NCI CENTER FOR CANCER RESEARCH

FELLOWS & YOUNG INVESTIGATORS NEWSLETTER

Volume 7 Issue 1 May 2008

From the Editor's Desk

Welcome to the spring issue of the CCR-FYI Newsletter with a slightly refreshed layout. Included in this issue is a review of the successful 2008 Colloquium held in March 2008, highlighting the various presenters, sessions and award winners. Also included is a candid interview with one of the 2007 outstanding mentor awardees, Dr. Sue Wickner. In addition, we have started an article highlighting fellow's research success so check out the article about explaining differences observed in the tumor micro-environment of prostate cancer patients. Finally, read about the trials and tribulations of teaching at a small college through a first hand experience. We hope that you enjoy these articles and if you have any suggestions or are willing to contribute an article, please contact us.

Tim Chan, Ph.D.
Michal Legiewicz, Ph.D.
Selinda Orr, Ph.D.
Raed Samara, Ph.D.
Editors

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IF YOU HAVE ANY COMMENTS, SUGGESTIONS OR WOULD LIKE TO CONTRIBUTE TO FUTURE NEWSLETTERS PLEASE EMAIL US AT
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CCR-FYI News

Summary of the 2008 Colloquium

The 8th Annual Fellows and Young Investigators Colloquium, previously referred to as the Retreat, was held this year in Ocean City, Maryland from March 3rd-5th. There were over 330 registered participants in attendance to hear a wide variety of outstanding presentations from the invited keynote speakers and the various oral presentations by current fellows and young investigators of the CCR. This year, we had the great pleasure of having Drs. Carlo Croce, John Schiller, Stefanie Vogel and Patricia Steeg as our keynote speakers representing a wide variety of research interests. Following the first meal, Dr. Croce spoke about his research involving the association of microRNAs with the formation of cancers. The following day, Dr. Schiller spoke to the audience about the characterization and development of the human papilloma virus (HPV) vaccine using virus-like particles and other methods such as carrageenan to further inhibit HPV infections. Dr. Vogel discussed the role of TLR4 in disease and has associated two TLR4 single nucleotide polymorphisms with susceptibility to RSV infection. The last keynote speaker, Dr. Steeg, presented data on the progression of brain metastasis from breast cancer patients with $HER2^{+}$ tumors and identifying possible treatments to improve the outcomes for patients with brain metastasis. In addition, Dr. Matthew Hall, was selected as the Outstanding Postdoctoral Fellow and his talk focused on the design of drugs that would improve action in multi-drug resistant tumors for improved responses.

Dr. Carlo Croce presents his work on MicroRNAs and Cancer.

Dr. John Schiller presenting at the 2008 Colloquium.

Dr. Jonathan Wiest, Associate Director of Training and Education, discusses mentorship.

Throughout the colloquium, there were six professional development workshops that examined various issues that a fellow and young investigator will come across during their career. These workshops covered the topics associated with becoming an independent researcher by discussing “Grant Writing”, “How to set up a lab” and “Scientific Management”. Several other workshops focusing on jobs and the scientific career were also emphasized in “CV Critique, Interviewing and Negotiating Skills”, “International Career Opportunities” and “Academia, Institute or Industry: Which one is for you?”. These workshops provided the unique opportunity for fellows to seek guidance from experts in the aforementioned areas in an informal setting and obtain insightful tips.

In continuance with the theme of career guidance, the colloquium provided another chance for young investigators to plan their future careers. The third annual career fair session was modified to a two-day event that attracted various companies, embassies and government institutions to attend. These organizations provided information on

Dr. Mark Udey, Deputy Director, during the Director’s Open Forum Session.

career opportunities and some organizations such as Pfizer even held on-site interviews with promising young investigators. The career fair exhibitors included the following: Canadian Embassy, Contact Singapore, Dendreon Corporation, DFG-German Research Foundation, Genentech Inc., Invitrogen Corporation, Lockheed Martin Corporation, NCI Cancer Training Branch, NCI Office of Science Planning and Assessment (OSPA), NCI Technology Transfer Center, NIH Division of International Services (DIS), NIH Fellows Committee (FELCOM), National Postdoctoral Association (NPA), Pfizer Inc., The Resume Doctor and U.S. Food and Drug Administration (FDA) Office of New Drugs.

Fellows and young investigators talking science during the poster sessions held during the two nights of the Colloquium.

