The Dossier

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

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this issue

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From the Editor

Welcome to the second issue of The Dossier, a newsletter dedicated to the Staff Scientists and Staff Clinicians (SS/SC) of the CCR! This issue introduces our Staff Clinician Co-Chair, contains important messages from the Director's Office, our Deputy Director of Intramural Research and a special article by Dr. Howard Young. A summary of our SS/SC retreat is also presented along with informative articles from the Professional Development Committee, details on the quadrennial review and information on bioinformatics resources at NCI. This issue also highlights the work of Dr. Julio Valencia (SS) and his successful experience with the Electron Microscopy Core. We hope to continue to provide relevant and pertinent information to aid in the success of SS/SCs. Please send your contributions and suggestions to budhua@mail.nih.gov.

Anuradha Budhu (SS)

Meet the SS/SC Clinical Co-Chair

John Morris is a board-certified medical oncologist and Staff Clinician in the Metabolism Branch, CCR, NCI. He also completed a post-doctoral fellowship at the bench in the laboratory of R. Michael Blaese, M.D. in the Clinical Gene Therapy Branch, NHGRI. For the past 10 years, John has been Co-Director of Clinical Trials in the Metabolism Branch, NCI. He is responsible for translating discoveries from the branch's laboratories into clinical trials, for the management of these studies and the care of patients. John has been a member of the Staff Scientist and Staff Clinician Organization since 2008 and has participated in the Career Development Committee. Now, as the Bethesda Staff Clinician Co-Chair, John continues to play an active role in initiatives such as the Translational Seminar to provide networking and collaboration between Staff Scientists and Staff Clinicians.

John C. Morris (SC)

Staff Clinician Co-Chair

From the Office of the Director

Excellence in research here at the Center for Cancer Research (CCR) stems from a flexible infrastructure that permits our staff scientists and clinicians to capitalize upon advances in knowledge and technology and forge ahead at the boundaries of the possible. It also stems from our ability to readily establish strategic collaborations wherever they are needed, whether inside or outside the government.

One of many ways we are increasing our ability to establish strategic collaborations involves shifting our culture toward team science. A difficult aspect of this transition toward team achievement is its requirement that researchers share scientific recognition and credit in a new way. Although the contributions and discoveries made by individual investigators remain the cornerstone of much new knowledge generation, effective exploitation of that knowledge now depends on the power of partnership and teamwork.

Another way is by streamlining our ability to interface with industry. We have established an umbrella CRADA to make such collaborations possible and easier to establish and expand. This approach already is increasing the partnerships between industry and our labs.

Still another route we take involves building partnerships with scientists in academia who are trained in complementary disciplines such as mathematics or physics. Partnerships like these enable our teams to come at biological problems from a variety of scientific perspectives, and this accelerates our progress.

CCR staff scientists and clinicians play a major role in all these strategic collaborations that underlie our success. Whether they are working with graduate students who come to our labs under academic partnerships with universities, or they are studying biological mechanisms of new cancer therapies developed in concert with industry under our universal cooperative research agreements, our staff scientists and clinicians are forging ahead as members of productive teams who are making effective inroads against cancer.

Robert Wiltrout, CCR Director, and *Lee Helman*, CCR Scientific Director for Clinical Research

The 2010 Staff Scientist and Staff Clinician (SS/SC) Retreat

Thank you Elaine Hurt and Jianbo Chen for organizing the Sixth Annual NCI CCR SS/SC Retreat. This year, the DCEG SS/SCs joined the retreat, making this a groundbreaking event. Dr. Niederhuber, who addressed the importance of SS/SCs to the mission of the NCI, successfully started the morning with welcoming remarks.

The keynote speaker, Dr. Craig Thompson, Director of the Abramson Cancer, University of Pennsylvania, proved to be the highlight of the meeting when he delivered an inspiring review of the current state of metabolic signaling as it applies to tumor growth and metastasis. The excitement generated by Dr. Thompson's presentation carried the group to the breakout sessions.

