THE DOSSIER

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

June 2013 Issue 13

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 Kathy Kelly, Ph.D. A summary of our recent SSSC Retreat is provided by Rimas Orentas, Ph.D., and Aleksandra Michalowski, Ph.D. We also introduce our new SSSC Officers who inform us of some of their goals over the next two years and feature an article by Yvona Ward, Ph.D., on revisions of the T42 tier designations in our new NIH SSSC Section. The work of Sergey Tarasov, Ph.D., and Siddhartha A.K. Datta, Ph.D., using the Biophysics Resource is highlighted and we also feature Jianjian Zhu, Ph.D., in our SSSC Corner. In addition, Natalie Abrams, Ph.D., of CCR's Bioinformatics Core, introduces us to tools, algorithms and guidelines for analyzing high-throughput data. We hope to continue to provide 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

Adam Metwalli, M.D., Clinical Co-Chair, Urologic Oncology Branch, metwallia@nih.gov

Connie Sommers, Ph.D., Bethesda Co-Chair, Lab of Cellular and Molecular Biology, sommersc@mail.nih.gov

Sergey Tarasov, Ph.D., Frederick Co-Chair, Structural Biophysics Laboratory, tarasovs@mail.nih.gov

From the Office of the Director

Identifying Strategic Collaborations to Refocus Our Resources

As a distinctive part of the Nation's investment in cancer research, the NCI Intramural Research Program has an obligation to taxpayers to do the type of work that is critical to research progress but which may be too costly, or require a longer time commitment, for industry or academia to pursue. As Congress continues to review federal budgets and to make tough funding choices, CCR's leadership has been working to strategically refocus some of our basic and clinical research goals to better leverage our distinctive collaborative culture through even more integration of intellectual expertise and resources in basic, clinical, and translational research.

Toward that end, we have identified several areas where we are well-positioned to make progress not easily made elsewhere, which could then contribute to broader applications across the larger cancer research community. In this context, we benefit from the unique expertise provided by all members of the CCR staff, particularly the essential role Staff Scientists and Staff Clinicians play in the successful outcomes of these initiatives and programs.

The development of new therapies for cancer is an important goal of CCR and NCI. The Drug Development Collaborative (DDC), which evolved from the Molecular Targets Faculty, provides the infrastructure to accomplish this goal. The DDC is a mechanism for intramural researchers to bring small molecules and biologics created in their labs to the drug development pipeline. The ultimate goal of the DDC is to bring promising compounds to the NCI Experimental Therapeutics (NExT) program, which is a partnership with the NCI Division of Cancer Treatment and Diagnosis, and then ultimately to deliver improved therapies to patients. To learn more about the DDC, please visit the DDC website at https://ccrod.cancer.gov/confluence/display/CCRMTF/Home.

The Rare Tumor Initiative was recently launched to integrate our existing basic and clinical study of rare tumors to more effectively translate potential new basic science discoveries at the bench to innovative therapies delivered at the bedside—and then return them back to the bench for refinement. During an initial pilot "precision medicine" project, basic research scientists are actively helping to identify targets that will better inform clinical protocol design. Clinical researchers, in turn, will provide tissues and clinical perspective to basic researchers for molecular characterization of tumors, which will better inform future clinical trials. This pilot phase will include projects specifically investigating Ras-related tumor types, including malignant peripheral nerve sheath tumors (MPNSTs) and plexiform neurofibromas, in addition to selected non-Ras-related sarcomas. A future goal is to expand the network of basic and clinical scientists to include study of other rare tumor types.

Research in RNA Biology addresses the many roles of RNAs in controlling cells and viruses. CCR has leaders in these areas including investigations of the details of transcription, splicing, RNA processing, regulation by miRNAs and shRNAs, control of the efficiency and location of translation of mRNAs, and the analysis of secondary and tertiary RNA structure. A CCR Initiative for RNA Biology is under early development to provide a forum to facilitate communication and collaboration among CCR laboratories interested in RNA Biology and to explore new research opportunities.

CCR's Staff Scientists and Staff Clinicians, working together with Principal Investigators, are an integral part of the intellectual foundation for CCR's strategic collaborations, and an important part of CCR's culture of collaboration. I encourage you to continue to be vigilant for new scientific opportunities that can be fostered by our application of community-wide expertise to difficult scientific problems.

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

The 9th Annual SSSC Retreat (April 22, 2013)

Why Haven't We Cured Cancer Yet?

The 9th Annual CCR and DCEG Staff Scientist and Staff Clinician Retreat of the National Cancer Institute was held on April 22, 2013, at the Natcher Conference Center on the NIH campus in Bethesda, MD. The response from our community was extremely supportive as the event was "sold out!" –meaning that we reached the room maximum of 180 attendees.

