

THE DOSSIER

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

March 2013

Issue 12



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 focused on CCR's Protocol Support Office and a special article by Michael Bustin, Ph.D. Information about the upcoming SSSC Retreat is provided by Rimas Orentas, Ph.D. and Aleksandra Michalowski, Ph.D. The Chair of the SSSC Professional Development Committee, Christophe Marchand, Ph.D., informs us about the SSSC Alumni Da-

tabase. We also highlight a study conducted at the NCI Laboratory of Cancer Biology and Genetics FACS Core Facility by Karen M. Wolcott and Melanie S. Vacchio, Ph.D. We are also very pleased to introduce our new SSSC section of the Dossier, which will feature the professional and outside activities of our SSSC and will be managed by our new Section Editor, Takashi Furusawa, Ph.D. 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

Anuradha Budhu, Ph.D. (SS)

Editor-in-Chief

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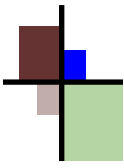
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From the Office of the Director

Making an Impact: The Protocol Support Office

Over the past few years I have personally heard from many of our Staff Clinicians and others who serve as Principle Investigators (PIs) on clinical protocols that the Protocol Support Office, created in 2010, is a highly valuable resource. Several years ago, the CCR clinical research community identified the increasing complexity and proliferation of administrative and regulatory requirements related to human subjects research as a significant barrier to developing high-quality clinical trials and opening them quickly. Through focus teams and working groups, a clear need was identified for support to protocol PIs and the CCR Protocol Support Office (PSO) was created in the Office of the Clinical Director as a result (<https://ccrod.cancer.gov/confluence/display/CCRCRO/Protocol+Support+Office>).

The PSO provides several services: (1) writing and editing, (2) advice and guidance on required processes and regulatory compliance, (3) protocol navigation and administration, and (4) administrative support to Scientific Review Committees (SRC). The PSO assists with the entire protocol lifecycle from initial Investigational New Drug (IND) application and Institutional Review Board (IRB) submission to continuing review applications, protocol amendments, and protocol deactivation. A key to success is that many protocol start-up activities are tackled in parallel rather than sequentially, saving time. For example, writing and regulatory review occurs in tandem with bi-directional dialogue and feedback between the PSO and the PI. Another key is that the PSO has standardized many processes and developed a tracking database that ensures smooth electronic submission to the Cancer Therapy Evaluation Program (CTEP).

Observing the success of the CCR PSO, NHLBI is in the process of implementing a similar protocol sup-

port office model, and National Institute on Minority Health and Health Disparities (NIMHD) has forged an agreement with CCR to use the PSO as a service center.

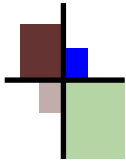
The PSO is improving the protocol development process in CCR. If you are interested in finding out more about these services, I encourage you to contact Nicole Grant (grantn@mail.nih.gov), Office Head, for more information or contact nciprotocolsupportoffice@mail.nih.gov.



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



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

The 9th Annual CCR and DCEG Staff Scientist and Staff Clinician Retreat will be held on Monday, April 22nd, 2013, from 8 AM to 5 PM at Natcher Auditorium (Bldg. 45).

The theme of this year's retreat is "Why Haven't We Cured Cancer Yet?" – a topic that has been much in the news lately. However, our goal is to put some scientific teeth into this question. We are excited to present world leaders in cancer research to share their ideas in a special interactive forum, as well as though our keynote speaker. Please come and join us for these exciting presentations and as fellow Staff Scientists and Clinicians from NCI and SAIC present their research in afternoon poster sessions. There will be three sections for posters: Basic Research; Translational, Clinical and Epidemiological Research; and Technologies and Methodologies Development. Travel awards for the winners of the poster competition in each category will be provided by NCI, DCEG, and SAIC.