This year the NCI Office of Workforce Development facilitated the ability of our organization to meet our goal of providing professional growth by leading two workshops (1) conflict resolution and (2) emotional intelligence. The immediate feed back from the participants carried over into lunch in the Natcher cafeteria and indicated that not only did we as a group learn new approaches to sometimes chronic work related problems but as individuals these classes gave us ways to improve our relationships with family.

The 2010 SS/SC Retreat (continued)

Our busy afternoon started with the Clinician's Address, which was given this year by Dr. Sharon Savage, a tenure track investigator from DCEG. Dr. Savage provided a glimpse of which cancer types are associated with shortened telomere length and how short telomeres contribute to the clinical manifestations of a bone marrow failure syndrome, dyskeratosis congenita.

Christophe Marchand's presentation on the current activities of the Professional Development Committee provided a great transition to this year's panel discussion given by Dr. Michelle Bennett, deputy director of the NCI, Dr. Mike Difilippantonio, program manager for therapeutic and diagnostic initiatives, DCTD and Dr. Chameli Jhappan, program director for tumor biology and metastasis branch in the NCI Division of Cancer Biology. This year the discussion focused on transitioning from the intramural to extramural programs at the NCI. In response to the question "How do we gain a better understanding of current and future directions for the NCI?" Dr. Bennett suggested reviewing the board of scientific advisors meetings. The links are available in the NCI Event-Cal electronically published to your desktop bi-monthly.

Following the panel discussion, the NIH Director's Innovation Award winners presented their research. Dr. Olga Sedelnikova provided a retrospective view of her group's studies into oxidative DNA damage induced by tumors in distal tissues. Dr. Xin Chen reported on the background of TNF receptor 2 in the expansion of regulatory T-cells, which led his group to propose that blockade of TNFR2 could be a relevant anti-cancer therapy.

The 6th annual retreat concluded with Dr. Jonathan Wiest's announcement of the winners of the 2010 SS/SC travel awards. The winners are listed on pp.8.

Zack Howard (SS) and Ofelia Olivero (AS)

The PI Corner

A major responsibility that we have at the NIH is the mentoring of students and fellows as they represent the future generation of scientists. Over my years at the NCI, I have interacted with a large number of students and developed a set "rules" that are meant to offer some guidance to students/trainees should they choose to pursue a career in biomedical research. I believe that mentoring of students is particularly relevant to Staff Scientists/Staff Clinicians since you are the ones who shoulder much of the mentoring in the lab.

I offer 10 of my rules here with a brief explanation of the rationale of my thinking behind each one. Please contact me if you are interested in the full list.

10 Rules to Remember for a Life in Science

1. "Choose a job you love, and you will never have to work a day in your life." (From Friends Reflections). *Rationale*: My colleagues and I don't come to "work". We come to the lab and few if any scientists I know consider their occupation as a "job". In my opinion, the freedom of being a biomedical scientist at the NIH is a special privilege and is indeed a job people love.

2. Never burn your bridges, especially if you pursue science as a career. *Rationale*: most scientists are at most 2 degrees of separation from each other. Almost certainly you will run into former colleagues at some meeting, even if you change fields. These are the same people that might be reviewing your papers or are asked to write letters for your job/promotion.

The PI Corner (continued)

3. Take your work seriously but not yourself seriously. *Rationale*: We all want to succeed at our science but if people take themselves seriously, it invariably ends up creating tension in the lab.

4. Your background and circumstances may have influenced what you are, but you are responsible for what you become. – Confucius *Rationale*: I tell students that it is OK to have people open doors for them but it is up to them to stay in the room. It is clear that some students may have gotten their positions because a friend, neighbor or relative works at the NIH but, to get invited to return, they need to prove that they have earned the privilege.

5. Only work with people who like chocolate. *Rationale*: If people get grumpy, a small piece of chocolate will make them smile.