We chose a provocative theme this year. We did so to arm, inspire, and inform ourselves about the many challenges and advances that currently face our field. In fact, at the very time that we need support from our scientific leaders, some have criticized the efforts of the cancer research community, and implied that not much new is happening. So, we raised the question ourselves. The importance of addressing this topic was highlighted by the full participation of the leaders in the cancer research community that we invited: Edward Harlow, Ph.D., Chair of Biological Chemistry and Molecular Pharmacology at Harvard School of Medicine, Barbara Wold, Ph.D., Bren Professor of Molecular Biology at the California Institute of Technology, Lee Helman, M.D., Scientific Director for Clinical Research at the CCR, Giorgio Trinchieri, M.D., Director of the CCR Cancer and Inflammation Program, and our keynote speaker, Richard Gilbertson, M.D., Ph.D., Director and Executive VP of the St. Jude's Children's Research Hospital Cancer Center. We felt uniquely blessed to have this world-class panel.

The retreat began with Dr. Richard Gilbertson giving an in-depth keynote address that demonstrated how new murine models of brain development and malignancy have led to the wholesale reclassification of human disease. The ability to use mouse models to tease apart a seemingly intractable clinical challenge was bench to bedside research at its best. We were impressed by Dr. Gilbertson's challenge to include every member of the research community, from genomics researchers, to bioinformaticians, to researchers in classical molecular and developmental biology, to a research-focused clinical team that could use this information to plan informed treatment approaches. As our ability to analyze each person's cancer increases, as well as our sophistication in following the natural history of the disease, and to determine individual therapeutic targets improves, this also feeds back to the creation of more refined animal models. He stressed that each member of the team was a key resource. This higher-level integration of laboratory disease modeling and clinical understanding of the disease process was a clear answer as to "how" the field is advancing in its approach towards a cure.

The interactive panel session at the 2013 SSSC Retreat. Pictured from left to right: Richard J. Gilbertson, M.D., Ph.D., Edward Harlow, Ph.D., Giorgio Trinchieri, M.D., Lee J. Helman, M.D., and Barbara Wold, Ph.D.

Following the keynote address, the retreat faculty panel each gave a brief introduction to their understanding of where the field stands, and gave clear answers and insights as to how the press towards a cure was continually advancing. Dr. Helman highlighted molecular high-throughput screening mechanisms that both took advantage of genomic analysis and posed new questions about mechanisms of resistance. Dr. Trinchieri revealed how our new understanding of inflammation in the cancer process was creating new avenues for intervention and prevention. Dr. Wold, who has a very global view of the analysis of genomic patterns in cancer, impressed us with how deep our knowledge at the genomic level of understanding cancer has become. Dr. Harlow shared from both his scientific knowledge about cancer signaling pathways and tumor progression, and his passion to keep the mechanics of research going even in these challenging times.

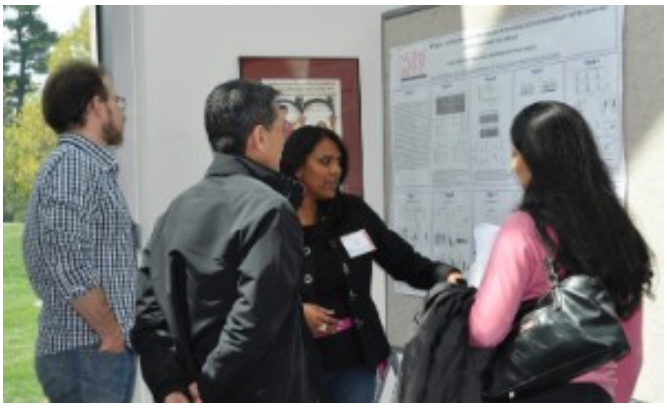
The retreat also featured an overview of the Quadrennial Review process by Lynne Rockwood, Ph.D., and Geoffrey Kidd, Ph.D., who oversee the review of Staff Scientists and Staff Clinicians, respectively. We also took a short time to greet our new Officers, as well as to hear about the Professional Development

The 9th Annual SSSC Retreat (April 22, 2013) Con't

Committee from Christophe Marchand, Ph.D. In response to issues raised in our retreat survey, we would like to emphasize that the retreat functions for us as a means to meet and greet one another, to build networks, and to share our research. Some attendants wanted more in the realm of Professional Development. Past retreats have tried to incorporate this, but that made for a very long day. To that end, the Professional Development Committee highlighted the offerings that are presented throughout the year. Please, lets all keep an eye out for these events, as they are essential to build our careers in science in the long-term. Importantly, Dr. Rockwood shared that NCI leadership is well aware of the challenges that we face with regards to travel and having the ability to demonstrate leadership (part of the Quad Review criteria) in the extramural community. For that reason, participation in our SSSC events and committees should be encouraged, and in her words "it counts!"

We should also note that there were discussions in government leadership to eliminate the Title 42 system, which many of us are hired under. This probably does not mean that our jobs would be eliminated, but it does mean that in times like these, it is important to stay together and stay informed. We heard about this possibility from panel members, as well as in Dr. Helman's closing remarks. We are very grateful for the support and encouragement Dr. Helman gave us with regard to the retreat, and our service here at the NIH. But many were surprised to know that if it were not for Francis Collins', M.D., Ph.D. strong defense of our current positions, and his taking the time to explain, defend, and share the unique culture of NIH to our government leaders, the coming year could have been more than a little turbulent.

