emory University. He has also previously served as a member of the Society's Prostate Cancer Committee, co-chaired the U.S. Surgeon General's Task Force on Cancer Health Disparities, and filled a variety of capacities at the National Cancer Institute (NCI), most recently serving as Assistant Director.

Currently, Dr. Brawley serves as a member of the Centers for Disease Control and Prevention Breast and Cervical Cancer Early Detection and Control Advisory Committee. He served as a member of the Food and Drug Administration Oncologic Drug Advisory Committee and Chaired the NIH Consensus Panel on the Treatment of Sickle Cell Disease. He is listed by Castle Connelly as one of America's Top Doctors for Cancer. Among numerous other awards, he was a Georgia Cancer Coalition Scholar and received the Key to St. Bernard Parish for his work in the U.S. Public Health Service in the aftermath of Hurricane Katrina.

Dr. Brawley is a graduate of University of Chicago, Pritzker School of Medicine. He completed his internship at University Hospital of Cleveland, Case-Western Reserve University, his residency at University Hospital of Cleveland, and his fellowship at the National Cancer Institute.

Larry Norton, MD

Memorial Sloan-Kettering Cancer Center

Cancer as a Disease of Cell Mobility

Abstract: The high cell density, rapid growth rate and large population size of cancer are conventionally attributed to a pathologically high ratio of cell production to cell death. Yet these features might also or instead result from inappropriate cell movement, already understood to underlie invasion and metastasis. This integrating concept could induce a broadening of our existing anticancer pharmacopoeia, which, with mitosis as its predominant target, is now seldom curative.

Norton, L. and J. Massague, *Is cancer a disease of self-seeding?* Nat Med, 2006. **12**(8): p. 875-8.

Bio: Larry Norton, M.D is Deputy Physician-in-Chief and Director of Breast Cancer Programs at Memorial Sloan-Kettering Cancer Center. He is Scientific Director of The Breast Cancer Research Foundation (BCRF), and has served as chairman of the BCRF Medical Advisory Board since its inception in 1993. Dr Norton is Past President of the American Society of Clinical Oncology, and Chair of the ASCO Foundation. A Presidential Appointee to the National Cancer Advisory Board of the NCI (1998-2004), he is the first incumbent of the Norna S. Sarofim Chair in Clinical Oncology at MSKCC and recipient of the American Society of Clinical Oncology's 2004 David A. Karnofsky Memorial Award.

After receiving his M.D. from the College of Physicians and Surgeons, Columbia University, he trained in Internal Medicine at the Albert Einstein College of Medicine. He then served as a Clinical Associate and Investigator at the NCI prior to joining the faculty of the Mount Sinai Medical Center in New York from 1977-1988. He is currently Professor of Medicine, Weill Medical College of Cornell University.

Dr. Norton has served on or chaired numerous committees of governmental and professional organizations, including the NCI's Cancer Clinical Investigations Review Committee, its Cooperative Breast Cancer Tissue Resource (Registry), and the Consensus Development Conference on Treatment of Early Stage Breast Cancer (1990). He has also served on several committees of the Institute of Medicine of the National Academy of Sciences. Dr. Norton is on the editorial board of several medical publications, and is an active clinical and laboratory investigator. He is the co-author of the Norton-Simon Model, which has broadly influenced cancer treatment and research for over twenty-five years.

Dr. Norton has received numerous honorary visiting professorships including the Belsky-Moranis Memorial Lectureship, New York University Medical Center; the Shoshana Biran Visiting Professorship, Hadassah University Hospital, Jerusalem; the Schlager Visiting Professorship, Dana-Farber Cancer Institute; the Vivian Saykaly Visiting Professorship, McGill University and Université de Montreal 2003; and the Paul Carbone Visiting Professorship, University of Wisconsin Comprehensive Cancer Center.

He has also been honored by many organizations including Y-ME National Breast Cancer Organization, the American-Italian Foundation for Cancer Research, the Don Shula Foundation, NABCO, Cancer Care, Share (NY), and the Susan G. Komen Foundation.

