THE DOSSIER

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

March 2011 Issue 4

From the Editor

Welcome to the March issue of The Dossier, a newsletter dedicated to the Staff Scientists and Staff Clinicians (SS/SC) of the CCR!

This issue contains important messages from the Director's Office and a special article by Dr. Amar Klar. Details on our 7th Annual SS/SC Retreat is also provided. A summary of the third block of our SS/SC Mid-Year Training Event is presented along with mentoring tips for your quadrennial review and information on bioinformatics resources at CIT. This issue also highlights the work of Drs. Donald Johann and Josip Blonder and their successful experience with the Laboratory of Proteomics and Analytical Technologies. 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, Ph.D. (SS)
Editor-in-Chief
Laboratory of Human Carcinogenesis

In This Issue

SS/SC Co-Chairs

Anu Puri, Ph.D.
Frederick Co-Chair
CCR Nanobiology Program
puria@mail.nih.gov

Marybeth Hughes, M.D., FACS
Clinical Co-Chair
Surgery Branch
hughesm@mail.nih.gov

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

From the Office of the Director

I would like to call your attention to a recent article in the *New England Journal of Medicine* that provided me with yet another reason to be proud of the contributions of CCR's staff clinicians. The paper examined the role of public-sector research in the discovery of novel biologics and vaccines. The authors found that among the new novel biologic and vaccine products approved by the FDA over the past 20 years, more than 25 percent were for hematology-oncology indications, and government labs played a significant role in delivering these products.

This is a very important finding because it shows how our staff clinicians fill an important gap in the drug pipeline by tackling rare cancers and then applying what they learn to develop drugs that could potentially serve a broader patient pool. By laying the preclinical groundwork for promising biologics and vaccines and then licensing the intellectual property to pharmaceutical companies so new treatments can come to market, your high-risk, high-impact labor brings hope for patients with rare cancers, and it at times also provides a proof-of-principle for new approaches to more commonly occurring cancers that continue to pose major challenges.

"…..our staff clinicians fill an important gap in the drug pipeline by tackling rare cancers and then applying what they learn to develop drugs that could potentially serve a broader patient pool. ..."

At a time when talk of government waste is endemic, it is good to stop and note this impressive return on investment for the country's research dollars. It is in large part, in an effort to expand this success at drug development, that the National Institutes of Health is creating a new translational science center to link even more basic discovery research to the development of drugs that can be used in clinical practice. By leading NIH in the licensing of patents and treatment innovations, you collectively represent a singular example of government at its best. Keep up the good work.

Lee Helman, M.D.
Scientific Director for Clinical Science,
Center for Cancer Research

Source reference: Stevens A, et al "The role of public-sector research in the discovery of drugs and vaccines" *N Engl J Med* 2011; 364: 535-541.

Please share this newsletter with your colleagues and visit the SS/SC website at
https://ccrod.cancer.gov/confluence/display/CCRSSSCArchive/Home

The 7th Annual SS/SC Retreat (April 11, 2011)

The 7th Annual CCR and DCEG Staff Scientist/Staff Clinician Retreat will be held on Monday, April 11, 2011 from 8am to 5pm at Natcher (Bldg. 45). This event brings together Staff Scientists and Staff Clinicians, which represent a unique sector of CCR and DCEG employees, to network, exchange ideas, present your research and learn. Come and find out what is going on in this active Staff Scientist/Staff Clinician community, and take advantage of everyone's knowledge to further your career!

To register and submit an abstract: http://web.ncifcrf.gov/events/clinicianretreat/2011/default.asp

Anuradha Budhu (SS) and Ewy Mathé (BSS)
(2011 SS/SC Retreat Co-chairs)