The survey responses indicated that the panel and keynote speakers were enjoyable, inspiring, and of the highest quality and value. But the single event that most respondents noted as being important to them was being able to network and meet others at the poster sessions. We had 71 posters in three categories: a) Basic Research, b) Translational, Clinical and Epidemiological Research, and c) Technological and Methodological Development. Travel awards were given to Yu Yanlin, Ph.D. (CCR) - "Identification of a novel Fcg gene that mediates metastatic tumor cell escape from immunosurveillance" in the Basic Research category; Jun Wei, Ph.D. (CCR) - "Massively Parallel Sequencing Reveals an Accumulation of De Novo Mutations and an Activating Mutation of LPAR1 in a Patient with Metastatic Neuroblastoma" in the Translational, Clinical and Epidemiological Research category; and Xiaoying Ye, Ph.D. (SAIC)-"Simultaneous Mapping of N and O Linked Glycosylation Sites in Renal Cell Carcinoma Cells" in the Technologies and Methodologies Development category. Actually, all of us who visited the posters and met our colleagues were winners, as the research we do, day in and day out, was highlighted and shared with each other. The depth and breadth of the research community in NCI is one of the best things about being here, and so it is always encouraging to get a bigger picture of all that is going on at our various campuses.



Swati Choksi, Ph.D. (SS) discussed her research during an afternoon poster session at the 2013 SSSC retreat.

The retreat was translated from an abstract idea into a real event through the dedicated participation of the retreat committee members: Drs. Gabriella Andreotti, Debbie Hodge, Maria Kireeva, Anu Puri, Christina Stuelten, Nadya Tarasova, Sergey Tarasov, and Jonathan Wiest. If you would like to participate in the planning of next year's retreat, please join the committee by contacting the co-chairs for the 2014 retreat: Anu Puri (puria@mail.nih.gov) or Rimas Orentas (orentasrj@mail.nih.gov).

We are very grateful and wish to thank all the volunteer judges who dedicated their time and expertise to evaluate abstracts and poster presentations: Stefan Ambs, Ph.D., M.P.H., Jonathan Ashwell, M.D., Yawen Bai, Ph.D., Federico Bernal, Ph.D., Christopher Buck, Ph.D., Yamini Dalal, Ph.D., David Danforth, M.D., David Goldstein, Ph.D., Tim Greten, M.D., James Gulley, M.D., Ph.D., Patricia Hartge, Sc.D., Zack Howard, Ph.D., Chand Khanna, D.V.M., Ph.D., Jackie Lavigne, Ph.D., M.P.H., Jadranka Lon-

The 9th Annual SSSC Retreat (April 22, 2013) Con't

-carek, Ph.D., Jordan Meier, Ph.D., Kumaran Ramamurthi, Ph.D., Jeffrey Rubin, M.D., Ph.D., John Schneekloth, Ph.D., Kandice Tanner, Ph.D., Xin Wei Wang, Ph.D., David Waugh Ph.D., and Kazimierz Wrzeszczynski, Ph.D.

We also thank Jonathan Wiest, Ph.D., Jackie Lavigne, Ph.D., M.P.H., David Heimbrook, Ph.D., Dwight Nissley, Ph.D., Robert Wiltrout, Ph.D., and Lee Helman, M.D., and all of the CCR and DCEG leadership who continue to encourage and support our retreat and the SSSC in general. We also thank Doug Nichols for website support, and Julia Lam for conference planning and support par excellence.

Looking forward to seeing you in 2014!

Your 2013 retreat co-chairs,

Aleksandra Michalowski, Ph.D. (SS)
Laboratory of Cancer Biology and Genetics

Rimas Orentas, Ph.D. (AS)
Pediatric Oncology Branch

The NIH SSSCO Corner

The NIH Staff Scientists/Staff Clinicians Organization (NIH SSSCO) represents all Staff Scientists and Staff Clinicians at the NIH. The intent of this organization is to promote exchange of ideas through networking and inter-institute collaborations among its members. In addition, the NIH SSSCO organizes workshops, seminars, and informational meetings designed to keep our Staff Scientists and Staff Clinicians well informed about topics such as emerging technologies, career development, mentoring opportunities, and visa regulations.

The most recent and topical initiative of the NIH SSSCO is to redefine the Title 42(g) Staff Scientist Tercile (Tier) designations. As you are probably aware, the tier-based salary designations that were in existence in 2010 are no longer relevant and current guidelines and regulations are being considered for revision. In order to allow Staff Scientists to be promoted in accordance with increased duties and/or outstanding performance, it is necessary at this time to uncouple Staff Scientists' promotions to the next tier from a mandated pay increase. At the request of Michael Gottesman, M.D., a working committee was formed from the NIH SSSCO membership to draft a new document that would clearly outline three performance-based tier levels accessible by Staff Scientists. Although the promotions would not be specifically linked to a pay increase, we hope that the level of performance will ultimately lead to an opportunity for compensation. The document proposing these changes to the tier designation is currently under review in Dr. Gottesman's office. The NIH SSSCO will continue to work with the NIH administration to provide fair and equitable opportunities for Staff Scientists to be reviewed, evaluated, and compensated for their contributions to the intramural program at the NIH.