6. When the lottery hits $100 million, get everyone in the lab to put in a dollar apiece (and only a dollar) and buy a pool of chances. *Rationale*: We have done this often and it gives lab members the chance to dream about what life would be like with financial independence. We did once win $150 but there were 35 people in the pool, so our path is still uphill. Of course I am not advocating gambling on a government facility……

7. Treat the administrators and administrative assistants that you deal with respect, for if you take care of them, they will take care of you. *Rationale*: This has been true through my entire career. It's easy to ignore or procrastinate about administrative requests but invariably you will need to request something from the administrative staff. If you have proven helpful to them in the past, your request will likely go to the top of their pile.

8. Free pizza (or chocolate) will get just about everyone to attend any talk you ever give. *Rationale*: This always works.

9. Don't let your hypothesis drive the interpretation of your data; rather, let your data drive the evolution of your hypothesis. *Rationale*: Students must appreciate that if an experiment does not fit their hypothesis and they have confirmed that the experiment (including controls) worked properly, they need to rethink their model. Too often people get tunnel vision, thinking that the experiments must fit either their model or existing dogma.

10. Everything in moderation except love, understanding and the number of experiments you do for your supervisor. *Rationale*: Can someone ever do enough experiments?

Mentoring is a big job and I salute all of you that have been mentors and will continue to mentor in the future. If you have additional advice that you give to students/trainees, don't hesitate to let me know. May all your students and fellows succeed and be a real credit to your laboratories.

Howard Young, Ph.D.

Deputy Chief, Laboratory of Experimental Immunology

Head, Cellular and Molecular Immunology

From the Deputy Director of Intramural Research

Future Directions for Staff Scientists and Staff Clinicians at the NIH

Sixteen and one-half years ago when I became Deputy Director for Intramural Research at the NIH, we were in the midst of a revolutionary re-thinking of how we should deploy our talented scientific staff to advance biomedical research and bring the fruits of our laboratory studies into the clinic. There was unanimous support for the creation of 2 new positions at the NIH, known as the Staff Scientist (for laboratory staff) and Staff Clinician (for M.D., D.D.S. and D.O. clinical staff), whose jobs were to bring highly specialized knowledge and training to bear on important research problems under the direction of an NIH principal investigator. We soon realized that there were Ph.D. scientists whose primary responsibilities were to provide clinical service and/or to participate in clinical research at the NIH and they got the subtitle Staff Scientist (Clinical). This was to be a time-limited, but renewable, appointment under Title 42, and it was appreciated that many (but not

From the Deputy Director of Intramural Research (continued)

all) of our Staff Scientists/Clinicians would be chosen from among the outstanding post-docs at the NIH who had evidenced the ability to work in teams and provide special expertise.

At that time, we discussed extensively the issue of career development and the need to provide potential pathways for our Staff Scientists/Clinicians who excelled and demonstrated the ability to function independently. The Associate Scientist position, a subset of Staff Scientists, was initiated several years ago to allow a small percentage of Staff Scientists to manage small research programs after rigorous review at the IC level, in part to deal with the need for career development of our most successful Staff Scientists. Most recently, there has been extensive discussion about the future for some of our most successful Staff Clinicians, and their role and career development will be addressed in the near future.

Let me assure you that the work that you do is essential to the success of the NIH Intramural Research Program, and your long-term commitment to research at the NIH is important to the leadership here. We will work together, within the existing framework, to develop opportunities for personal fulfillment and career development.

Michael M. Gottesman, M.D.

Chief, Laboratory of Cell Biology

Head, Molecular Cell Genetics

The Quadrennial Review Corner

Quad Review Tips – How to do Your Best

The Quadrennial Review process has been standardized over the past few years to fairly evaluate Staff Scientists despite their various roles. The review of each Staff Scientist and Clinician's performance is based on how they fulfill their role in the Lab/Branch – whether it's providing an essential core service, functioning like a PI, or giving scientific continuity to their PI's program. Additionally, reviewers take into consideration mitigating issues such as the scientific environment of the lab, mentoring by the PI, a poorly prepared package, etc. Staff Scientists and Clinicians are not just evaluated by their publication record. They are expected to provide scientific leadership, collaborate with groups beyond their lab, mentor and teach fellows, and participate in the scientific community.

