THE DOSSIER

The Digest on Staff Scientists and Staff Clinicians: Information, Employment and Research

June 2011 Issue 5

From the Editor

Welcome to the June issue of The Dossier, a newsletter dedicated to the Staff Scientists and Staff Clinicians (SSSC) of the CCR!

This issue contains important messages from the Director's Office and a special article by Elaine S. Jaffe, M.D. An overview of our 7th Annual SSSC Retreat is also provided. A summary of a workshop series for SSSC, provided by the NIH Office of Intramural Training and Education is presented along with information on Bioinformatics resources at the NIH Library. This issue also highlights the work of Michael Tangrea, Ph.D., Jeff Hanson, M.S., and Jaime Rodriguez-Canales, M.D. and their successful experience in the Laboratory of Pathology. In this issue, we also welcome Caterina Bianco, M.D., Ph.D. and Anne Gegonne, Ph.D., who are our new Section Editors for the *PI Corner* and *Core Corner* of The Dossier, respectively. We hope to continue to provide relevant and pertinent information to aid in the success of SSSCs. Please send your contributions, suggestions and comments to budhua@mail.nih.gov.

Anuradha Budhu, Ph.D. (SS)
Editor-in-Chief
Laboratory of Human Carcinogenesis

In This Issue

SSSC Co-Chairs

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Christophe Marchand, Ph.D., Bethesda Co-Chair, Lab of Molecular Pharmacology, marchand@mail.nih.gov

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From the Office of the Director

Our Innovative Staff Scientists

The NIH Office of Technology Transfer (OTT) works with NCI's Center for Technology Transfer (CTT) to improve both the country's public health and its economy by bringing inventions that are made in government labs to the public sector for commercialization. While it is well known that researchers at the Center for Cancer Research (CCR) produce a large portion of all NIH-licensed inventions, it is less well known that CCR Staff Scientists contribute to a significant number of these innovations.

Examples of impressive Staff-Scientist contributions to this year's inventions available for licensing include quantum dots for labeling cells expressing specific carbohydrate-binding proteins on their surface; a high-throughput screening assay for pro- and anti-angiogenic drugs; and highly defined antibody conjugates with broad utility that can target and deliver small synthetic molecules to various cell surface receptors.

OTT and CTT work hand in hand to move to market inventions such as these, and many more. Whether it is a new treatment approach or a technology, when a Staff Scientist contributes to an invention to a point where non-government enterprise can better accelerate progress, OTT and CTT step in to help. They make sure our scientists have the proper filings in place for disclosure and the protection of intellectual property. This process of technology transfer permits our Staff Scientists to bring in-demand inventions outside government labs when a major scale-up is needed to meet market and public health demands.

"…..CCR staff scientists contribute to a significant number of these innovations……This process of technology transfer permits our staff scientists to bring in-demand inventions outside government labs…. to meet market and public health demands."

CCR leadership acknowledges with gratitude the innovative talent of our Staff Scientists who, year after year, contribute to development of new technologies and, with the help of OTT and CTT, move them out to be licensed and developed in commercial markets.

Robert Wiltrout, Ph.D.
Director, Center for Cancer Research

Please share this newsletter with your colleagues and visit the SSSC website at sssc.nci.nih.gov

The 7th Annual SSSC Retreat (April 11, 2011)

The 7th Annual Center for Cancer Research and Division of Cancer Epidemiology and Genetics Staff Scientist and Staff Clinician (SSSC) Retreat was held on April 11, 2011 at the Natcher building at NIH. This event is particularly important to our SSSC community as it highlights our research, enables networking and provides valuable career development tips. The retreat was very successful this year with interactive participation and some new additions to the agenda.

The retreat was kicked off with introductory remarks from two of the new Chairs of the SSSC Association, Drs. Christophe Marchand and Anu Puri, followed by Drs. Lee Helman and Martha Linet who both highlighted the importance of SSSCs in the greater NCI community. Our fist keynote speaker, Christopher Loffredo, Ph.D., Associate Professor of Oncology and Biostatistics at Georgetown University, gave an engaging presentation on the epidemiology of hepatocellular carcinoma conducted in multiple studies worldwide. He presented on the aspects of risk, prevention and challenges of this disease spanning from the development of the studies, to the data analysis, to current establishment of task forces to address issues highlighted in the findings. Ron Evans, Ph.D., Professor and Howard Hughes Investigator in Molecular and Developmental Biology at the Salk Institute, our second keynote speaker, presented on nuclear receptor pathways and their roles in the circadian clock and muscle endurance.

