THE DOSSIER

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

March 2012 Issue 8

From the Editor

Welcome to the March 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 Jeffrey S. Rubin, M.D., Ph.D. The agenda and registration site for the 8th annual SSSC retreat is provided. Our series on summarizing Information Technology resources at NCI continues along with an article by Ofelia Olivero, Ph.D. (AS), describing an exchange program with Brazil aimed to connect and promote emerging female leaders. We highlight the work of Anu Puri, Ph.D. (SS), and her successful experience with the Protein Chemistry Laboratory and the Laboratory of Proteomics and Analytical Technologies. We also provide important news on the SSSC Quadrennial Review and on the SSSC Professional Development Series. We hope to continue to provide relevant and pertinent information to aid in the success of SSSCs. Please send your contributions, suggestions and comments to budhua@mail.nih.gov.

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

In This Issue

SSSC Co-Chairs

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From the Office of the Director

In last summer's issue of the *Dossier*, I discussed our Major Opportunity (MO) initiative, part of CCR's ongoing protocol reengineering efforts. This initiative is identifying exciting clinical research areas where focused effort on achieving specific clinical goals within 3-5 years may lead to significant leaps forward in the field of oncology medicine. I invited you to participate in our survey to identify these areas and to our retreat.

More than 100 CCR researchers and clinicians participated in the Major Opportunities Retreat on October 21, 2011, at the Bethesda Marriott. About one-third of the attendees were basic scientists. Many of them told me personally how excited they were to participate in this effort and to collaborate with their clinical colleagues. As a result of the retreat, where each proposed MO was presented and discussed, and through a follow-up survey afterward, eight MOs were refined. These eight are now being prioritized using feedback from the CCR community, the Board of Scientific Counselors, CCR senior leadership and the NCI director.

The eight MOs under consideration are:

- Targeting Inflammation in Cancer
- Matrix Drug Screening for Combination Therapies in Cancer
- Treatment of Cancers Based on "Driver Mutations" Independent of Histology or Site
- Monitoring and Manipulating the Epigenome in Human Cancers
- Target Therapy Combining Immunotherapy and Pharmacology
- Attacking Cancer Based on Its Metabolic Basis
- Rare Cancers and Genetic Tumor Predisposition Syndromes (GTPS)
- Characterizing the Transition from Premalignant or Early Stage Cancers to Lethal Tumors

" ….our Major Opportunity (MO) initiative…. is identifying exciting clinical research areas where focused effort on achieving specific clinical goals within 3-5 years may lead to significant leaps forward in the field of oncology medicine."

CCR will be announcing the MOs that will be supported soon. I hope many of you will take an active role moving those projects forward.

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

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

The 8th Annual SSSC Retreat (April 17, 2012)

The 8th Annual CCR and DCEG Staff Scientist and Staff Clinician Retreat will be held on Tuesday, April 17, 2012, from 8am to 6pm at Natcher Auditorium (Bldg. 45).

The general theme of this year's retreat is increasing the effectiveness of our work through collaborations. The event will bring together not only NCI Staff Scientists and Staff Clinicians, but also Scientists from SAIC. Two poster sessions will include four sections: Basic Research, Epidemiology/Bioinformatics, Translational/Clinical Research and Technologies Development. Travel awards for the winners of the poster competition will be provided by NCI and SAIC.

To register and submit a poster abstract log in at: http://web.ncifcrf.gov/events/SSSCRetreat2012/default.asp

Nadya Tarasova, Ph.D. (SS) and Sergey Tarasov, Ph.D. (SS)
(2012 SSSC Retreat Co-Chairs)

Agenda

8:00 am Poster setup and registration

8:30 am Opening remarks: Dr. Robert N. Hoover

8:45 am Keynote speaker: *Dr. Bahija Jallal, MedImmune Executive Vice President, R & D.*

10:00 am Poster session I

11:45 am Topic lunch (choice of one):
1. IP, Technology Transfer and collaboration with the industry
2. Collaboration between clinicians and bench scientists
3. Life in the new budget
4. Quadrennial review, professional growth and career paths

1:00 pm Poster session II

2:45 pm Special highlight presentation: *Mathew Zachary, Radio Talk Show Host, Recording Artist and Founder/CEO of I'm Too Young For This! Cancer Foundation*

4:00 pm Management workshops (choice of one):
1. Creating Motivating Environments
2. Making the Transition to Manager (includes power and influence)