Franco Cavalli, MD

Oncology Institute of Southern Switzerland

The Worldwide Fight Against Cancer: Problems and Hopes

Abstract: In 2030 we could have 27-28 million of new cancer cases yearly with 80% of the deaths occurring in low- and middle income countries. As a comparison in 2002 there were 11 million new cases of cancer and in 1980 the number of deaths was the same in developing and in the developed world. This evolution is linked to the demographic changes, but also to the increased risk in developing countries, in which there are still the poverty related tumors (e.g. cervical cancer, liver cancer, esophageal cancer), but increasingly also the tumors related to the Western style of life (cancer of the breast, prostate, GI, lung). Moreover, due to the lack of prevention, early diagnosis and resources for treatment, the outcome is much worse in the developing countries than in the high income countries. The magnitude of the problem is as yet not well recognized in the media, among politicians and to some extent also in the professional organizations. This is one of the main reasons why the UICC has launched for the first time in Washington, D.C. in 2006 the World Cancer Declaration, which has just been updated in Geneva (August 2008). This Declaration is setting targets for 2020-2030, which will be explained in details, problems and hopes in this worldwide fight against cancer will be discussed in depth.

Bio: Franco Cavalli obtained his M.D. from the Medical University, Bern (Switzerland) and upon completing his studies he joined the Department of Internal Medicine, Inselspital, Bern and then the Institute of Medical Oncology at the same institution until 1978.

He has been Head of the Division of Oncology, Ospedale San Giovanni, Bellinzona (Switzerland) since 1978 and was appointed Honorary Professor in internal medicine, specialising in oncology, on the Medical Faculty at the University of Bern. He has been Director of the Oncology Institute of Southern Switzerland (IOSI), Bellinzona since 1999.

His expertise is also called upon by countless Scientific Boards, Committees and Task Forces, the most recent include the Scientific Board of the Istituto Nazionale dei Tumori Regina Elena, on which he serves as Member, the Scientific Committee of the European School of Oncology (ESO) in the capacity of Vice-President. He was appointed President of the International Union Against Cancer (UICC) in 2006 and also currently serves as Board Member of ECCO – the European CanCer Organisation.

Franco Cavalli is author of 500 publications, work which has been recognised through several Awards and Prizes of prestige, the most recent include the Swiss Award (Man of the Year) for Societal Merits, and the Montaigne Prize, the Toepfer Foundation.

Robert Weinberg, PhD
Keynote Speaker

MIT and Whitehead Institute for Biomedical Research

Mechanisms of Malignant Progression

Abstract: The progression of primary tumors to states of invasiveness and metastasis represents a problem of great complexity that must be addressed, since metastases represent the causes of 90% of cancer-associated mortality. The formation of macroscopic metastases represents the end-point of a long sequence of changes that together is termed the invasion-metastasis cascade. More specifically, cells within the primary tumor acquire invasiveness, intravasate, translocate through the circulation, extravasate, form micrometastases; the latter may, with low probability, grow into macroscopic metastases, this last step being termed colonization.

A series of transcription factors have been identified that appear to play key roles in this process by programming a transdifferentiation process termed the epithelial-mesenchymal transition (EMT). These transcription factors (TFs) are normally operative in early embryogenesis, where they organize key steps of morphogenesis. In doing so, they impart to epithelial cancer cells many of the cell-biological phenotypes of mesenchymal cells, thereby causing these cells to become motile, invasive, and relatively resistant to apoptosis. By opportunistically accessing and expressing these latent TFs, cancer cells acquire the multiple attributes that enable them to complete most of the steps of the invasion-metastasis cascade, up to but not including colonization.

Recently researchers in my laboratory have discovered that, induction of the EMT confers on epithelial cells, perhaps unexpectedly, many of the attributes of stem cells, including the phenotype of self-renewal. By doing so, the EMT empowers cancer cells to acquire the replicative potential that they need in order to spawn macroscopic metastases at sites of dissemination. The consequences of this acquisition of stem cell-like phenotypes will be discussed.

Bio: Dr. Robert A. Weinberg is a founding member of the Whitehead Institute for Biomedical Research and the Director of the Ludwig Center for Molecular Oncology at the Massachusetts Institute of Technology (MIT). He is an internationally recognized authority on the genetic basis of human cancer.