Throughout the day, brief presentations specific to SSSC's interest and development were given, including tips on collaborations with the extramural community by Dr. Melissa Maderia, Bioinformatics resources by Dr. Sean Davis, career development by Dr. Christophe Marchand and the Quad Review by Drs. Lynne Rockwood and Jeffrey Strathern. Drs. Ofelia Olivero and Anuradha Budhu also provided information on an up-and-coming Mentoring Forum and The Dossier, respectively. Further career development events included the Office of

Dr. Christopher Loffredo (Top Panel) and Dr. Ron Evans (Bottom Panel) provide keynote presentations at the 2011 SSSC Retreat.

Workforce Development workshops on Emotional Intelligence and Conflict Resolution. These workshops were highly attended, very interactive and allowed everyone to participate. This year, we introduced lunch topics, which gathered a smaller number of participants to discuss various subjects including, team science, visibility in committees, grants and much more. Participants enjoyed lunch while experts on the particular topic moderated the discussion. Further networking was feasible through the poster sessions, which were well-attended with over 70 abstracts submitted.

The 7th Annual SSSC Retreat (Con't)

Congratulations to our six awardees who received travel awards that can be used to attend scientific conferences within one year (Drs. Swati Choksi, Phuong Mai, Rimas Orentas, Ana Robles, Binwu Tang and Enrique Zudaire). Thanks to Drs. Jonathan Wiest and Jackie Lavigne for the support of these awards. To wrap up the eventful retreat, Dr. Robert Wiltrout provided closing remarks, once again highlighting the important contribution of the SSSCs to the NCI community. Our thanks to all of the participants and organizers for a successful and engaging day!

Anuradha Budhu. Ph.D. (SS) and Ewy Mathé, Ph.D. (BSS)
(2011 SS/SC Retreat Co-Chairs)

Introducing our new Dossier Section Editors

Please welcome ***Caterina Bianco, M.D., Ph.D. (AS)***, our new Section Editor for the PI Corner of The Dossier. Dr. Bianco received her M.D. from the University of Naples Federico II, Italy, in 1991 and her Ph.D. in Genetic Disease and Gene Therapy from the University G. D'Annunzio, Chieti, Italy, in 2003. Following an oncology residency program at the University of Naples Federico II Medical School, she joined the Tumor Growth Factor Section of the Mammary Biology & Tumorigenesis Laboratory at the NCI in 1996 as a postdoctoral fellow and in 2001 she became a Staff Scientist. In 2011, Dr. Bianco was promoted to an Associate Scientist position. Dr. Bianco's research program focuses on the role played by the embryonic gene Cripto-1 in the pathogenesis of breast cancer. If you would like to write an article for The PI Corner, please email: biancoc@mail.nih.gov with subject title "The PI Corner".

We also welcome ***Anne Gegonne, Ph.D. (SS)***, our new Section Editor for The Core Corner of The Dossier. Dr. Gegonne did her Ph.D. research at the Pasteur Institute of Lille, France, where she contributed to the discovery and initial characterization of the Ets1 proto-oncogene, the founding member of the now large family of Ets transcription factors. After a post-doctoral stint at the Institut Curie in Orsay, France, where she investigated how Ets proteins promote transcription, she joined the laboratory of Dr. Alan Wolffe at NICHD in 1995, where she worked on the role of nucleosome positioning in the control of transcription. In 1998, she joined the laboratory of Dr. Dinah Singer in the Experimental Immunology Branch, where she became a Staff Scientist in 2003. Her research investigates the function of TAF7, a 'basal' transcription factor assembled in a large complex needed to recruit the RNA polymerase II at the transcription initiation site. If you would like to write an article for The Core Corner, please email: gegonnea@mail.nih.gov with subject title "The Core Corner".

The Quadrennial Review Corner

The 2011 Quad Review Summary

When the three quad review panels met this year, the government was operating under a series of short term continuing resolutions and the NIH was preparing for a possible shutdown. The difficult funding environment translated into a more stringent review than previous years. Here is an overview of the three panels' actions this year.