5:00 pm Award ceremony
Closing remarks: Dr. Robert H. Wiltrout

A CCR Staff Scientist Visits Brazil

The Governments of the United States and Brazil have an Memorandum of Understanding aimed at advancing women in both countries. One of the first priorities under the agreement as expressed by the Brazilian side was for emerging women science leaders to visit the United States. The U.S. hosted eight scientists during the Commission on the Status of Women meeting held in NYC in 2011, then arranged for them to visit several NSF grantee institutions. From a group of more than 500 applicants, eight U.S. women scientists were selected to visit Brazil through a reverse exchange program led by the Office of Women's Issues of the U.S. Department of State. The delegation left the U.S. on December 4 to 14, 2011. I was very happy to share the trip with seven colleagues representing different fields of STEM (Science, Technology. Engineering and Mathematics). The group was diverse, composed of an architect, two engineers, a post doc, a graduate student, a neuroscientist, and a geologist. So the already inspirational experience of visiting this country was enriched because we learned a lot from each other.

Front row from the left: Norma Santos Paes (Brazilian representative), Parinaz Massoumzadeh, Diane Wray-Cahen, Erin Pettit and Ofelia Olivero.

Back row from the left: Amy Patrick, Donnette Sturdivant, Candace Carroll, Lauren Armstrong and Beatriz Helena Matte Gregory (Brazilian representative).

As a Staff Scientist it is important to have had the chance to participate in an experience like this and I urge all of us to keep looking for opportunities that help enrich our careers and growth. The incredible journey that we experienced is hard to describe on paper. We visited four different cities: Recife, Belem, Rio de Janeiro and the capital Brasilia. We had the chance to meet scientists working for translational science centers, museums in the Amazonian region as well as archeologists, physicists, curators, experts in science policy, diplomats, and more. Many connections were established and a report providing a list of recommendations and ways to implement them in the short and long term is being performed by the delegation.

The U.S. State Department organized this event with the purpose of generating awareness of other countries' initiatives to promote women in science.

I would like to share with my colleagues what the delegation and I learned.

- The Brazilians are passionate and can make any difference possible with their strong beliefs. However, commitment from the top is an essential component to make this possible. We learned that the president of Brazil, a woman, has allocated monetary support to fund 100,000 scholarships for female students and graduates to train outside the country. Half will train in the U.S. In addition, she has created the Ministry of Women, where issues regarding women's rights are a priority.

- Outreach to the community from scientific organizations is very important in Brazil and I believe that this could be used as a model from which to learn. Organizations want to show their communities their treasures and enhance awareness of natural resources and conservation of the environment, particularly among their youth; certainly, a lesson to bring back home.

- Lastly, we realized that engagement of additional women in STEM in Brazil or in the U.S. would be based on commitment

A CCR Staff Scientist Visits Brazil Con't

from the top, not on the knowledge we acquired.

- Overall, formal and informal exchanges with Brazilians helped us understand that global challenges require global solutions, and this program was a true attempt to start a global dialogue that will not be interrupted.

Ofelia Olivero, Ph.D. (AS)
Laboratory of Cancer Biology and Genetics
Carcinogen-DNA Interactions Section

The PI Corner

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

I've served on the Promotion Review Panel that evaluates applicants for the Staff Scientist position since 2000. For the past few years I've been fortunate to have a gifted researcher, Dr. Yoshimi Greer, working in my lab as a Staff Scientist. These experiences have provided an in-depth perspective of the position and the individuals who fill it.

The Staff Scientist plays a central role in the research of most labs while assisting junior members in learning techniques and helping in other ways to further their projects. Circumstances vary within different groups, but the common denominator is expertise in a critical area of research and an ability to work well with others. Staff Scientists are highly valued for their scientific knowledge, technical skills, leadership and the continuity they provide to the group.

"Staff Scientists are highly valued for their scientific knowledge, technical skills, leadership and the continuity they provide to the group."

In the challenging budgetary times we currently face, the Staff Scientist is especially important. Our continued success will depend on this core of talented, highly motivated individuals who share a passion for research. Staff Scientists and PIs can work together to ensure that the path forward is productive. These efforts should be imbued with mutual respect, and PIs should be mindful of their partners' needs which include recognition of their accomplishments, opportunities to present at meetings, a network of professional contacts and time to devote to classes and NIH community service. Particularly when times are difficult, we should appreciate and nurture the combination of intelligence, skill, dedication and drive embodied in the Staff Scientist.