Dr. Weinberg and his colleagues isolated the first human cancer-causing gene, the ras oncogene, and the first known tumor suppressor gene, Rb, the retinoblastoma gene. The principal goal of his current research program is to determine how cancer cells collaborate with normal cells to create viable tumors and ultimately metastases. Much of his current research is focused more specifically on how primary tumor cells metastasize and how this process depends on the formation of cancer stem cells.

Dr. Weinberg is the author or editor of five books and more than 350 articles. Three of his books intended for a lay audience, are "One Renegade Cell", "Racing to the Beginning of the Road: The Search for the Origin of Cancer" and "Genes and the Biology of Cancer," co-authored with Dr. Harold E. Varmus, former Director of the National Institutes of Health. More recently, he has published a textbook "The Biology of Cancer", which is intended for doctoral students learning about this disease. He is an elected Member of the U.S. National Academy of Sciences and the Institute of Medicine and is a Fellow of the American Academy of Arts and Sciences.

Among Dr. Weinberg's honors are the Discover Magazine 1982 Scientist of the Year, the National Academy of Sciences/U.S. Steel Foundation Award in Molecular Biology, the Sloan Prize of the General Motors Cancer Research Foundation, the Bristol-Myers Award for Distinguished Achievement in Cancer Research, the Landon Prize of the American Association for Cancer Research, the Gairdner Foundation International Award, the Keio Medical Foundation Prize, and the 1997 National Medal of Science. He has served on scientific advisory boards for the Institute of Molecular Pathology in Vienna, Austria and the Massachusetts General Hospital in Boston.

Born in Pittsburgh in 1942, Dr. Weinberg received his B.S. (1964) and Ph.D. (1969) degrees in Biology from MIT. He did postdoctoral research at the Weizmann Institute in Rehovoth, Israel and the Salk Institute in La Jolla, California, and then returned to MIT in 1972. In 1982, he was appointed Professor of Biology at MIT and also became one of the five founding Members of the Whitehead Institute. He has been an American Cancer Society Research Professor at Whitehead and MIT since 1985.

Michael F. Clarke, MD

Stanford Institute for Stem Cell and Regenerative Medicine

Consequences of Utilization of Stem Cell Pathways by Cancer Cells

Abstract: Most common cancers, such as cancers of the breast and colon, arise in organs such as the breast that contain a small population of stem cells that constantly replenish the mature cells of the tissue. Stem cells are defined by the ability to divide and give rise to a new stem cell (self-renewal), as well as the ability to give rise to the differentiated cells of an organ, and thus are the only long-lived cell population in many tissues. Epithelial tumors consist of a heterogeneous population of cancer cells that differ in their apparent state of differentiation, suggesting that solid tumors might represent aberrant organs containing a cancer stem cell population that maintains the ability to self-renew. Indeed, using a xenograft model of human breast, colon and head and neck cancers, a phenotypically-distinct subset of the cancer cells (cancer stem cells) has been found to have the exclusive ability to form tumors. The remaining cancer cells, which often form the bulk of the tumor, are unable to self-renew or sustain tumorigenesis. Recently, it has become apparent that some oncogenes and tumor suppressor genes also regulate self-renewal, the process by which both normal and malignant stem cells maintain themselves. The process of self-renewal is de-regulated in cancer stem cells resulting in tumor formation. Extensive molecular and cellular analyses of normal and malignant breast, head and neck, and colon stem cells will be discussed. These analyses have revealed new pathways that regulate self renewal as well as resistance to cytotoxic therapies in normal and cancer stem cells.

Bio: Dr. Michael F. Clarke is an International Leader in the area of Stem Cell Biology. Dr. Clarke is the Associate Director of the Stanford Institute for Stem Cell Biology and Regenerative Medicine. In addition to his clinical duties in the division of Oncology, Dr. Clarke maintains a laboratory focused on two areas of research: i) the control of self-renewal of normal stem cells and their malignant counterparts; and ii) the identification and characterization of cancer stem cells. In particular, his laboratory is pursuing how Cancer Stem Cells self-renew to maintain themselves and escape the genetic constraints on unlimited self-renewal that regulate normal stem cell numbers. His laboratory has discovered that the proto-oncogene Bmi-1 regulates stem cell self-renewal via an epigenetic mechanism. By investigating the pathways upstream and downstream of Bmi1, the laboratory is actively investigating the molecular pathways that regulate self-renewal. His focus is to aid in the development of more effective treatment therapies for various forms of Cancer. Dr. Clarke's group has developed a technique that allows the isolation and characterization of tumorigenic and non-tumorigenic populations of cancer cells present in human breast, colon and head and neck cancer tumors.