Nineteen Staff Scientists were quad reviewed by a panel of nineteen reviewers. The Promotion Review Panel (PRP) was supplemented with six ad hoc reviewers who were invited to participate because they had new Staff Scientists in their labs. Of the nineteen Staff Scientists reviewed this year, there were four outstanding individuals whose performance in every aspect evaluated was markedly superior to all the other Staff Scientists reviewed this year. The delineation between Outstanding and Excellent groups was unequivocal. Nine Staff Scientists were rated Excellent. This group had substantial accomplishments, but the Outstanding group set the bar really high. There were three Staff Scientists rated Good, and three were Satisfactory. Extremely low productivity was the one factor that, in the end, made it impossible for the panel to rate these six people any higher. All the Staff Scientists rated Good performed significantly better overall than the Satisfactory group. In some instances, mentoring and opportunities may be an issue.

Seven Staff Clinicians were reviewed by the Clinical quad review panel. Four were rated Outstanding, and three were Excellent. The entire Clinical quad review process is actively under revision. The review committee will consist of a PI representative from each Branch. The review criteria will be more applicable to the unique responsibilities of Staff Clinicians, including patient care, clinical protocol support, and training/mentoring activities. The changes will be in place for next year's review. I will outline the new process in a subsequent article.

This is the second year that CCR has done Quad reviews of Bioinformatics Staff Scientists. Four Bioinformatics Staff Scientists were reviewed, two were rated Excellent, one Satisfactory, and one Good. CCR created a separate review panel for Bioinformatics Staff Scientists, with reviewers who rely on bioinformatics tools in their research and are sensitive to the differences between bench and Bioinformatics Staff Scientists. Adjustments in review-

"…..The entire Clinical quad review process is actively under revision……Adjustments in review criteria have been made to acknowledge differences in culture between bench and Bioinformatics Staff Scientists….."

criteria have been made to acknowledge differences in culture between bench and Bioinformatics Staff Scientists. For example, peer reviewed publications are an important measure of productivity, but also considered are database development, development of bioinformatics tools for use by NCI and extramural scientists, or public release of widely used software, even if not published in conventional journals. One concern about using publications as measures of productivity is that there may be a different attitude about granting authorship to those who provide bioinformatics analysis.

Bioinformatics Staff Scientists are a growing group that meets a critical need for computational support across CCR. However, fundamental questions remain regarding hiring mechanism, performance expectations, and review criteria. These will only be resolved at the NIH level, but CCR has definitely started the conversation. The CCR Staff Scientist/ Staff Clinician Organization has also taken a keen interest in this subject. Their advocacy will be a powerful voice, but Bioinformatics Staff Scientists will also benefit from taking more initiative on their own behalf.

Lynne Rockwood, Ph.D.
Office of Scientific Programs

The Bioinformatics Corner

Bioinformatics Support at the NIH Library

Overwhelmed by sequence data? Confused about which tools to use to analyze? How to use those tools can be a struggle in itself. Fortunately, the NIH Library's Bioinformatics Support Program (http://nihlibrary.nih.gov/Bioinformatics) can help.

The program was founded in 2009 by Dr. Medha Bhagwat, who worked previously at the National Center for Biotechnology Information (NCBI). Bhagwat updated a series of courses that she had developed over the past 11 years at NCBI. These courses cover sequence analysis, genome browsers, identifying pathogenic mutations, and more. The program often invites outside trainers to give presentations about their products. The classes are held in the NIH Library's state-of-the-art training room where students are provided a laptop with which they can follow a demonstration exercise and then try one on their own. The courses are in great demand and have been attended by over 1800 participants so far. Current class schedule can be obtained from http://nihlibrary.nih.gov/bioinformatics/training. Bhagwat also teaches an FAES course "BIOL 429 *Practical Bioinformatics"* for credit which includes many of these courses.

Want to learn at your leisure from your computer? The program provides access to a number of free online tutorials and has also purchased over 100 bioinformatics on-line tutorials from Open Helix. The tutorials can be accessed from http://nihlibrary.nih.gov/bioinformatics/online .

The program also provides one-on-one consultations to the researchers on their research projects. NIH Library has recently hired Dr. Lynn Young to provide programming support. Young was formerly at NCI-Frederick and CIT's Division of Computational Bioscience.

The NIH Library has purchased two high performance workstations (64 bit architecture, 24-48Gb RAM and 2TB disk space) dedicated to high throughput data analysis for NIH staff to use. The NIH Library has also been focusing on licensing bioinformatics software for NIH staff. Some of these are available as network licenses that can be accessed from any NIH computer and some are loaded on the workstations in the Library. The list of licensed resources

"…..Dr. Bhagwat updated a series of courses that she had developed over the past 11 years at NCBI. These courses cover sequence analysis, genome browsers, identifying pathogenic mutations, and more. ….."

and instructions on how to register for them are available at http://nihlibrary.nih.gov/bioinformatics/licenses .