The colloquium was also a time for attendees, ranging from fellows, graduate students and post bacs, to present their work to their colleagues. There were 35 oral presentations and two poster sessions with travel awards presented for outstanding presentations in both the oral and poster sessions. Travel awards were presented on the final day of the colloquium. Congratulations to Drs. Snehalata Pawar, M. Raza Zaida, Aaron Schetter and Daniel Fitzgerald for exceptional oral presentations and to Drs. Jie Li, Jong Heun Lee, Lisa Wright Nolan and Anil Shanker for outstanding poster presentations. These eight individuals were awarded $1000 travel awards to be utilized for attendance at scientific conferences. In addition, a raffle was held to win one of four Ipod Shuffles upon submission of both the colloquium and general scientific surveys. The results from both of these surveys are currently being compiled and this data will help highlight future issues that both the colloquium and the Steering Committee can address.

Dr. Robert Wiltrout providing some words of wisdom

The 2008 CCR Fellows Colloquium provided a great opportunity for members of the CCR to broaden their knowledge in various fields of research. The sessions enabled the colloquium attendees to network and start collaborations, which may be sustained for the rest of their scientific careers. This should create a highly productive network for scientists to advance cancer research.

Participation in this event was an invaluable training experience for those individuals who organized, moderated and executed the colloquium. We would like to thank the CCR Office of the Director, under the guidance of Dr. Robert Wiltrout, for the continuing financial support to provide the fellows and young investigators with this invaluable opportunity. Special thanks also go out to Dr. Jonathan Wiest, the Associate Director of Training and Education, and to Palladian Partners, who worked closely with the organizing committee. We would also like to acknowledge all of the individuals who volunteered many countless hours in order to make this colloquium a success.

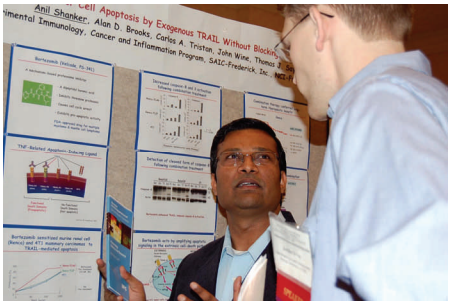
2008 Members of the Steering Committee.

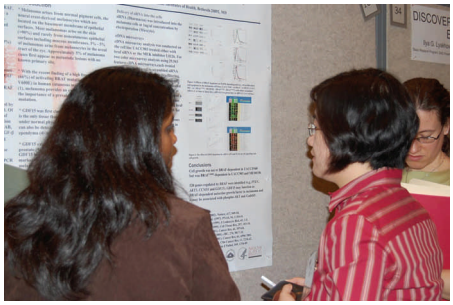
Submitted by:
Selinda Orr, Ph.D.
Tim Chan, Ph.D.
2008 Colloquium Committee Co-chairs

Pictorial Highlights of the 2008 Colloquium

8th Annual Fellows & Young Investigators

Colloquium





Articles

Recognizing Outstanding Mentors

On September 14, 2007, Dr. John Niederhuber announced the Outstanding Mentor and Mentors of Merit Awardees. The awardees have been chosen each year since 2001 through a competitive review conducted by a panel of postdoctoral fellows. The review focuses on seven separate criteria addressing the quality of the nominee's mentoring: mentoring record, professional expertise, accessibility, communication, training environment, provision of visibility for trainees, and commitment to trainee career development.

The 2007 Outstanding Mentor Awardees from the Center for Cancer Research were Curtis C. Harris, M.D. and Sue Wickner, Ph.D. In the last issue of the newsletter, we highlighted Dr. Harris' mentoring achievements. This issue spotlights Dr. Sue Wickner.

Dr. Sue Wickner

Dr. Sue Wickner has been the Chief of the Molecular Biology of DNA Section in the Laboratory of Molecular Biology since 1994. During that time she has successfully mentored 7 postdoctoral fellows, including her current fellows, as well as 10 postbaccalaureate fellows and students. It is clear that Dr. Wickner has made a positive impact on the young investigators who trained under her. When I was asked to write this article, I decided to ask the individual that nominated Dr. Wickner for the award why she felt that Dr. Wickner was an outstanding mentor. One answer I received was that Dr. Wickner promotes a good balance between work and personal life, a balance she exhibits in her own life and career. Her trainees are also very enthusiastic about the highly collaborative research environment that Dr. Wickner promotes. She selects individuals with various research interests, skills, and expertise to join her group and encourages lab members to work together to move projects forward. Additionally, she advises them to seek collaborations outside the lab. As part of the collaborative research environment within her lab, she provides fellows with the opportunity to gain their own mentoring skills by encouraging fellows to mentor both postbaccalaureate fellows and summer students on a regular basis.