Agenda

8:00 am	Poster set-up and registration
8:30 am	Opening remarks by Drs. Anuradha Budhu and Ewy Mathé and SS/SC Committee Chairs
8:40 am	Opening remarks by Drs. Lee Helman and Martha Linet
9:00 am	Keynote Address 1: "Hepatocellular Carcinoma: Risks, Prevention and Challenges Ahead—Dr. Christopher Loffredo
10:00 am	Break and Poster Session I
10:45 am	Workshop on Emotional Intelligence
11:30 am	Collaborations with Biotech/Extramural—Dr. Melissa Maderia
12:00 pm	Topic Lunch
1:15 pm	Workshop on Conflict Resolution: Getting to Win/Win
2:00 pm	Keynote Address 2—Dr. Ron Evans
3:00 pm	Career Development Panel (Including a summary of mid-year activity, handbook, fall census and other things to come)
3:30 pm	Break and Poster Session II
4:15 pm	Poster Awards
4:25 pm	Quadrennial Review—Drs. Lynne Rockwood and Jeffrey Strathern
5:00 pm	Closing Remarks by Dr. Wiltrout and Adjourn

The 2010 Staff Scientist and Staff Clinician Mid-Year Training Event

The Career Development Committee held the first NCI Mid-Year Training Event for SS/SC on September 13, 2010 in the Natcher Building, NIH.

The first Staff Scientist and Staff Clinician Mid-year Training Event took place on September 13th, 2010 at Natcher (Bldg. 45). The event, organized by the NCI SSSC Professional Development Committee, was open to all NIH Staff Scientists and Staff Clinicians. General information on the event has been posted, and a summary of the first two blocks was published in the November 2010 issue of *The Dossier*. The third block, entitled **"Staff Scientists and Staff Clinicians: Our Issues, Our Solutions"**, was held in the afternoon and was organized in the format of four mini Think Tanks. Each group was given the mission of developing ideas about particular Professional Development issues for SSSC.

Unlike most workshops, which focus on presentation of information, this workshop was all about exploration. It was the job of the coordinators to make certain the issue to be discussed was clear, encourage all members of each group to contribute to problem-solving and to develop a sensible action plan, all within the time limit. The four topics were:

A. Moving on: How can we provide support to SSSC who want or need to leave the NIH?
Moderated by Therese Brendler and Martin Playford

B. How can SSSC increase their visibility and integration into the NIH?
Moderated by Ofelia Olivero, Karen Kurdziel and Ana Robles

C. How do we address policy and procedural issues that impact the careers of SSSC?
Moderated by Zack Howard and Connie Sommers, this session was structured as an informational panel with invited experts: Larry Samelson, Investigator, LCMB; Patrick Miller, Director, Workforce Management Resource Center; and Marianne Henderson, Chief, ODOA.

D. What information pertaining to SSSC should be included in a new hiring manual?
Moderated by Alison Rattray and Dale Lewis

After a brief introduction by workshop organizers Victoria Virador and Pat Sokolove (OITE), the four groups separated in different rooms and conducted their deliberations, which were summarized back in the auditorium at the end of the session. The main results are presented here, as starting points for future initiatives within Career Development Committees of the various Institutes or NIH-wide.

Group A. Moving on: How can we provide support to SSSC who want or need to leave the NIH? In preparation for these deliberations, Therese Brendler had tried to find information about SSSC who had left NIH in previous years. She found it was hard to get a sense of the turnover, indeed, hard numbers were almost impossible to get because most ICs did not reveal the data or simply did not keep any records. Michael Espey, chair of the Trans-NIH SSSC, informed her that tackling this issue is one of his priorities. Therese provided her attendees with some questions prior to their meeting:

1. Will you be displaced in the next two years?

2. Who have you talked to? What options were discussed? Were you satisfied?

3. Do you think it would be beneficial if each IC had a designated person to act as an advisor and coach for SSSC in transition?

4. What other ways do you think the NIH could support SSSC in transition?

5. FelCom has a voluntary alumni database for networking and a source of peer advice for those fellows seeking jobs. Should we implement this idea in the SSSC organization? Should we restart the practice of listing job openings culled from USAJOBS or JOBS@NIH?