The program recently began management of the web site "Molecular Biology at NIH and Beyond": http://nihlibrary.nih.gov/molbio . This site was formerly of the CIT Helix group.

The program's first venture into social networking is Twitter: http://nihlibrary.nih.gov/socialnetworking .

Two articles about the Program were published in the NIH Catalyst and can be accessed from http://nihlibrary.nih.gov/bioinformatics/catalyst and http://nihlibrary.nih.gov/bioinformatics/catalyst2

For more information about the NIH Library Bioinformatics Support Program, please visit the program's webpage, http://nihlibrary.nih.gov/Bioinformatics or contact the Program Coordinator Dr. Medha Bhagwat .

Medha Bhagwat, Ph.D.
Coordinator, Bioinformatics Support Program
NIH Library

The PI Corner

Section Editor: Caterina Bianco, M.D., Ph.D. (*AS*)

The PI Corner column has focused primarily on the role of the Staff Scientist at the NCI. As my perspective is more clinical, I would like to offer a few thoughts on the role of the Staff Clinician. The NIH is known for its often ground breaking basic research, but the patients that come to the NIH and enroll on clinical trials look to the NIH for its excellence in patient care. This superb reputation stems from the expertise and caring of NIH's Staff Clinicians, Research Nurses, and Nurse Practitioners. In part due to the protocol-driven nature of the NIH patient population, sometimes attracting very rare diseases, Staff Clinicians often develop unique skill sets that may be lacking elsewhere.

I would like to highlight a few of the superb diagnosticians working in the Laboratory of Pathology. David Kleiner, M.D., Ph.D. is an internationally recognized authority on hepatitis and liver disease. Martha Quezado, M.D. provides expertise in gastrointestinal pathology, while also being a proficient neuropathologist. The Flow Cytometry service is staffed by Maryalice Stetler-Stevenson, M.D., Ph.D. and Connie Yuan, M.D., Ph.D., both of whom are leaders in their field. Stefania Pittaluga, M.D., is an expert in neoplastic hematopathology, and a specialist in congenital immunodeficiency disorders. These Staff Clinicians, like so many others, are looked to by their peers in the extramural community as leaders, with exceptional clinical and diagnostic skills. They are critical to maintaining high standards in patient care, but also vital to the research mission of the NIH.

Elaine S. Jaffe, M.D.
Head, Hematopathology Section,
Laboratory of Pathology

From The Professional Development Committee

The Office of Intramural Training and Education (OITE) continues to be a resource for Staff Scientists' Career Development. This year, OITE director Sharon Milgram announced the launch of a four-part series for NIH Staff Scientists and Staff Clinicians looking to move to the next stage of their careers or exploring options for the future.

Two of the sessions took place in March, covering an introduction to career planning as well as essential tips for CVs and resumes. A third session focused on career networks took place in April. The sessions were videocast and can be found on the OITE webpage (https://www.training.nih.gov/career_development_ss/sc). I find networking to be the common denominator when it comes to receiving career advice. As Lori Conlan put it in her April presentation, this is a word that sends shivers down the spine of many of us, introverted, dedicated scientists. Yet, we all see the need for networking in order to expand our career. Lori's lively presentation encouraged us to network according to our own personality and style. She covered different networking events as well as how to use conversational skills in them. She spent a good deal of the talk encouraging the use of LinkedIn (http://www.linkedin.com) as a tool to build our networking map. Lori offered to share additional great tips about the use of LinkedIn and other networking opportunities, just send her a note (conlanlo@mail.nih.gov)!

Victoria Virador, Ph.D. (SS)
Medical Oncology Branch

The Core Corner

Section Editor: Anne Gegonne, Ph.D. (*SS*)

Expression Microdissection (xMD) for High-Throughput Analysis of Tissue Specimens