How can you do your best in the Quadrennial Review? Remember that the reviewers only have the information in your package to assess your achievements – your PI's recommending memo, your CV and bibliography, and letters from collaborators. Work with your PI on the recommending memo. Make sure your duties and responsibilities in the lab are clearly spelled out and your accomplishments are highlighted. There is no page limit for your CV, so include supporting details.

What are your contributions to collaborations? Who have you mentored, do they have accomplishments that reflect your training and guidance – publications, posters, talks, academic or career steps? Give a complete account of meetings attended and talks and posters presented. What do you do in the lab to keep things running?

Between 2006 and 2009, 110 staff scientists were Quad-reviewed. Of these, 42% were rated Outstanding, and 44% were rated Excellent. The Quadrennial Review recognizes and rewards the extraordinary expertise and commitment of CCR's Staff Scientists and Clinicians.

Lynne Rockwood, Ph.D.

Office of Scientific Programs

From the Professional Development Committee

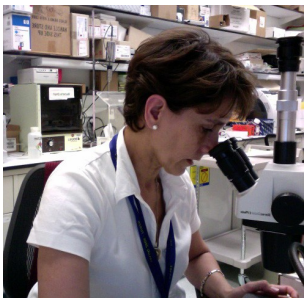
The SS/SC Professional Development Committee began working in March of 2010. The original members were Christophe Marchand, Victoria Virador, and Alison Rattray. In May, Therese Brendler, Zack Howard, Debbie Hodge and Dale Lewis joined. Our immediate goal is to launch the first **September Midyear training activity for NCI SS/SCs.** Our long term plans include maintaining updated information on the Professional Development web page and providing a strong resource for SS/SC looking to further their career at NIH.

The first **September Midyear training activity for NCI SS/SCs** will be held September 13, 2010 in Natcher (Balcony C). We are actively organizing three separate training modules and we expect registration to go live by mid/end July. Interested SS/SCs will be able to sign up for one or all modules. The tentative schedule is as follows: BLOCK I: 9-11am. How to organize a scientific meeting; facilitated by the OWD. BLOCK II: 11:45-1:45am. Grants for SS/SCs. Moderated by Jonathan Wiest, this block will focus on grant sources available to SS/SCs. BLOCK III: 2-4pm. Staff Scientists, Our issues, Our solutions. Facilitated by Sharon Milgram from the OITE, this block will encourage Senior SS/SCs and Associate Scientists to discuss and put forward proposals for selected issues. A short survey will be sent to the SS/SCs in preparation for this module.

Christophe Marchand (SS), Victoria Viirador (SS),

Therese Brendler (SS), Debbie Hodge (SS),

Dale Lewis (SS) and Alison Rattray (SS)



The Core Corner

Uncovering the Complex Routes of Pmel17 Trafficking Required in the Formation of Melanosomes

Establishing the identity and function of a normal cell is called differentiation. All cells take several steps to protect this process since loss of identify and function results in de-differentiation and starts the oncogenic process. However, many “normal” processes remain apparently unchanged when in fact had been modified by transformed cells. One of the hallmarks of melanocytic cells is their ability to engage in melanogenesis, the production of pigment, which requires the formation of a unique organelle called the melanosome. During malignant transformation, melanoma cells usually lose this ability, resulting in the loss of expression of Pmel17, a differentiation marker that is involved in the fibril formation of melanosomes and also is a key immunological marker of melanocytic cells.

Our goal was to characterize and identify whether changes in processing and/or trafficking are involved in the loss of Pmel17. To achieve our goal, we analyzed the trafficking pattern of Pmel17 and the effects of post-translational modifications (involving the addition of N- and O-glycan chains) on Pmel17 delivery to melanosomes and subsequent melanosome formation.