6. In what other ways do you think the SSSC organization could support SSSC in transition?

It was recognized that each person's situation is unique, which makes placement of displaced SSSC complicated. Four current methods of dealing with displaced SSSC were identified:

1. Earl Stadtman Tenure Track Investigator Program.

2. Placement with a Senior Investigator who has an opening.

The 2010 Staff Scientist and Staff Clinician Mid-Year Training Event (Continued)

3. Temporary placement in the Office of the Laboratory Chief while the SSSC is detailed to a non-tenured Investigator.

4. SSSC applies for jobs in industry and academia or an administrative job in the government.

Nadya Tarasova discussed her experiences as a displaced SSSC after the sudden death of her Principal Investigator, Christopher Michejda. She stressed the importance of developing collaborations within the IC, and applying for outside grants. Other specific suggestions from group deliberations are as follows:

1. The SSSC positions need to be defined in terms commonly used by academia and industry (i.e., Associate Research Professor). Those evaluating applications for positions outside NIH do not know if the SSSC is qualified because they are unfamiliar with the duties and the qualifications of an SSSC position.

2. The NIH should make it easier for displaced SSSC to obtain government jobs within the NIH by allowing SSSC to directly transition into GS-13 level jobs.

3. The Office of the Director could be approached with a proposal to establish a Think Tank composed of Staff Scientists. Displaced SSSC could apply to this Think Tank.

4. The NIH could support preferential hiring of displaced SSSC by establishing a databank of displaced SSSC that PIs could search before hiring a new SSSC.

5. The Office of the Director or the NIH SSSC Organization could establish a networking database for SSSC.

6. SSSC should be encouraged to apply for independent funding within the mission of the Lab/Branch.

7. SSSC should be encouraged to establish collaborations within the IC and also other government agencies (e.g. the FDA).

Group B. How can SSSC increase their visibility and integration into the NIH? Coordinated by Ofelia Olivero, Ana Robles and Karen Kurdziel.

Although the group valued some of the visibility opportunities within CCR, they considered that there is room for improvement. Some of the challenges that were brought up concerned the ability of the SSSC to obtain independent funding, which would give the SSSC a certain degree of scientific freedom, always within the scope of the Section or Branch' mission.

Authorship constitutes another challenge that SSSCs face. In many cases the customary ranking of SSSC, as a "middle author" is detrimental for the career progression of the SSSC and their evaluation by the Quadrennial Review Committee.

Problem-solving ideas were:

*To consistently encourage SSSC to access their personal WEB sites, populate them and use them as a window to showcase research abilities and attract potential collaborations.

*To create a platform for the exchange of abilities/skills/background. This effort should be focused on the organization of a listing (virtual/Web-based) populated by available/interested SSSCs. This would also facilitate mobility between ICs and would alleviate the persistent challenge of displacement.

*Because of the nature of the SSSC position, accessibility to peers is warranted and with that a good amount of potential for collaborative research. SSSCs should strive to make the most of these opportunities.

*To amend the perceived lack of career progression by providing remunerated promotions.

Overall the group thought that many challenges could be addressed by the collaborative effort of the SSSC Organization and the Office of the Director.

The 2010 Staff Scientist and Staff Clinician Mid-Year Training Event (Continued)

Group C. How do we address policy and procedural issues that impact the careers of SSSC? Coordinated by Zack Howard and Connie Sommers.

The coordinators brought in three administrative experts to discuss issues such as job security and compensation. Marianne Henderson – Chief, Office of Division Operations and Analysis, NCI/DCEG, Larry Samelson – Deputy Director, NCI/CCR, and Patrick Miller – Director, Workforce Management Resource Center, NCI assisted in the deliberations. The discussion focused on the following issues:

Retention/Job security: Since the majority of SSSC are Title 42 employees, their contracts are time-limited and renewable. In NCI/CCR, the terms are usually 4 years, and renewal depends on the level of support from the PI, site visit evaluation of the PI, and quadrennial review of the SSSC. In order to maximize potential for renewal, SSSCs need to consider the importance of the quadrennial review. NCI has developed a form to provide feedback to individuals after their quadrennial review. SSSC from other institutes are welcome to ask for this form and develop some similar evaluation mechanisms.

The other level of evaluation is the PMAP system. SSSCs need to be savvy and work with the system as it can provide an opportunity to communicate with their PI about how he/she views the progress and status of the SSSC.