The field of molecular pathology has grown tremendously over the past two decades with the advent of the human genome project and the ubiquitous use of high-throughput molecular analysis methods. Thus, the ability to profile patient specimens has become critical to the discovery and validation of novel biomarkers and biological findings. However, working with tissue samples is a challenge due, in part, to the effect of tissue fixation on biomolecular integrity and the complex, multi-cellular nature of the specimens themselves. Today, there are few technologies that allow for high-quality analysis of tissue sections. To this end, our laboratory, the Pathogenetics Unit (PGU) in the Laboratory of Pathology, focuses on the development of novel technologies for the molecular analysis of tissue specimens. One such technology, Expression Microdissection (xMD), was developed in our laboratory in 2004 (1). xMD enables a high-throughput, unsupervised microdissection process. Based on the use of antibodies for molecular targeting, xMD allows for the procurement of histological targets as determined by the local deposition of the 3,3'-diaminobenzidine (DAB) stain via standard immunohistochemistry (IHC) techniques (Figure 1). Initially, we developed an xMD prototype with our collaborators, Robert Bonner, Ph.D. and Tom Pohida, M.S. Their expertise and the original prototype were essential in advancing the technology forward. The movable stage and fixed laser source of the initial instrument enabled us to dissect epithelial cells at a rate of thousands of cells per second, allowing for a truly high-throughput dissection process.

Using the xMD technology, we completed several DNA methylation studies of the prostate tumor microenvironment, characterizing both tumor-associated stromal and endothelial cells (2, 3). Since the IHC stain defines what is to be procured, the xMD technology enables very fine dissections (on the order of microns), which is beyond the capabilities of current commercial instruments. This allowed us to dissect and analyze cells with challenging morphology, such as blood vessels within the tumor, with an unmatched precision. In addition, this novel approach eliminates the need for visual inspection by an investigator trained in histology or a pathologist to determine which cells are to be dissected.

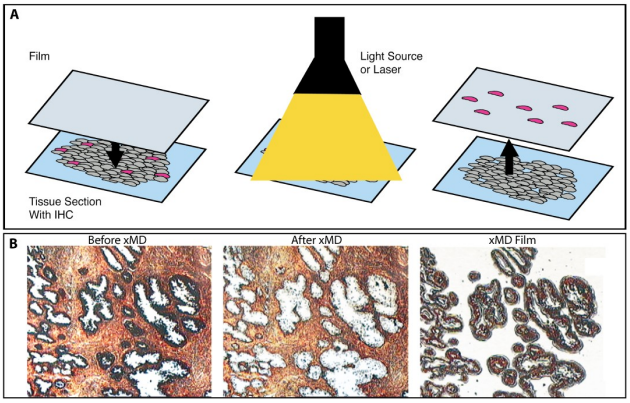


FIGURE 1: Schematic illustrations of expression microdissection (xMD). A) Overview of the xMD method using a flashlamp light source. Cells highlighted in magenta represent those targeted by immunohistochemistry (IHC). B) xMD dissection of prostate specific antigen (PSA) positive epithelial cells from ethanol-fixed paraffin-embedded prostate tissue. Figure adapted from Tangrea *et al*, Diagnostic Molecular Pathology, 2004.

Until recently, xMD studies have been restricted to the experimental prototype. However, to allow for greater public access of the xMD technology, we recently adapted xMD to commercially available laser capture microdissection (LCM) instruments in collaboration with the LCM core facility in the Laboratory of Pathology (4). Michael Emmert-Buck, M.D., Ph.D., one of the inventors of the original LCM technology, supervises the LCM core lab, which consists of Jeffrey C. Hanson, M.S. and Jaime Rodriguez-Canales, M.D. The LCM core lab provides free access to LCM instruments to the entire NIH research community, as well as training on LCM techniques, tissue handling and pathology review. Dr. Rodriguez-Canales is a pathologist and Mr. Hanson is a biologist and biomedical engineer. Both have an excellent understanding of the LCM technologies and are experts in the field. Relying on their expertise was key to adapting the xMD technology to three commercially available LCM machines, the PixCell II, the Veritas, and the Arcturus^{XT}, all of which are available in the LCM core.

The xMD technology relies heavily on close contact between the clear xMD film and the immunostained tissue (Figure 1A). To achieve the optimal contact, Mr. Hanson developed a method of "pre-melting" the xMD film onto the stained tissue slide at a temperature below the film's melting temperature.