Jill Bargonetti, PhD

Hunter College City, University of New York

Pharmacogenomics for Cancers with Compromised p53

Abstract: The genetics of each cancer differs in subtle and apparent ways. While mutations and oncogenic proteins are used to sabotage normal cell growth programs, increasing evidence underscores the single hub pathway of the p53 regulatory circuit as a critically apparent Achilles heel. Oncogenic Mdm2 variations subvert the normal function of the p53, as do mutations within the p53 gene itself. Our laboratory investigates how to capitalize on the genetic changes to better target the type of death pathways that function in tumor cells with compromised p53 that result from either a single nucleotide polymorphism in the mdm2 gene or mutations in the p53 gene. The compromised p53 molecules in these two scenarios are different but early evidence suggests that some small molecules and DNA damaging drugs are effective at killing cells with either disrupted pathway. Using human cancer cell lines and *C. Elegans* we are comparing the influence of small molecules, gene silencing and DNA damaging agents on inhibiting the growth of cells with these altered p53 pathways. We have found that targeting the absence of p53 tumor suppressor activity can be very powerful. Results from experiments targeting the Mdm2 pathway and the lack of p53 pathway will be presented along with an explanation of the possible benefits for targeting cancers with compromised p53.

Bio: Molecular biologist Jill Bargonetti is a cancer researcher, and tenured Professor at the City University of New York with a joint appointment at Hunter College and the Graduate Center. Professor Bargonetti has done extensive research on the p53 protein, which assists in the suppression of tumor cell growth. Mutation of the p53 gene is found in numerous different tumor types. Prior to arriving at Hunter College in 1994, Bargonetti was a post-doctoral fellow at Columbia University (1990-1994). Jill Bargonetti holds a M.S. and a Ph.D. in Molecular Biology, both from New York University (1987 and 1990 respectively) and a B.A. from SUNY Purchase.

Awarded the prestigious Presidential Early Career Award for Scientists and Engineers by President Bill Clinton in 1997, Bargonetti has received numerous research grants from the National Science Foundation and the National Institutes of Health as well as grants from the American Cancer Society and the Department of Defense Breast Cancer Research program. The most recent prestigious grant funding is from the Breast Cancer Research Foundation. She was a member of the National Cancer Policy Board from 2002 until 2005 (a board of the Institution of Medicine and National Research Council of the National Academies).

Neil Bander, MD

Weill Cornell Medical College/
New York-Presbyterian Hospital

Targeted Treatment of Metastatic Prostate Cancer with a Radiolabeled Antibody

Abstract: Serum Prostate Specific Antigen (PSA) testing has ushered in an era of far earlier diagnosis of prostate cancer (PC). Nevertheless, PC remains the second most common cause of cancer deaths in US men. Despite earlier diagnosis, patients who undergo surgical or radiation treatment for clinically localized cancer have approximately a 1 in 3 chance of developing recurrent disease due to micro-metastatic disease present at the time of diagnosis. It is estimated that of the >2,000,000 men in the US with a diagnosis of PC, as many as 1,000,000 have rising PSAs after local therapy prior to developing overt metastatic disease. These patients represent an ideal setting for a therapeutic intervention as they are easily identified, easily categorized as to level of risk (e.g., by PSA doubling time) and they have a very low disease burden.