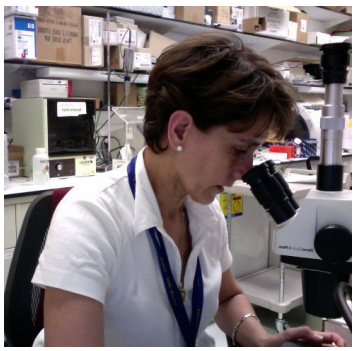
In addition to doing their jobs well, SSSCs need to publish, network, collaborate and find one or more mentors.

Compensation: There are 4 types of raises: (1) COLAs, which are usually automatic and initiated at the NIH Director level, (2) annual pay adjustments, which are merit-based and can be up to 2% (and in NCI/CCR have to average to 1%); these are initiated at the laboratory level, (3) performance bonuses, which are one-time awards, initiated at the laboratory level or above and (4) quadrennial review pay adjustments, the largest possible pay increases. The score on a quadrennial review sets the amount of increase; the actual % increase for a given score varies annually based on the NCI budget.

Promotion: In CCR/NCI, promotion to Associate Scientist and Senior Associate Scientist levels is possible (but rare). In other institutes this may refer to Tiers II and III. The pay scales for these positions can be found at the NIH OHR website.

Displaced SSSC: Patrick Miller spoke for NCI/CCR and said that CCR makes every effort to place displaced SSSCs. If a contract will not be renewed, the SSSC is given one year's notice before non-renewal. This one-year notice is not codified and may not be uniform across the NIH.

Group D. What information pertaining to SSSC should be included in a new hiring manual? Led by Dale Lewis and Alison Rattray, the group reviewed a document created by Alessandra Rovescalli of the NHLBI. The group discussed expanding this document to include information pertaining to NCI and other Institutes. The NCI SSSC Professional Development Committee is currently continuing the work that was started in this session. They hope to have a final hiring manual ready within the current year.



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

-with additional commentary by the Professional Development Committee and Coordinators of the SSSC Mid-Year Training Event

The PI Corner

It is a worthwhile question to address the purpose of the Staff Scientist positions at NCI. Why do we have them, how do they help a Staff Scientist's career development, and how do these positions serve the mission of NCI? In academia, only Senior Faculty, those who have been successful in competing for ever-shrinking funds, usually from their grants, use such positions. At NCI, the Staff Scientist essentially acts as an experienced, right-hand person of the PI, helping to train newcomers to the laboratory and run day-to-day operations of the laboratory. Biological research presently involves expertise in many different techniques that the PI alone can't master; therefore, the best use of the Staff Scientist position is to help bring the needed technical expertise to the laboratory. Science is becoming more and more a group effort; therefore, this position helps in accomplishing the twin goals of NCI, to conduct health-related research and train tomorrow's scientists in biomedical research. Moreover, it has always been the case that not all deserving postdoctoral trainees get independent positions in academia or in industry, some don't even want to take up independent positions, and hence, Staff Scientist positions provide opportunity for further training of such well-qualified persons. As this is not a permanent position at NCI, those individuals should exploit this opportunity to advance their career, with the goal to move from strictly a designated collaborator of the PI on to an independent position in the future.

Amar Klar, Ph.D.
Head, Developmental Genetics Section,
Gene Regulation and
Chromosome Biology Laboratory

The Quadrennial Review Corner

Mentoring Tips

CCR's Staff Scientists and Clinicians function in many different capacities, but they all are expected to serve as mentors to students and fellows in their labs. Mentoring has a vital role in the scientific community, as indicated by the inclusion of mentoring as part of the review criteria at many levels of scientific review, including site visits and the Quad review. It is a complex relationship that is both personal and professional. Ideally both parties benefit.

A career in scientific research is complex and demanding. The mentor serves as a guide and a role model in this professional environment. Explicit conversations about expectations and goals are important to both sides of the mentoring relationship. Be available and really listen to your mentee. Set a great example; model professional behavior and remember that your enthusiasm is infectious. Share your insights and experiences. Introduce your mentees to the culture of the NIH. Encourage them to get out of the lab and engage in the larger scientific community - attend lectures and meetings, present posters, join interest groups and take courses. Offer increasing responsibility in the lab and let your mentees take credit for their findings. Help them gain experience and confidence in communicating their work by drafting papers and giving talks in a variety of settings. Recognize and celebrate their accomplishments.