The Core Corner (Continued)

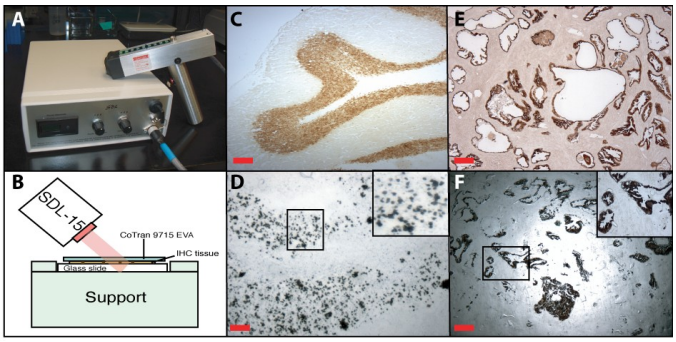


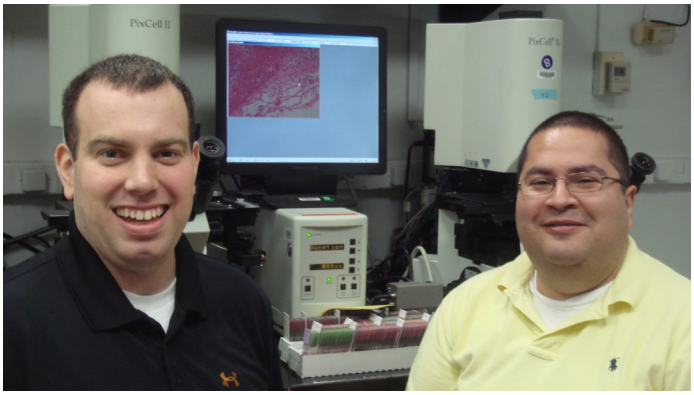
FIGURE 2: A) SDL-15 laser diode. B) Schematic diagram showing the positioning of the SDL-15 for xMD. C) NeuN IHC staining of nuclei in frozen rat brain cerebellum. D) Procurement of NeuN targeted nuclei by handheld xMD. E) Cytokeratin-stained epithelium in a human prostate section. F) Dissection of targeted prostate cells. Figure adapted from Hanson *et al*, Nature Protocols, 2011.

This gentle heating, in combination with the application of physical rolling over the xMD film, ensures the necessary contact for a successful dissection. At the same time, the "pre-melt" step does not increase the amount of non-specific tissue pick-up.

The PGU then utilized this "pre-melting" approach to establish close contact between the tissue and the film as we adapted the xMD technology to an inexpensive, handheld laser source (4). Now, it is possible to perform an xMD dissection on an entire tissue section in minutes, using a laser source that costs ~$1200 (Figure 2).

Our goal has always been to develop xMD and disseminate the technology to the public. Through a productive collaboration with the LCM core lab, we were able to achieve this objective. Currently, collaborators are beta-testing the xMD technology for specific microdissection projects, and we invite all NIH investigators interested in this technique to contact the LCM core lab (ncilcmcore@mail.nih.gov). Our hope is that researchers will find this technology useful and contribute to the improvement and development of xMD in biological research studies and future clinical applications.

Michael A. Tangrea, Ph.D. (SS)
Pathogenetics Unit, LP, CCR



Jeff C. Hanson, M.S.
Biologist
LCM Core Laboratory, LP, CCR

Jaime Rodriguez-Canales, M.D.
Research Fellow
LCM Core Laboratory, LP, CCR

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Announcements

Congratulations!

Join us in congratulating the SSSC 2011 Retreat Travel Award Winners!

From left to right: Drs. Swati Choksi, Phuong Mai, Enrique Zudaire, Rimas Orentas, Binwu Tang and Ana Robles

	Basic Science	Clinical & Translational Research	Epidemiology/ Bioinformatics
First Place	Swati Choksi, Ph.D.	Enrique Zudaire, Ph.D.	Phuong Mai, M.D.
Second Place	Binwu Tang, Ph.D.	Rimas Orentas, Ph.D.	Ana Robles, Ph.D.

Complete or Update your CCR Website!

All Staff Scientists and Staff Clinicians are part of CCR's online Research Directory and should be listed on the Senior Staff Index. If your name is not on this index, or to set up access for you to update your Web content, please contact Ave Cline or Sue Fox, CCR Office of Information Technology. Senior staff members are also listed on each Lab/Branch Home page on the left sidebar.

Please check your Home page. If the information displayed is incomplete, you need to complete it. You can complete or update your Web page content via the CCR Portal Login page at: https://ccrintra.cancer.gov/cms/login/login.aspx and enter with your **NIH login.**

A Call for Content

We need your input! Send your articles or suggestions with subject title "The Dossier" to: budhua@mail.nih.gov

This newsletter is an avenue for you to express your ideas and thoughts regarding being a Staff Scientist or Staff Clinician at CCR and to make pertinent announcements.

Your contribution is very important to the success of The Dossier. Please send us your commentary, announcements and suggestions for topics/subject manner and we will do our utmost to include your material in upcoming issues.

Join one of these SSSC Committees

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