You should have received a copy of the "Proposed Changes to Title 42(g) Staff Scientist Tercile (Tier) Designations and Descriptions" document to review before it was sent to Dr. Gottesman's office. On behalf of the NIH SSSCO, I would like to thank all of you for your insightful ideas and suggestions. All of

The NIH SSSCO Corner Con't

your comments were read carefully even if we could not address them all in the current document. Please recognize that this proposal is a first step in the process rather than a definitive solution and the NIH SSSCO will continue to voice the concerns of our members.

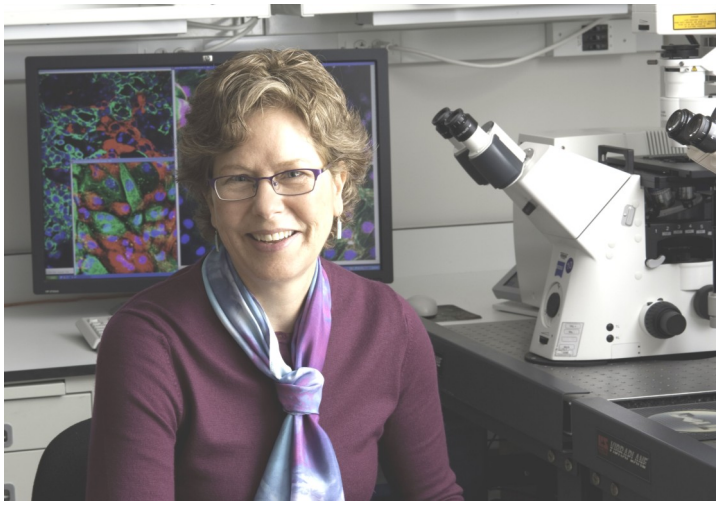
If you would like to be an NCI representative to the NIH SSSCO and participate in the meetings, please contact Yvona Ward at wardy@mail.nih.gov.

For more information about the NIH SSSCO, please go to the following link http://sigs.nih.gov/NIH_SSSC/Pages/default.aspx

Yvona Ward, Ph.D. (SS)
Chair, NIH Staff Scientists/Staff Clinicians Organization
Cell and Cancer Biology Branch

The PI Corner

Section Editor: Lakshmi Balagopalan, Ph.D. (*SS*)



These are challenging times. We have witnessed a nearly ten-year contraction in government funding for all biomedical research, intramural and extramural, with the most recent challenge being the "sequester." Especially now, I am struck by the important role that Staff Scientists and Staff Clinicians play in stabilizing and moving our research efforts forward as intramural programs become smaller. As postdoctoral fellows leave and are not replaced, the institutional memory of Staff Scientists becomes even more critical for efficient and successful operation of laboratories. This often times means incorporating additional sophisticated methods into an already extensive technical repertoire or remaining aware of unpublished but useful data for fledgling projects. Staff Scientists often help stretch shrinking supplies and service budgets by sharing reagents and other experimental materials with a network of colleagues

"...the institutional memory of Staff Scientists becomes even more critical for efficient and successful operation of laboratories."

built over their career and by using their knowledge of vendors who return the best value.

The Cell and Cancer Biology Branch is fortunate to include two talented and motivated Staff Scientists Yvona Ward, Ph.D., and Swati Choksi, Ph.D. Yvona and Swati exemplify the many hats worn by Staff Scientists. Yvona heads a confocal core facility that services and trains individuals from several laboratories within CCR. In addition, Yvona manages a successful independent research project concerning the relationship of specific G-protein receptor coupled signaling pathways to metastasis. Swati, who is a member of Zheng-Gang Liu's laboratory, designs and performs experiments for an exciting independent project investigating cell death pathways in cancer. Swati also serves as supervisor and mentor to incoming fellows and students in the Liu lab. In addition, Yvona and Swati are active contributors to CCR community-based activities. In closing, I hope and expect that government support for biomedical research will increase as the economy improves. As we meet the current challenges, the knowledge, experience, and dedication of Staff Scientists and Staff Clinicians are more important than ever.

Kathy Kelly, Ph.D.
Head, Signal Transduction Section,
Chief, Cell and Cancer Biology Branch

The SP1 Region of HIV-1 Gag Functions as a Molecular Switch During Assembly

The Retroviral Assembly Section of the HIV Drug Resistance Program, Center for Cancer Research, focuses on understanding the mechanisms involved in the assembly of retroviruses, including HIV. The principal building block of retrovirus particles is the Gag protein; its sole expression in mammalian cells is sufficient for the production of immature virus-like particles (VLPs) (Fig 1a and 1c). All retroviral Gag proteins have Matrix (MA), Capsid (CA), and Nucleocapsid (NC) domains (Fig1b). Addition of single stranded nucleic acid (DNA or RNA) to purified, recombinant Gag leads to spontaneous assembly of VLPs *in vitro* (Fig 1d). By cryo-tomography, the architecture of these VLPs are indistinguishable from that of immature virus particles made in cells. VLPs expressed in cells always contain nucleic acid. *In vivo*, when the NC domain which binds nucleic acid, is replaced with leucine or isoleucine zipper protein-protein interaction domains, it still leads to VLP assembly. These zipper VLPs do not contain nucleic acid. How does NC-RNA binding (or zipper oligomerization) trigger VLP assembly mediated by the CA domain?