Mentoring can create lifelong interactions and expand your network of collaborators as mentees evolve into mentors and collaborators themselves.

Lynne Rockwood, Ph.D.
Office of Scientific Programs

The Core Corner

Towards Cancer Biomarker Discovery *via* Targeted Clinical Proteomics

As effective biomarkers are incorporated into clinical practice, patient outcomes usually improve rather dramatically, due to the feedback provided to physicians that enables a more rational approach to therapies and customized care plans. This has certainly been the case for cardiovascular disease where blood pressure and lipid profiles greatly facilitate tailoring of medications and thus reducing risk, as well as HIV/AIDS, where CD4 counts, viral loads and genotypes have allowed for better customization of complex combination antiviral therapies. Why has the use of biomarkers been difficult to incorporate into the practice of clinical oncology? Through our collaboration, we sought to scientifically explore this question, and develop novel approaches directly addressing this oncologic issue.

Although cell lines and even animal models have been extremely important in the efforts to better understand cancer, they do have significant limitations. Due to the lack of a tumor microenvironment, and deranged or significantly different enzyme systems, we choose to concentrate our efforts on the direct analysis of human tissues. Our first clinical proteomics collaborative publication was focused on the pros and cons of analyzing human tissue versus fluids versus both (1). We proposed to use both, employing a tissue-directed proteomics strategy where solid tumor tissue is examined first, in order to map driver proteins, followed by blood-based identifications.

Given the heterogeneity present in solid tissue and tumors in particular, we next hypothesized that a functional linkage between laser capture microdissection (LCM) and MS may provide an innovative platform for the molecular profiling of fresh frozen tumor tissue. Subsequent experiments resulted in our next collaborative publication (2). We continued by developing a method capable of identifying tumor proteins in blood using a unique experimental design coupled with a novel bioinformatic platform (figure 1). We analyzed in parallel solid tissue and blood from a patient with a newly diagnosed non-metastatic renal cell carcinoma (RCC), which successfully identified a panel of eight proteins/markers in the blood (3). This discovery has also resulted in a patent application.

In this study, proteins were extracted from the tumor, normal adjacent kidney, and a pre-operative blood specimen and then subjected to multi-dimensional liquid chromatography tandem MS analyses. The identified proteins from each tissue type were then filtered to isolate: i) those found in the tumor but not the kidney, ii) found in the blood specimen along with a higher spectral count in the tumor tissue versus blood (indicating a gradient or leaking phenomena). Cross validation Western-blot analyses confirmed the presence of cadherin-5, cadherin-11, DEAD-box protein-23, and private kinase in the blood of the patient under study, as well as four additional patients diagnosed with RCC, but not in the blood of a matched healthy donor. Interestingly, all peptides (from tumor and blood) identified from cadherin-5 came from the same extracellular domain. Thus, an active role of cadherin-5 in the RCC molecular biology of our patient was considered, and since this protein has been described as an antiangiogenic drug target, it may be incorporated into an individualized adjuvant therapy plan.

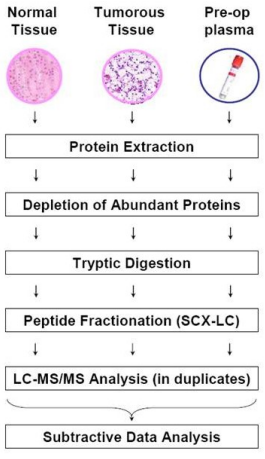


Figure 1. Experimental Design

In summary, our method represents a small but significant step toward improved proteomic analysis of solid tumors. Given the number of new drugs for RCC and the fact that no validated biomarkers exist, these results are timely. High-throughput techniques

The Core Corner (Continued)

utilizing immunoassays (ie, ELIZA) or MS-assays (ie, MRM) may be used for a larger RCC cohort or application in a clinical trial. Finally, this concept may help accelerate the transformation of oncology from a discipline of categorically assigned treatments derived from population statistics to one where therapy is derived following a rational molecular profiling of the patient's actual tumor.

Finally, special thanks to the Laboratory of Proteomics and Analytic Technologies where this work was done, and the CCR for funding and establishing access to the instrumentation required for this work.