In addition to being a remarkable scientific mentor, Dr. Wickner is an excellent role model for early-career scientists. Within the NIH community, she has recently served on the NCI Promotion Review Panel and the NIH Central Tenure Committee. Dr. Wickner is also an active member of the scientific community at-large, engaging in many responsibilities outside of NIH. She has served on the Editorial Board of PNAS, multiple section panels for the American Academy of Arts and Sciences, as well as various committees for the National Academy of Sciences and ASBMB. Dr. Wickner has also chaired a multitude of sessions at national scientific meetings. In 2004, Dr. Wickner was elected to the National Academy of Sciences, one of the most prestigious achievements in the scientific community.

When Dr. Wickner was asked what she sees as the most important aspects to successfully mentor fellows, she indicated that it's critical to speak to her fellows daily, whether it be about their current project, overall direction of their work, future plans, or the skills needed (beyond publications) to be successful in science. The most enjoyable part of mentoring for Dr. Wickner is seeing fellows and students do well as a result of their hard work.

Many of the fellows who have trained under Dr. Wickner have moved on to successful positions in both academia and government. She feels that the most important trait her trainees should possess is self-motivation and therefore seeks out individuals who "really want to do it." From there, she guides and facilitates them to gain the tools needed to achieve both success in the laboratory and well-rounded CVs for their continuing careers.

It is a challenge to identify all of characteristics that have made Dr. Wickner such a well-

respected and outstanding mentor to the fellows and students who have trained with her over the last 14 years. The fact that Dr. Wickner was nominated for and received the 2007 Outstanding Mentor Award demonstrates that her trainees truly appreciate the time and effort Dr. Wickner puts forth to mentor them to become successful in their careers and life in general.

Article submitted by Krista Zanetti, Ph.D., M.P.H.

Bethesda CCR Fellows PASS

(Presentation Skills Seminar)

Every 2nd and 4th Tuesday of the month from 3:30 - 4:30 pm
(in Building 37, 4th Floor Conference Room)

NCI-Frederick Postdoc Seminar Series

Starts again in September

Every 1st and 3rd Tuesday of the month
Bldg 426 Conference Room

This seminar series is designed as a platform on which to practice conference/job talks and receive constructive feedback from other Fellows
You will Improve your Speaking and Presentation Skills, Learn about Ongoing CCR Research & Meet Other Fellows and Young Investigators

For more information:
Bethesda PASS - contact Brid Ryan : ryanb@mail.nih.gov
NCI-Frederick - contact Madeline Knoebel: wilsonmk@ncifcrf.gov

Interested in joining the Steering Committee?

Attend one of our monthly video-conference meetings on the last Thursday of each month

Where: Bethesda: Bldg 31 Conference Room Rm 3A11
Gaithersburg ATC: 8717 Grovemont Circle, Rm 142
Frederick: Bldg 549, Conference Room A

Time: 11:00 AM– 12PM
http://ccr.nci.nih.gov/careers/fellows

Significant Differences Exist in the Tumor Microenvironment of Prostate Cancer between African-American and European-American Patients

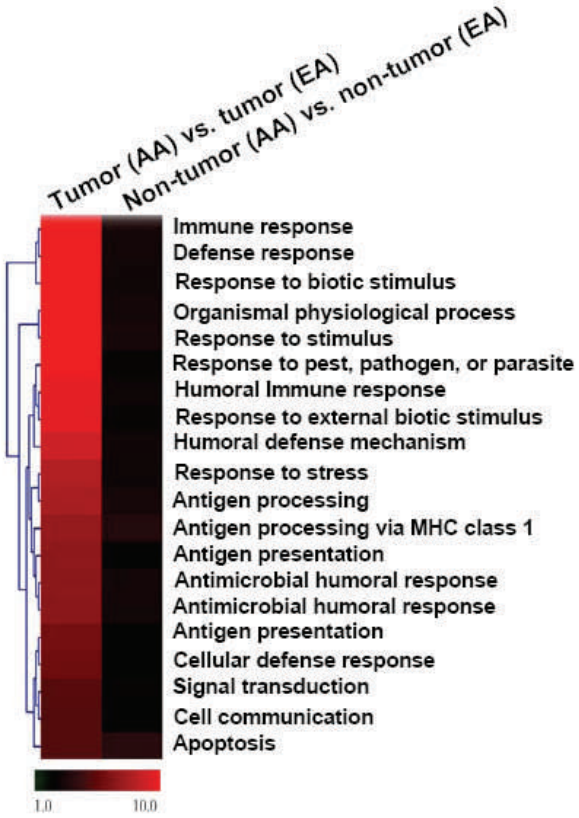
African-American men experience the highest prostate cancer incidence and mortality rates in the United States. Race/ethnic differences in tumor biology may account for this well-established cancer health disparity.