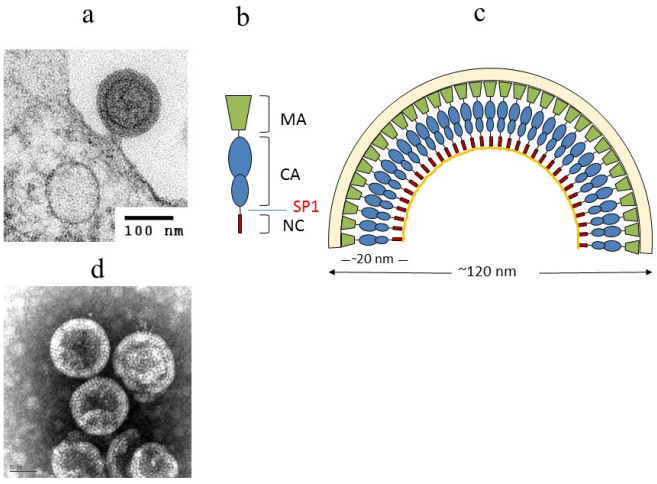


Figure 1. (a) Budding immature VLP (b) Domain structure of Gag (c) Organization of Gag in VLPs (4) In vitro assembled VLPs

SP1 is a 14 amino acid (aa) linker domain connecting NC and CA. The effect of single aa deletions in this "linker" was tested *in vivo*. The first four aa's are critical for correct assembly - deletions result in the formation of misassembled structures including blobs and tubes. Deletion of residue 5 or 6 shows partial effects; however, deletion of residue 7 does not have an effect on VLP morphology. Introducing missense mutations to these linkers was impactful. Helix breakers such as G or P, or charge reversal have the most dramatic effects, though some synonymous changes are tolerated. Molecular dynamics (MD) modeling suggested that the structure of this region was extremely sensitive to environmental conditions (dielectric). As the dielectric is lowered, the structure should undergo a concerted transition from an unstructured state to form an amphipathic helix.

To test the MD predictions, the properties of a peptide spanning the CA-SP1 junction, 18 aa in length, were investigated. Monitoring the change in peptide secondary structure as a function of environmental conditions could give insight. Circular dichroism (CD) instrumentation at the Biophysics Resource (BR) was critical to address this question. We found that the peptide undergoes solvent-dependent changes to a helical form in helical-promoting solvents (halogenated alcohols) and also in organic solvents that are not specifically helix-promoting but which alter the environmental dielectric. Remarkably, the peptide also undergoes the same transition in absence of modifying solvents, simply as it is concentrated: this region switches from an unstructured to a helical conformation as a function of its own concentration. The exquisite sensitivity of SP1 to mutational changes and its ability to undergo a concentration-dependent structural transition raise the possibility that SP1, as part of Gag, could act as a molecular switch to prime HIV-1 Gag for VLP assembly. We suggest that the nucleic acid binding (or association by zipper domains) plays a non-specific role in concentrating the Gag molecules, whereupon changes in the local environment of SP1 might trigger this switch (1). These properties render it an attractive target for anti-assembly drug design.

Current experiments are underway to investigate the structure of the SP1 helical bundles, forced to oligomerize as zipper chimeras. Facilities at the BR, including CD, differential scanning calorimetry, mass spectrometry and fluorescence spectroscopy are being used in this endeavor.

The Core Corner Con't

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

The BR http://ccr.cancer.gov/resources/sbl/BR/Default.aspx is an open, shared use facility; in general, BR users get training from BR staff members to run their own experiments with the help of nine modern biophysical techniques. For the most complex studies, BR staff members (Sergey Tarasov, Ph.D., and Marzena Dyba, M.S.) collaborate with users by providing experimental design, data analysis, and interpretation. Since its foundation in 2001 to its current form, more than 160 CCR scientists have conducted collaborative research with the BR or have been trained to use BR instrumentation and 142 scientific publications and patents were prepared in collaboration with BR or with BR acknowledgement.

Sergey G. Tarasov, Ph.D. (SS)
Head, Biophysics Resource
Structural Biophysics Laboratory

Siddhartha A.K. Datta, Ph.D. (SS)
Retrovirus Assembly Section
HIV DRP Retroviral Replication Laboratory

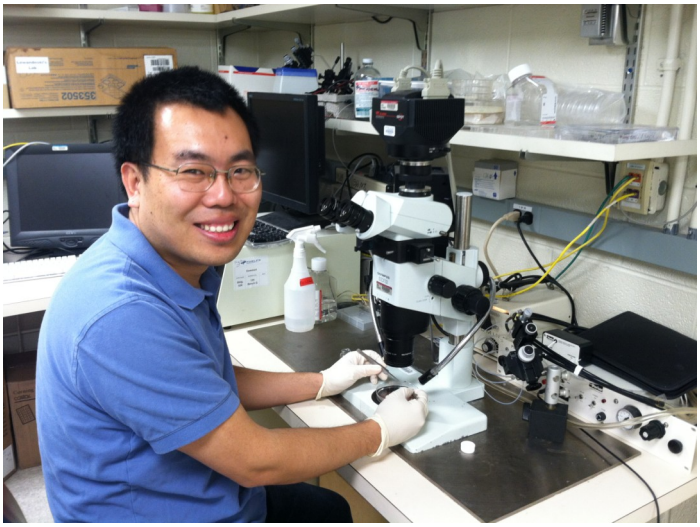
References:

1. *Datta, S.A.K. et al. On the role of the SP1 domain in HIV-1 particle assembly: A molecular switch? J Virol*. 2011 May; 85(9):4111-21.