Jeffrey S. Rubin, M.D., Ph.D.
Senior Investigator
Laboratory of Cellular and Molecular Biology

The Information Technology Corner

PIV cards, facts and helpful links

Personal Identity Verification (PIV) card has become a fact of life for staff at the NIH. This article will discuss some facts about the PIV card itself as well as current plans for how PIV cards will be used at the NIH.

The idea of a standard federal ID was turned into action in 2004 when the President signed Homeland Security Presidential Directive 12 (HSPD-12), titled "Policy for a Common Identification Standard for Federal Employees and Contractors." In HSPD-12, the National Institute of Standards and Technology (NIST) was required to develop a set of guidelines for how common identification would be implemented. NIST has created several documents for this purpose, with the main one being Federal Information Processing Standard 201 or FIPS 201.

These standards have allowed the development of smart cards, card readers, and software that work together to provide identity verification both physically and electronically. Some PIV card facts include the following:

- The use of a PIV card with its PIN is called two-factor authentication. Something you have (PIV card) and something you know (PIN).
- The PIV card and PIN provides us a very secure way to identify ourselves.
- The PIV card contains a digital certificate that allows us to sign and encrypt email and other documents.
- HHS wants NIH to develop plans for how we will replace the use of username and password for authentication with PIV card and PIN.
- All computers that are not part of a scientific equipment installation should have a PIV reader and software installed.

How will the current and new PIV card policies impact us, day to day and long term?

- PIV cards are now our standard badges. They can be used to gain entrance to both the Bethesda and Frederick campuses.
- The certificates on our PIV cards have a 1- or 2-year life span. You will be notified when the expiration date nears.
- Both Mac and PC computers can be configured to allow the use of PIV cards for computer login, web site login, email encryption and VPN login.
- VPN login will be the first mandated two-factor service.
- On March 1 all VPN access to the NIH network from outside of NIH will be done via two-factor authentication. This will be accomplished mainly with PIV card and PIN. Some staff will have to use a RSA token for devices that don't support PIV cards, or for contractors that physically can't get a PIV card issued to them.
- In the future, all standard laptops will require PIV card and PIN to login.

The main site for PIV card information at NIH is here: http://smartcard.nih.gov

NCI Bethesda PIV information: http://itss.nci.nih.gov/piv.html

NCI Frederick PIV information: http://css.ncifcrf.gov/information/piv/

As always, please email me with any questions or concerns at jdshilling@nih.gov

Jeff Shilling
IT Architect
CCR Office of Information Technology

The Quadrennial Review Corner

Quadrennial reviews will occur in March for both Staff Clinicians and Staff Scientists. For Staff Clinicians only, we are inviting branch chiefs to the Clinical Review Panel meeting to confidentially discuss (5-10 minutes) the unique and critically important role each Staff Clinician plays in their branch, as well as in CCR and NIH, as appropriate.

CCR OD

The SSSC Professional Development Series

The SSSC Professional Development Committee and the Office of Workforce Management and Development have crafted a series of free quarterly 2-hour workshops on professional development for SSSC. The first session was held on January 31 in Building 40 and was about DiSC, an assessment tool that identifies a person's preferred behavior style among four quadrants (Dominance, Influence, Steadiness and Conscientiousness). During two hours of extremely interactive activities and discussions, participants identified their own DiSC behavioral styles. They also learned how to recognize and how to interact effectively with other DiSC styles.

Some of the participants who had previously received a full DiSC assessment from the Office of Workforce Management and Development found the session very useful due to the in-depth analysis of the four different DiSC behavioral styles.

The April session will be about enhancing your emotional intelligence (EI) by understanding what EI is, knowing EI competencies and identifying strategies to build EI competencies.

We hope to see an increasing participation of the SSSC community.

"*We cannot become what we need by remaining what we are*." — John C. Maxwell

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

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

Development of Lipid-based Photo-triggerable Platforms for Delivery of Anticancer Drugs

In the Membrane Structure and Function Section (MS&F) in the Nanobiology Program, headed by Dr. Robert Blumenthal, we focus on the molecular mechanisms of viral fusion and triggerable drug carriers. Dr. Anu Puri (SS in the MS&F section) devotes her research efforts to develop Intelligent Drug Delivery platforms to improve the therapeutic index of anticancer agents and nano-scale diagnostic tools for detection of pathogens and cancer biomarkers. She has developed nanoparticles (liposomes) by utilizing light-sensitive lipids[1]. These nanoassemblies of lipids (designed based on the criteria of stability/on-demand release potential, Figure 1) include a matrix lipid, a phototriggerable lipid ($DC_{8,9}PC$, Figure 1A) and a pegylated lipid (for stealth properties) (Figure 1B).