Dr. Tiffany Wallace

Prostate cancer is the second leading cause of cancer mortality for men in the United States. In addition to age and family history, race/ethnicity is an established risk factor for prostate cancer. Specifically, African-American men have the highest incidence and mortality rates of prostate cancer for all race/ethnic groups. The increased mortality is partly explained by an earlier onset and a more rapid progression of the disease. While socioeconomic factors contribute to this health disparity, they do not fully explain the excess burden in incidence, morbidity, and mortality that are seen amongst African-American men. We hypothesized that racial differences in tumor biology exist, and they contribute to more aggressive prostate tumors in African-Americans. The results of this study appeared in the February 1 issue of *Cancer Research*.

To identify biological differences between race/ethnicity groups, the gene expression patterns of prostate tumors from African-American men and European-American men were compared. Numerous differences between the two patient groups were found. Most notably, many of the differentially expressed genes between African-American and European-American men were related to immune and inflammatory responses. Furthermore, several known metastasis-promoting genes were more highly expressed in the tumors from African-Americans.

Gene expression differences were investigated in prostate tumors from 33 African-American and 36 European-American men. All tumors included in the studies were well matched for clinical parameters to obtain the most unbiased results possible. In addition to the prostate tumors, surrounding non-tumor tissues from a subset of the patients were also analyzed.



Pathway analysis reveals that differentially expressed genes between African-American and European-American patients have a common association with immune response pathways.

Disease association and pathway analysis were used to identify biological networks that are functionally different in tumors from African-American and European-American men. The disease association analysis, which is a bioinformatics tool that can associate dysregulated genes with other common diseases, revealed a significant relationship of the differentially expressed transcripts with autoimmune disease and various inflammatory disorders. These findings were strengthened by pathway analyses, which showed that immune-specific processes are highly enriched when comparing African-

American men with European-American men (Figure). Interestingly, the heightened immune and inflammatory responses seem to be specific to the tumor microenvironment because these pathways were not altered in the non-tumor tissues.

Interestingly, several well-characterized tumor progression genes were differentially expressed between the two patient groups. Most notable were a subset of metastasis-associated genes that were expressed at higher levels in the tumors from African-American men. We hypothesize that the heightened expression of these genes may correlate with increased aggressiveness and poorer outcome in this patient group.

The cause of the altered immune response in tumors from African-American men remains to be elucidated. We hypothesize that the heightened immune response in African-American patients could be the result of predisposing factors. We found that many interferon-related genes were higher expressed in the tumors from African-American men. This distinctive interferon signature may indicate possible viral involvement in this African-American patient population, however further investigation is needed before any firm conclusions can be made. Alternatively, there could be a more general difference in immune function between the two patient groups. Recent studies of healthy volunteers reported gene expression variations in immune-related pathways between Caucasians and Africans from Nigeria.

Although preliminary, these findings may have important implications toward the advancement of cancer therapy. Immunotherapy is a promising therapeutic approach for the treatment of prostate cancer and has recently been the focus of numerous clinical trials. Our data suggest that African-American patients and European-American patients may respond differently to these types of therapies. In addition, the observed differences may offer opportunities to develop tailored therapies designed to target specific immune functions in the cancerous prostate.

In summary, this study identified differences in tumor biology between African-American and European-American prostate cancer patients. The differences may contribute to the disease aggressiveness in African-American men and could influence the patients' response to therapy.

Dr. Tiffany Wallace is a fellow in the Laboratory of Human Carcinogenesis with Dr. Stefan Ambs.