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

The SSSC Corner

Section Editor: Takashi Furukawa, Ph.D. (*SS*)



I came to NIH as a postdoctoral fellow after finishing my Ph.D. in China. My graduate work focused on developing new approaches for cancer treatment. To pursue my interest in cancer biology, I joined Dr. Susan Mackem's lab at NCI. Her group was studying Sonic Hedgehog (Shh) signaling that is involved in carcinogenesis and is also very critical for embryonic development. This gave me a unique opportunity not only to follow my interest in cancer studies, but also to learn a completely new field of developmental biology. I am amazed by the learning opportunities available at NIH. The NIH Intramural Program has provided me with chances to learn new subjects via a wide range of courses and hands-on training on cutting-the-edge technologies. I have had the privilege to access and interact with the worlds' leading scientists in various fields. This training experience has broadened my knowledge in many aspects of science and has helped me become a better scientist.

After my postdoctoral training, I was promoted to Staff Scientist in the same laboratory. The Staff Scientist position was ideal for me as I could carry on high-risk, innovative research. For example, the classical spatial/temporal gradient models of Shh function in the developing limb have been widely accepted in the field, but my initial work on this subject contradicted that dogma. It would have been extremely difficult to move these studies forward at any other place due to its high risk and bleak funding opportunities. Luckily, with the extended support provided to me as a Staff Scientist from Dr. Mackem, I was able to pursue these studies and have since proposed a new biphasic model. This groundbreaking finding is not only important in the limb field, but can also be applied to cancer studies. I really appreciate the freedom of exploring novel ideas as a Staff Scientist.

Jianjian playing Tic-Tac-Toe with his 4-year-old son David, photographed by his 9-year-old daughter Hannah.

Aside from my research in the lab, I love to spend quality time with my family. My 9-year-old and 4-year-old kids love to play with me in and out of the house. It always surprises me how easily they are satisfied, e.g. by a small toy or by playing Tic-Tac-Toe with me. I am enjoying every moment with them before they are teenagers and get busy with their studies and friends. Besides work and family, I love to volunteer in my local community and am involved in church activities in my spare time.

Jianjian Zhu, Ph.D. (SS)
Regulation of Vertebrate Morphogenesis Section,
Cancer and Developmental Biology Laboratory

The Bioinformatics Corner

Getting Publishable Results from High-Throughput Data: Experimental Design Initiatives at CCR

As high-throughput (HTP) technologies increasingly becoming a staple of biomedical research, many CCR labs have been embracing these new tools to attain a more detailed and quantitative view of cancer and its progression. CCR Staff Scientists and Clinicians (SSSC) have been at the forefront of this effort, often being the first in the lab to adopt next-gen sequencing, microarrays, proteomics, metabolomics, or related technologies. Since many HTP instruments such as Illumina HiSeq sequencing systems produce terabytes of data in a single run, early adopters often faced significant challenges when they tried to analyze, visualize, and integrate these large datasets across platforms and with existing public data.

Fortunately, over the last several years hundreds of bioinformatics analysis tools and algorithms have been developed to help researchers conduct progressively complex analysis that go far beyond simply enumerating transcripts, proteins, or metabolites. In CCR, several biologist-friendly commercial tools such as Partek, Genomatix, Ingenuity, and CLC Bio have been made available through the Office of Science and Technology Partnerships (OSTP). Additional help is offered through the CCR Bioinformatics Core (CCRIFX), which opened in 2011 to assist CCR investigators and staff in data analysis and experimental design. To extract meaningful information from complex and noisy HTP data, CCRIFX analysts use state-of-the-art commercial and open-source tools to conduct analysis, provide insight as well as deliver publication quality results.

In addition to sophisticated bioinformatics analysis tools, much more advanced approaches have been developed to optimize the design of next-gen sequencing and other HTP studies. Over the past two years, the CCRIFX core has assisted in over 100 requests for support. This experience has provided a unique opportunity to capture several key data quality metrics that can be used to enhance the design and minimize the costs of experiments. Without increasing costs, a few changes in the design of the study can help elevate its scientific impact, potential for clinical application, and chance of being published in a top-tier journal. Some of these enhancements are specific to small- and medium-scale projects, while others overlap with the guidelines proposed by TCGA, ICGC, ENCODE, and other large-scale projects proposed for common omics technologies.

To take this promising development further, in collaboration with CCR investigators and staff, the CCR Sequencing Facility, as well as the Bioinformatics Support Group (BSG) of the Advanced Biomedical Computing Center (ABCC), the CCRIFX has initiated efforts within the CCR community to draft practical guidelines on experimental design and data quality thresholds. The first guidelines will be developed for the four most common HTP technologies used by CCR including Exome-Seq, ChIP-Seq, RNA-Seq and microarrays. As consensus builds around the guidelines, preliminary information will be made available on the CCRIFX website in order to help inform future HTP experiments, to gather input from the larger CCR community, and to incorporate this input into recommendations.