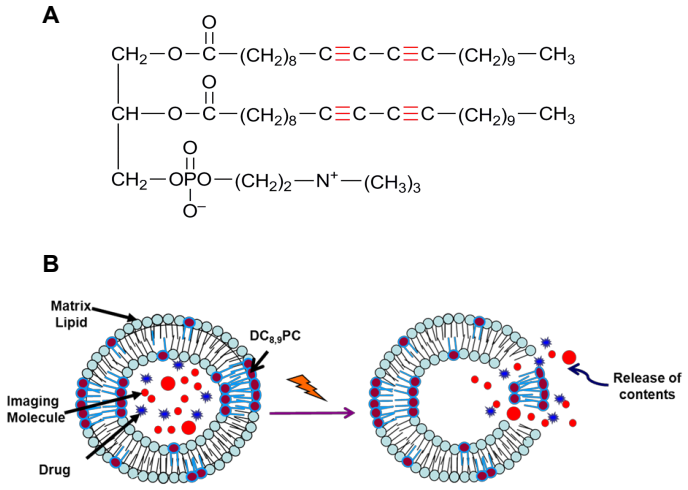


Fig 1. Design principle of photo-triggerable liposomes. (A) Chemical structure of $DC_{8,9}PC$. Diacetylene groups are shown in red. (B) A diagram showing various components of DPPC:$DC_{8,9}PC$ liposomes including a matrix lipid (DPPC), photo-triggerable lipid ($DC_{8,9}PC$), stabilizing lipid (DSPE-PEG2000) and entrapped anticancer drug or imaging marker. The cartoon also shows light-induced defects in the lipid membrane resulting in release of entrapped molecules.

The core of these particles includes an anticancer agent (such as doxorubicin) or a model fluorescent marker (such as calcein). We have demonstrated that visible light activation increases cytotoxicity of liposomal doxorubicin in cell culture-based assays when light-sensitive formulations are used[2]. Figure 2 shows the potential mechanisms of light-enhanced cytotoxicity. Our studies also demonstrate that clustering of the polymerizable lipid, $DC_{8,9}PC$ in the lipid bilayer (liposomes) is critical for light-triggered release of encapsulated contents[3]. Activation by light sources ranging from UV to visible to near-IR results in release of contents albeit via different mechanisms. For example, UV-triggered release occurs via the polymerization of $DC_{8,9}PC$ monomers. In contrast, visible light treatment does not promote photopolymerization of $DC_{8,9}PC$ monomers. Biochemical assays show a role of reactive oxygen species (ROS) in releasing the contents in latter case.

At this juncture, it became important to analyze light-induced modifications and any potential degradation byproducts in the lipid molecules, and hence led to a long-standing and fruitful collaboration with the investigators of two ATP laboratories: Protein Chemistry Laboratory (PCL) and Laboratory of Proteomics and Analytical Technologies (LPAT).