Teaching at Small Colleges: Myths vs Reality

I was invited to prepare an article with the title above, and I gladly accepted. However, as I sit down to write, I realize I am probably not much of an expert on the myths (I'm kind of curious as to what they might be these days) but I do know some of the reality. I came to my position in the Department of Biology at Hood College almost 20 years ago following my Ph.D and a three year post-doctoral experience. In those years I have taught introduction to biology, microbiology, biochemistry, general genetics, prokaryotic genetics, genomics, cell biology and courses titled Society, Science and Technology and an honors course on science and science fiction. This illustrates what I see as one of the central realities of faculty members teaching at small colleges – they must be generalists.

Dr. Craig Laufer

This requirement for generalization comes precisely because we work in small colleges with relatively small academic departments. By small college standards, my department is probably a bit on the large size (10 full-time faculty) and yet each of us, over the course of our careers, have taught many different subjects. Although my teaching responsibilities have largely fallen in the area of cellular/molecular biology, colleagues from departments of three to five end up teaching some really disparate topics (this is not to mention those who teach in the "science department" where you may teach courses as diverse as organic chemistry and human anatomy). In many cases you will not consider yourself an expert in a subject that you will have to teach. To be a successful faculty member at a small college you will have to be that life-long learner who is adept (and confident) in learning new tricks.

Being a generalist has its rewards. I find it professionally and personally enriching to regularly delve into new areas. I also find myself making connections between subdisciplines that I might otherwise have overlooked if my focus was narrower. Although my formal training in microbiology was limited to one undergraduate general microbiology course, I have come to be fascinated by the tremendous diversity of the microbial world, its amazing biochemistry and physiology, and its preeminence in so many biological phenomena. I also believe, particularly for an undergraduate audience, that being a generalist makes it easier to teach effectively. We need to convey the "big picture" to our students, emphasizing connections between topics and providing a conceptual framework for students to "hang" new facts onto. The specialist who has worked on the same or closely related problems and has taught the same subject matter for many years, would, I expect, not have this come as naturally.

Being a generalist has its frustrations too. The reality is that most research today is highly specialized, requiring an on-going effort at maintaining specific expertise and an intimate familiarity with a relatively narrow slice of the literature. Another reality is that the research resources, although highly variable from institution to institution, at small schools are generally not comparable to those available at large, research universities. Of course in addition to expertise and resources the other great requirement for participating in cutting edge, competitive research is having the time to pursue it.

This brings me to the next reality – the typical small college faculty member's time is highly divided. Foremost is the time devoted to one's teaching responsibilities. This is a day to day call on one's time. Unlike research or grant-writing, where the time frame for completing a proposal or project is months or years, there is always a new lecture or new lab that needs to be prepared for the next day or the next week. While worrying about whether your latest proposal will be funded certainly can be stressful, pulling together a lecture or lab exercise a few hours before class time and then having to do a new one again in two days time (and again and again) can also be stressful. Although teaching is most always the primary responsibility of the small college faculty member it is almost never the exclusive one. Academic advising is another typical duty. I often feel like I am running a small career planning and placement and employment agency out of my office between trying to help students find internship opportunities, getting them accepted into graduate and professional schools and finding them employment. Academics in general, and I think small college academics in particular, are infamous for their penchant for meetings and committee work. This can be a good thing. You get to work with interesting colleagues from different disciplines and there is the opportunity for shared governance of the institution between faculty and administration. I probably average around five to ten hours per week, depending on my committee assignments that year, in one kind of meeting or another. As one advances in the academic ranks it is likely you will assume some administrative duties (remember these are small departments so almost everyone will be a chairperson or program director at one time or another). I have served as Department Chair and as Director of a Masters program. These responsibilities can consume enormous time and effort.

What about research and publication and grant funding? The requirements in this area are highly variable from school to school and department to department. In speaking with colleagues from other schools my sense is that some modest level of research productivity is the normal expectation. Accomplishing this is quite a challenge in that the day to day calls on one's time tend to displace your efforts on those projects that have longer time horizons. On the other hand, getting that paper accepted for publication or getting external funding for your research is all the more special given the relative infrequency and the obstacles that have to be overcome.

I find teaching at a small college to be a challenging, and rewarding experience. I do believe that it is a very different career from that of a

faculty position at a research university or a staff position in a government or private lab. A year-long sabbatical at NIH doing only research made the contrast very stark to me. Being able to devote all (or most) of your energies to focus on a specific problem or a set of related problems has its own challenges and rewards. This is not the life of the typical small college faculty member. You will be torn in many directions, teaching multiple subjects at different levels, attending to the various needs of your students, helping to administer your departmental and college-wide programs, working on research projects, writing grants and papers and trying to make a reasonable balance of it all.