If you are in the design phase of a new HTP project, it is never too early to contact CRIFX by submitting a request for an experimental design consulation at: http://ccrifx.cancer.gov/experimentaldesign. If you would like to be involved in the CCR data quality initiative, please contact Natalie Abrams, Ph.D., (natalie.abrams@nih.gov) or Eric Stahlberg, Ph.D., (stahlbergea@mail.nih.gov).

Natalie Abrams, Ph.D.
Bioinformatics Manager/ Scientific Lead
CCR Bioinformatics Core
Advanced Biomedical Computing Center (ABCC)
Information Systems Program, SAIC-Frederick, Inc.
Frederick National Laboratory for Cancer Research

Our new SSSC Officers

The mission of the CCR SSSC Organization is "to advance the professional goals and scientific careers of CCR Staff Scientists and Staff Clinicians (SSSCs)." As Bethesda officers, Christophe Marchand and I are committed to achieving those goals. Our quadrennial reviews are important to all of us and we would like to help SSSCs do as well as possible on quadrennial reviews and further their careers. How will this happen? Our committees are working to help you achieve your goals. I hope you were able to attend the CCR SSSC Annual Retreat on April 22, 2013. The Annual Retreat Committee plans the retreat with several goals in mind: to educate SSSCs, to provide networking opportunities to SSSCs and to give SSSCs an opportunity to ask questions of scientific and administrative personnel. Additional networking opportunities are provided by our Social Networking Committee. In the past, the committee has planned social events, and in the future, the committee hopes to also establish an online forum for SSSCs to ask scientific and other questions of other SSSCs. I know I have personally made contacts through social networking that led to collaborations and collaborative publications. If you went to the Retreat, you also heard Christophe speak of the tremendous impact that professional training has had on his career. The Professional Development Committee provides links to many training opportunities for SSSCs. And finally, the Communications Committee maintains our very useful website and publishes this newsletter, *The Dossier*.

Although we have a number of good committees at work, there is still more to do. We are working CCR-wide and NIH-wide to improve opportunities for advancement for SSSCs, even in the current funding climate. Specifically, we are trying to help redefine tercile designations and descriptions that will be NIH-wide. We would also like for all SSSCs to be well-educated about the quadrennial review process. In particular, what qualifications will result in ratings of outstanding, excellent, good, satisfactory or unsatisfactory?

In terms of a personal introduction, I am a SS working in Dr. Larry Samelson's lab in the Laboratory of Cellular and Molecular Biology. I have been a SS in Larry's lab since 2000 and have previously served on the Quadrennial Pay and Promotions committee, the Annual Retreat Committee and currently serve on the Social Networking Committee. My area of expertise is in transgenic mouse models and the study of T cell signal transduction. Christophe has been a SS in the Laboratory of Molecular Pharmacology since 2006. He serves as chair of the Professional Development Committee and was instrumental in establishing SSSC Mid-year Training opportunities and in publishing the CCR SSSC Handbook. In the lab, he has developed novel high-throughput screening assays for the discovery of Human tyrosyl DNA phophodiesterase I (Tdp1) inhibitors.

Christophe and I hope that you will contact us about issues of concern to CCR SSSCs.

Connie Sommers, Ph.D. (SS)
Laboratory of Cellular Molecular Biology
Bethesda Co-Chair

Christophe Marchand, Ph.D. (SS)
Laboratory of Molecular Pharmacology
Bethesda Secretary

Our New SSSC Officers Con't

Through almost ten years of its existence, the CCR SSSC organization has been very successful in consolidation of SSSC efforts to achieve their professional goals. The organization is doing many great things, including yearly Retreats, Professional Development Committee actions, Frederick bimonthly seminars, informational and educational web-based support, our newsletter, *The Dossier*, as well as social events, etc. However, the more I praise the SSSC organization, the more evident is the fact that only a small fraction of the SSSCs take part in these activities. For example, our Retreat registration list, from year to year, only covers roughly half of all the SSSCs. So, what's wrong? Aren't star-like events such as the forum "Why Haven't We Cured Cancer Yet" at the recent Retreat worth every CCR researcher's time?

Why does this happen? Is it due to the fact that some people are busier than others? I don't think so. I believe it is all about personal values. Beginning in my college years, I could always watch the social extraverts and introverts, as they differed in their appreciatation of values of open scientific society. There are always easy-goers, whom it is easy to recognize by the expression of interest in their eyes, and those whose eyes you actually don't have a chance to see, because they are not frequently "in public", either at scientific or public events.

Could I be wrong? Do I unfairly treat those who prefer to spend all of their time working hard in their labs, escaping unnecessary (in their opinion) "distractions"? I would insist that the SSSC organization's activities are serving to enhance our professional goals by all possible means and, therefore, has no rational ground to be considered as a loss of time. Doesn't the consistent stream of information about the Quadrennial Review throughout the last several years serve as an outstanding example of the organization's support for professional and career growth?