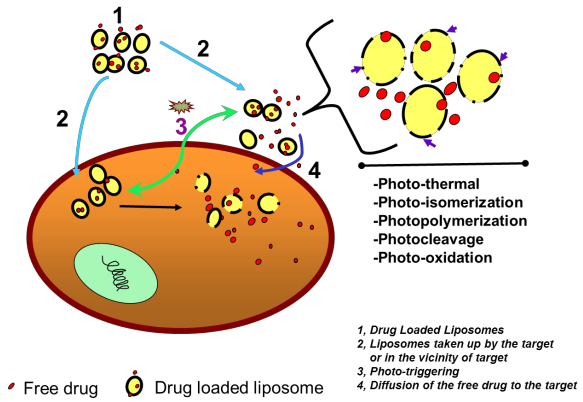


Fig 2. Release mechanism(s) of liposome-encapsulated drugs by photo-triggering

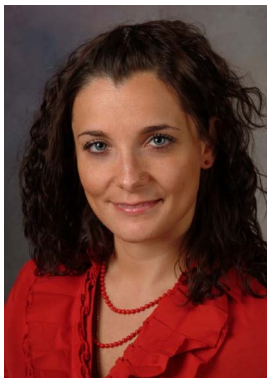
At the PCL, Drs. Simona Colantonio and Jack Simpson developed an assay to quantitate the levels of lipids using NALDI (nanostructured assisted laser/desorption and ionization)-TOF technology using a Bruker UltraFlex III mass spectrometer. NALDI allows lipids and other biomolecules to be analyzed within relatively complex mixtures without the use of any traditional matrix. Irradiation with a laser causes the molecules within the sample to be ionized and desorbed into the gas phase enabling them to be analyzed using mass spectrometry (MS)[4]. This new

technology bears the merit of broad-range applications for lipid analysis.

The LPAT possesses state of the art instrumentation including nuclear magnetic resonance (NMR), liquid chromatography and gas chromatography coupled tandem mass spectrometry (LC-MS) to solve challenging analytical problems in the fields of proteomics and metabolomics. In collaboration with Drs. Timothy Veenstra and Athar Masood (LPAT) we utilized a different approach to quantitate the ratios of lipids and the degradation products following photoactivation by light. The lipid analysis was performed using the LC-MS and quantitated using the selected reaction monitoring (SRM) protocol using the TSQ Discovery triple quadrupole mass spectrometer (Thermo Scientific, San Jose, CA) coupled to a Shimadzu UFLC XR HPLC system. The outcome of these efforts led us to map light-induced changes in the lipid molecules in our formulations and this information will be instrumental for further development of suitable drug delivery carriers.

This project illustrates an excellent example of the ability of the ATP to target specific molecules within mixtures. While mass spectrometers are often thought of as high-throughput protein sequencers capable of identifying thousands of proteins or metabolites in complex, they are also capable of characterizing a specific molecule with high sensitivity and accuracy. Whether your interest is in targeting a molecule or characterizing a complex mixture, the ATP may have the technology and scientific expertise you need.

Anu Puri, Ph.D. (SS)
CCR Nanobiology Program
Membrane Structure and Function Section



Simona Colantonio, Ph.D.
Protein Chemistry Laboratory

Timothy Veenstra, Ph.D.
Laboratory Director
Laboratory of Proteomics and Analytical Technologies

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2. Yavlovich A, Singh A, Blumenthal R, Puri A. A novel class of photo-triggerable liposomes containing DPPC:DC(8,9)PC as vehicles for delivery of doxorubcin to cells. *Biochim Biophys Acta.* Jan;1808(1):117-26, 2011.

3. Puri A, Jang H, Yavlovich A, Masood AM, Veenstra TD, Luna C, Aranda-Espinoza H, Nussinov R, Blumenthal R. Material Properties of Matrix Lipids Determine Conformation and Intermolecular Reactivity of a Diacetylenic Phosphatidylcholine in the Lipid Bilayer. *Langmuir : the ACS journal of surfaces and colloids*. 27(24): 15120-8, 2011.

4. Colantonio S, Simpson JT, Fisher RJ, Yavlovich A, Belanger JM, Puri A, Blumenthal R. Quantitative Analysis of Phospholipids Using Nanostructured Laser Desorption Ionization Targets. *Lipids*. 46(5): 469-77, 2011.

Announcements

Congratulations!

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

Francis A. Flomerfelt, **Ph.D.,** Experimental Transplantation and Immunology Branch

Romina S. Goldszmid, Ph.D., Laboratory of Experimental Immunology

Paola Scaffidi, Ph.D., Laboratory of Receptor Biology and Gene Expression

Wanping Xu, **M.D., Ph.D.,** Urologic Oncology Branch

Attend

The 8th Annual CCR and DCEG SSSC Retreat

Abstract submission deadline: March 30, 2012

Registration deadline: April 9, 2012

http://web.ncifcrf.gov/events/SSSCRetreat2012/default.asp

CCR SSSC Professional Development Series

Enhancing your Emotional Intelligence (EI)

April 10, 2012; 10-12pm

Building 40, Rm 1201/1203

A Call for Content

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

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

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

Join one of these SSSC Committees

Professional Development: Contact Christophe Marchand, Ph.D.

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

SSSC Retreat: Contacts: Sergey Tarasov, Ph.D.
Nadezhda Tarasova, Ph.D

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