Given the relative radiation-sensitivity of PC and the existence of a well established, cell surface, PC-restricted antigen—Prostate-Specific Membrane Antigen (PSMA)—radio-immunotherapy represents a reasonable approach to treat patients with after micro-metastatic disease in an effort to prevent the inexorable progression to metastatic disease followed by death. Virtually all PCs express PSMA at high levels. We have developed a high affinity humanized anti-PSMA mAb, J591, that has now undergone testing in several hundred patients in a series of phase I and II clinical trials. J591 has proven to be highly efficient and accurate at targeting disseminated PC in approximately 95% of unselected patients with clinically evident metastatic PC. In order to treat micro-metastatic disease, we have coupled 177Lutetium (177Lu), a radiometal ideal for radiating lesions of 1-3 mm, to J591. Although 177Lu is not optimal for patients with more advanced, bulky disease, we felt it necessary/appropriate to first establish the safety and tolerability of 177Lu -J591 in late stage patients who had exhausted all standard therapies. In a recently completed phase 2 trial in this advanced disease setting, a single dose of 177Lu -J591 proved to be well tolerated and 47% of the patients treated at the maximum tolerated dose had major PSA responses. We are now at the point of applying this therapeutic to the micro-metastatic patient population that is far more appropriate for the physical characteristics of 177Lu —those with small volume disease measured in millimeters. A randomized, multi-center trial is about to begin to determine whether we can significantly alter the natural history of PC in this clinical setting and perhaps prevent the development of clinical metastatic disease that otherwise ultimately leads to PC mortality.

Bio: Dr. Bander graduated from The Johns Hopkins University and received his MD degree from the University of Connecticut. After completing surgical and urological residencies, Dr. Bander completed a NIH Immunology Training Fellowship in the laboratory of Lloyd Old and was a Ferdinand C. Valentine Fellow in urological oncology under Willet F. Whitmore, Jr. at Memorial Sloan-Kettering Cancer Center. In 1983, he joined the faculty at Cornell Medical Center where he is now the Bernard and Josephine Chaus Professor at The New York Presbyterian Hospital-Weill Medical College of Cornell University and Member in the Department of Urology at Memorial Sloan-Kettering Cancer Center.

Dr. Bander initially concentrated his efforts in the area of kidney cancer where he developed the world's largest collection of monoclonal antibodies to normal kidney and kidney cancer-related antigens. In the 1980's, his studies defined the antigenic profile of normal and cancerous kidney cells and further elucidated the histogenesis of renal cancer. He defined multiple subtypes of renal cancer, at the molecular level, long before it was recognized that there were multiple varieties of renal cancer, before it was recognized that these subtypes had distinct clinical behaviors and long before molecular profiling of cancers came into vogue. His efforts led to, and as Principal Investigator he directed, the first clinical trials of monoclonal antibodies in kidney cancer.

In the early to mid '90s, Dr. Bander turned his attention to the field of prostate cancer. His laboratory developed the first monoclonal antibodies to the extracellular domain of prostate-specific membrane antigen. The lead antibody has completed phase 2 trials and will enter phase 3 trials in the near future.

Dr. Bander has authored more than 100 peer-reviewed publications in the fields of monoclonal antibodies, immunotherapy and urological cancers. He is considered the world's authority on the use of antibodies for imaging and therapy of patients with urological malignancies. He serves on several journal editorial boards, review committees for the Department of Defense Prostate Cancer Program, NIH, the Kidney Cancer Association Medical Advisory Board, is a member of numerous professional societies and several biotech advisory boards. His contributions have been recognized by the American Urological Association as well as the Urological Associations of Germany and Japan. He has won several awards including the Society of Surgical Oncology Ewing Research Award, the German Urology Association Research Award, and 8 consecutive Prostate Cancer Foundation Awards, and has been a Visiting Professor on 4 continents.

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Thank you for attending the 22nd Annual International Symposium of the Hunter College Center for Study of Gene Structure & Function.

This event is sponsored by Weill Cornell Medical College, Clinical & Translation Science Center (CTSC) and Hunter College of the City University of New York.

This symposium is dedicated to the memory of Erwin Fleissner PhD
From Erwin Fleissner's book: Vital Harmonies: *Molecular Biology and Our Shared Humanity* (Columbia University Press, 2004).

"We are part and parcel of the world that we live in. We are part of a process that has been going on on Earth for a very long time. It is now our responsibility to take care of this process and the new dimension that has been realized by the creation of human culture. This is our touchstone for ethics.

We cannot predict the ill fate that might come our way. The heroism of life comes from its fragility. All the best things that we strive for can be destroyed—they are mortal, just as we ourselves are. I am convinced that evolution on this planet, in its human phase, has been partly a heroic effort to construct and preserve a kind of life that is worth living. It is not an effort guaranteed to succeed, and only with hope, intelligence, and hard work can we sustain it."

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