Donald J. Johann, Jr., MD
Assistant Clinical Investigator
Medical Oncology Branch

Josip Blonder, MD
Head, Clinical Proteomics Group
Advanced Technology Program, SAIC-Frederick, Inc.

References:

1. Johann DJ, Blonder J. "Fluids vs. Tissues vs. Both", ***Expert Reviews in Molecular Diagnostics***. **2007**.Sept; 7(5):473-5.

2. Johann DJ, *et al*. Approaching solid tumor heterogeneity on a cellular basis by tissue proteomics using laser capture microdissection and biological mass spectrometry**.** ***J Proteome Res***. **2009** May; 8(5):2310-8.

3. Johann DJ, *et al*. Combined Blood/Tissue Analysis for Cancer Biomarker Discovery. ***Analytical Chemistry.*** **2010** March 1;82(5): 1584-8.

The Bioinformatics Corner

Looking for a place to analyze your microarray data? Want to visualize your data for a presentation? Need to use statistics without creating an Excel formula?

Welcome to mAdb. The microArray Database (mAdb) is a web-based resource which allows researchers to analyze and explore their own microarray data. Scientists can access this easy-to-use interface to evaluate the quality of their microarrays or use a variety of analytical approaches to decipher array data in a meaningful way.

We have standard statistical tools (e.g. t-test, ANOVA), but have also incorporated BioConductor tools, such as SAM (Statistical Analysis of Microarrays) and GSEA (Gene Set Enrichment Analysis). Calculations are done on our servers, so a user does not need a powerful computer even for large datasets. Analysis output can be shared with a PI or downloaded in an Excel format for input to other tools. Some view their data in heat maps or other graphical formats. Data are annotated with gene and pathway information and include links to sites at NCBI, GO and KEGG.

Though mAdb started over ten years ago by supporting in-house arrays printed at the Advanced Technology Center, most submissions now are commercial arrays from Affymetrix (including new support for the gene expression ST arrays), Agilent and Illumina Beadarrays. We securely store your data and make it accessible to you wherever you have an internet connection.

Need some help with your analysis? We offer training classes, but we are also available for one-on-one consultation. Ready to publish? The mAdb staff can help prepare your data for submission to a public repository (GEO) as required for publication.

Want more information? Contact us at madb-support@bimas.cit.nih.gov or point your browser to https://madb.nci.nih.gov/ and request an account.

Esther Asaki
(SRA International)
Center for Information Technology

Announcements

Join us at the 7th Annual CCR & DCEG Retreat!

The 7th Annual CCR & DCEG
Staff Scientist and Staff Clinician Retreat

When: Monday, April 11, 2011 (8am-5pm)
Where: Natcher (Bldg. 45), NIH, Bethesda, MD

Attend:	Keynote presentations by Drs. Ron Evans and Christopher Loffredo
Present:	Posters (Basic science, Translational science, Epidemiology & Bioinformatics)
Network:	Select topics during registration to discuss with experts at lunch tables
Learn:	Quadrennial review, Career development, Collaborations, Training

For more details, registration and abstract submission, go to:
http://web.ncifcrf.gov/events/clinicianretreat/2011/default.asp

Congratulations!

Join us in congratulating the SSSC 2011 winners of the NCI Director's Innovation Awards!

Izumi Horikawa, Ph.D., Laboratory of Human Carcinogenesis

Christophe Marchand, Ph.D., Laboratory of Molecular Pharmacology

Masaki Terabe, Ph.D., Vaccine Branch

Enrique Zudaire, Ph.D., Radiation Oncology Branch

Election Results are in!

Thank you for participating in our SS/SC Fall elections. Congratulations to our new Officers. They have taken office in January 2011 and will serve for two years.

Co-Chairs: Marybeth Hughes, Christophe Marchand and Anu Puri
Secretaries: Jianbo Chen and Christina Stuelten

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 SS/SC Committees

Professional Development
Communications
SS/SC Retreat

Please share this newsletter with your colleagues and visit the SS/SC website at
https://ccrod.cancer.gov/confluence/display/CCRSSSCArchive/Home