The SSSC organization is a completely voluntary association. We can't force anybody to visit our Retreats or professional trainings or social events. However, I need to admit that so far, we have not reached the soul and heart of every potential member, in spite of our rich and vibrant SSSC organization activities. Maybe, it is just due to the fact that some individuals do not consider it "rich and vibrant" or are just too busy. But what can be done? Should we have a program like "No Staff Scientist Left Behind"? Has everyone already made their choices and thus any effort to increase the pool of active participants futile? Perhaps it may be true for those SSSC who have held their positions for 15-20 years. But it can't be true for those who just became a SSSC. That's why the SSSC organization pays so much attention to newly appointed scientists, and the recently implemented "CCR SSSC Handbook" is the best example of that.

I would like to finish with an appeal that is one of the focus areas for me as one your new representatives: Let's do our best to bring CCR SSSCs TOGETHER to appreciate the advantages of an integrated SSSC scientific community and benefit from it both socially and scientifically. We will be looking for ways to find an individual approach for every member of the SSSC group to make it happen, starting with improving our notification system and working on agendas of regular meetings to make them more attractive for everybody.

Sergey Tarasov, Ph.D. (SS)
Structural Biophysics Laboratory
Frederick Co-Chair

Our New SSSC Officers Con't

The old adage "*you cannot see the forest for the trees*" is nowhere more applicable than here at the NIH where Staff Scientists and Staff Clinicians are universally engaged in undeniably important work throughout the campus. We are all so focused on what we do that many of us cannot tell you what goes on in the clinic or lab two floors above our own, much less what work is being done in the building next door. As a perfect example of this, I recently discovered that a colleague in another branch has seen as many or more patients with a particular disorder than has ever been reported in the medical literature. For him it was the occasional rare case, but for our branch it was a revelation within our own discipline. The chance for this sort of exchange of information and ideas is among the many things which make the NIH a unique and special place. But how many golden opportunities are missed because these exchanges often only occur by happenstance? I believe the Staff Scientists and Staff Clinicians Organization (SSSCO) is a means to promote this type of collaboration among experts who may not otherwise ever cross paths.

We have all spent innumerable years acquiring expertise that allow us to perform the critical work that each of us does. A common consequence of this type of intense training is a focus that can often manifest as tunnel vision which makes each of us an expert in our field but also makes us equally unfamiliar with issues outside of our field of study. While none of us would ever think twice about engaging in ongoing education within our own disciplines, it is somewhat unnatural for us to consider training in how to manage our careers as equally important and worthy of our time. As a result, many of us are less prepared to promote our own careers and navigate the labyrinthine organizational structure of the organizations for which we work. Yet none of us would ever doubt the value of scientific cross-pollination between different disciplines.

The purpose of the SSSCO is to foster not only career growth for Staff Clinicians and Staff Scientists but also to create a mechanism by which previously unforeseen collaborations can be conceived and mentored. One of the primary motivators for most Staff Scientists and Staff Clinicians is career advancement through professional achievement. Unfortunately, that association is not as linear as we would all like to think it is, and I believe one of the roles of the SSSCO is to help the SSSC community better understand that career advancement has to be planned and promoted; it does not just "happen" magically. In addition, I believe the SSSCO has an obligation to help facilitate career progression for as many in the community as possible. The founders of the SSSCO have done remarkable work in establishing and growing this organization, and it is my privilege to continue that work to raise awareness of the benefits of the SSSCO to a wider audience. As a representative to the SSSCO, I will work to help more of the Staff Scientist and Staff Clinician community to see the forest as well as the trees.

Adam Metwalli, M.D. (SC)
Urologic Oncology Branch
Clinical Co-Chair

Announcements

Congratulations!

Join us in congratulating this year's SSSC winners of the Best Poster Awards at our Annual Retreat!

Jun Wei, Ph.D., Pediatric Oncology Branch

Xiaoying Ye, Ph.D., Laboratory of Proteomics and Analytical Technology

Yanlin Yu, **Ph.D.,** Laboratory of Cancer Biology and Genetics

Congratulations!

Ofelia Olivero, Ph.D.: Recipient of the 2013 AWIS Bethesda Mentoring Award

Anu Puri, Ph.D.: Recipient of a 2013-14 Intramural to India Grant

SSSC Ice Cream Social!

Date: Wednesday, July 17, 2013
Location: Bldg. 37, North entrance park benches (in case of inclement weather: Bldg. 37, Rm 2107/2041)
Time: 3:00-4:00 pm

Looking for Editorial Experience?

The Dossier is looking for SS or SC to participate as Section Editors. If interested, please contact Anuradha Budhu at budhua@mail.nih.gov

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 a SSSC Committee

Professional Development:
Contact Christophe Marchand, Ph.D.

Communications:
SSSC Website: Contact Sharon Moore, Ph.D.
***The Dossier*:** Contact Anuradha Budhu, Ph.D.

Social Networking:
Contacts: Smitha Antony, Ph.D.
Swati Choksi, Ph.D.
Connie Sommers, Ph.D.
Aleksandra Michalowski, Ph.D.

SSSC Retreat:
Contacts: Rimas Orentas, Ph.D.
Anu Puri, Ph.D.

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