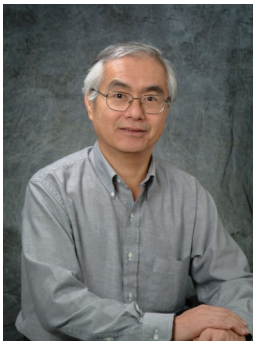
The Core Corner (continued)

Using subcellular fractionation and analysis of those fractions with mass spectrometry, we determined that different adaptor proteins (APs) are involved in a complex trafficking pattern and that such trafficking is influenced by changes in Pmel17 glycan compositions. Indeed, using a combination of molecular organelle markers and a novel antibody against Pmel17 (Pep25h), we discovered that direct or indirect delivery of Pmel17 to melanosomes requires association with two APs (AP1 and AP2), a process that is influenced by changes in O-glycosylation. Using immunofluorescence analysis, we confirmed such an association but with limits, due to a widespread distribution of individual vesicles and markers.

Since post-embedding immunoelectron microscopy (IEM) is the method of choice to localize and visualize target proteins at high resolution, we collaborated with the Electron Microscopy Laboratory (EML), a core facility at NCI-Frederick. IEM localizes targets using electron-dense markers (usually immunogold particles, e.g., IgG-conjugated gold nanoparticles). Indirect dual immune labeling was performed on thin-sectioned melanoma cells that had been previously fixed and infiltrated in a mixture of 100% cold ethanol and embedded in a special resin called LR White (low-viscosity acrylic resin). Thin sections were then incubated with anti-Pmel17 polyclonal antibodies (Pep13h or Pep25h) and either AP1 or AP2 monoclonal antibodies. Dual immunogold labeling was performed using gold particles with different diameters (e.g., 10 nm or 25 nm).

Since the success of IEM greatly depends on how well the proteins are preserved in the cells and how strong and specific the primary antibodies are, the basis for a successful experiment requires close work and trust between the involved parties during the validation and the collection processes. Note IEM is a very challenging task that needs to be addressed on a case by case basis since one successful protocol may not work in other cases.

As a result of our collaboration, we confirmed, with extreme detail, how the different glycoforms of Pmel17 traffic towards the plasma membrane in vesicles containing either AP1 (from the cytoplasm) or AP2 (from the plasma membrane). We also discovered that changes in the O-glycan composition alter the ability of Pmel17 to form melanosome fibers. The results of our collaboration were published in two papers (Valencia *et al.*, 2006;Valencia *et al.*, 2007), which have been cited several times in the literature.



Julio C. Valencia[1]*, MD (SS)* , and *Kunio Nagashima*[2]*, MS*.

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[2]Electron Microscopy Laboratory, NCI, Frederick, MD.

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Send your articles or suggestions with subject title "The Dossier" to:

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We need your input!

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 or suggestions for topics/subject manner and we will do our utmost to include your material in up-coming issues.

Get Involved!

Join a Staff Scientist and Staff Clinician Committee!

Choose from the following committees:

* SS/SC Retreat
* Quadrennial Review
* Career Development & Promotion
* Communications
* Translational Seminars

The Bioinformatics Corner

The need for Bioinformatics spans from data management to software development and training. With large amounts of data in hand, the tasks can sometimes be daunting and it can be difficult to know where to get useful information. Here are some links to NCI resources that may help get you started:

Site-licensed software available to NCI: http://ostp.nci.nih.gov

CIT tools and resources: http://cit.nih.gov/Science/ToolsResources/

Bioinformatics-related listservs (i.e. microarrays, bioinformatics): https://list.nih.gov/

High computing servers, Biowulf and Helix: http://helix.nih.gov/

ABCC at NCI-Frederick: http://isp.ncifcrf.gov/abcc/

Ewy Mathé (SS)

Announcements

Congratulations to the following Staff Scientists and Staff Clinicians as recipients of the 2010 SS/SC Retreat Travel Awards!

Dr. Atsushi Terunuma - Outstanding Clinical/Translational Research

Dr. Stephanie Weinstein - Merit Clinical/Translational Research

Dr. Xiaolan Qian - Outstanding Basic Science Research

Dr. Yanlin Yu - Merit Basic Science Research

Visit the CCR Staff Scientist and Staff Clinician Homepage:
https://ccrod.cancer.gov/confluence/display/CCRSSSCArchive/Home