Craig Laufer, Ph.D.
Associate Professor, Department of Biology
Director, Biomedical Sciences Graduate Program
Hood College

Congratulations!! 2008 Director's Innovation Award Recipients

The NCI Director's Intramural Innovation Award Program was established in 2006 and offers Career Development awards, valued at $10,000, for fellows. The goals of this award are to support novel proposals that are considered "high-risk" or projects with a potential for high scientific impact in the field, or the ability to generate new technology or intellectual property. This year, 73 proposals from CCR were submitted of which 20 of them were successful and 16 of them are Career Development Awards. The award recipients were recognized during the NCI Intramural Retreat on January 8th, 2008.

The Career Development Award recipients are:

- **Samuel F. Bunting, Ph.D.**, Experimental Immunology Branch
  Mapping Chromosome Breaks in B Lymphocytes Using ChIP-Seq
- **Orla M. Casey, Ph.D.**, Cell and Cancer Biology Branch
  Generation and Characterization of a Transgenic Mouse for the Prostate Cancer Fusion Protein TMPRSS2-ERG
- **Yoshimi Endo, M.D., Ph.D.**, Laboratory of Cellular and Molecular Biology
  Analysis of Wnt Antagonist Gene Methylation in Circulating DNA as a Biomarker for Renal Cell Cancer
- **Theresa M, Geiman, Ph.D.**, Laboratory of Cancer Prevention
  Isolation and Characterization of Cancer Stem Cells Using a Tagged ES Cell Gene Marker
- **Jordan D. Irvin, Ph.D.**, Gene Regulation and Chromosome Biology Laboratory
  Study of Transcriptional Fidelity In Vivo
- **Michal Legiewicz, Ph.D.**, Retroviral Replication Laboratory, HIV Drug Resistance Program
  Arti N. Santhanam, Ph.D., Laboratory of Cancer Prevention
  Structural Determinants at 5' UTR of Cancer Relevant mRNAs Regulated at the Level of Translation
- **Amy E. McKee, M.D.**, Pediatric Oncology Branch
  Neuroblastoma: Every Cell Is a Tumor-Initiating Cell
- **Gianluca Pegoraro, Ph.D.**, Laboratory of Receptor Biology and Gene Expression
  A Functional Screen for the Discovery of Novel Protein Quality Control Factors in Mammalian Cells
- **Ashutosh Rao, Ph.D.**, CCR Office of the Director
  A Mitochondrially Targeted Redox Agent for Enhanced Tumor Killing and Cardioprotection from Doxorubicin
- **Joseph Riss, Ph.D.**, Laboratory of Cancer Biology and Genetics
  Cancer as Wounds That Do Not Heal: In-Vitro and In-Vivo Testing of RCC Combinational Drug Therapy
- **Krisada Sakchaisri, Ph.D.**, Laboratory of Protein Dynamics and Signaling
  A Novel Method (PCAT) for Selective Purification of Dimeric DNA-Binding Proteins
- **Misako Sato, Ph.D.**, Laboratory of Cancer Biology and Genetics
  High Throughput Screening for Drugs that Restore Tumor Suppressor Responses to TGF-beta in Cancer
- **Yih-Horng Shiao, Ph.D.**, Laboratory of Comparative Carcinogenesis
  Pyrosequencing with Terminator Chemistry for Allele-Specific Haplotyping and DNA Methylation
- **Diana A. Stavreva, Ph.D.**, Laboratory of Receptor Biology and Gene Expression
  Real Time Interactions of the p53 Tumor Suppressor with Its Regulatory Elements in Living Cells
- **Christine Tomlinson, Ph.D.**, Laboratory of Cancer Biology and Genetics
  Generation, Characterization and Oncogenic Manipulation of Mammary Progenitor Cells from ES Cells
- **Shinji E. Tsutsumi, M.D.**, Urologic Oncology Branch
  Molecular Determinants for Extracellular Secretion of Heat Shock Protein 90

Applications for the 2009 Director's Innovation awards will be announced later this summer with Letters of Intent (LOI) due in September and the proposals submitted in October.

Written by Tim Chan, Ph.D.