To register and submit a poster abstract, log in at <http://ncifrederick.cancer.gov/events/SSSCRetreat2013/default.asp>

Rimas Orentas, Ph.D. (AS) and Aleksandra Michalowski, Ph.D. (SS)
(2013 SSSC Retreat Co-Chairs)



Agenda

8:00 am **Registration and poster setup, light refreshments**

8:30 am **Welcome and Opening remarks**

Dr. Margaret A. Tucker, M.D., Director, Human Genetics Program and Acting Director, NCI/DCEG

MORNING SESSION: "WHY HAVEN'T WE CURED CANCER YET"

9:00 am **Keynote speaker**

Richard J. Gilbertson, M.D., Ph.D., Director, Comprehensive Cancer Center and Executive Vice President, St. Jude Children's Research Hospital

10:00 am **Panel Presentations**

Edward E. Harlow, Ph.D., Chair, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School; Special Advisor to the NCI Director

Lee J. Helman, M.D., Scientific Director for Clinical Research, NCI/CCR

Barbara Wold, Ph.D., Bren Professor of Molecular Biology, California Institute of Technology

Giorgio Trinchieri, M.D., Director, Cancer and Inflammation Program, NCI/CCR

Richard J. Gilbertson, M.D., Ph.D., , Director, Comprehensive Cancer Center and Executive Vice President, St. Jude Children's Research Hospital

Continued on pp. 4

Agenda continued

Moderators:

Nadya I. Tarasova, Ph.D., Head, Synthetic Biologics and Drug Discovery Facility, NCI/CCR

Rimas J. Orentas, Ph.D., Associate Scientist, Pediatric Oncology Branch, NCI/CCR

The panel will discuss current challenges focusing on:

- Inhibiting non-druggable oncoproteins
- Understanding how drivers work in cancer cells
- Tumor heterogeneity and resistance to therapy
- Immune suppression

12:15 pm **Lunch Break**

12:45 pm **Poster Session 1**

2:00 pm **Poster Session 2**

3:15 pm **Quadrennial Review**

SS Overview: **Lynne Rockwood, Ph.D.**, Scientific Program Specialist, NCI/CCR/OD

SC Overview: **Geoffrey Kidd, Ph.D.**, Scientific Program Specialist, NCI/CCR/OD

3:35 pm **SSSC Communications**

SS/SC Officer Transition

Professional Development Committee presentation: **Christophe Marchand, Ph.D.**, Staff Scientist, Laboratory of Molecular Pharmacology, NCI/CCR

3:55 pm **Closing Remarks**

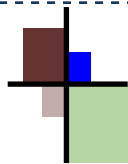
Lee J. Helman, M.D., Scientific Director for Clinical Research, NCI/CCR

4:15 pm **Award Ceremony**

Jonathan S. Wiest, Ph.D., Associate Director for Training and Education, NCI/CCR

4:30 pm **Adjourn**



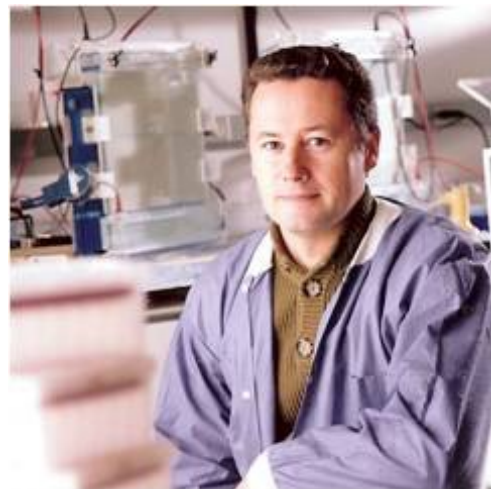


The Professional Development Corner

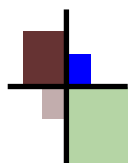
Building a SSSC Alumni Database

The NCI SSSC Professional Development Committee has been working on the development of a NCI SSSC Alumni database. With the help of CCR, the committee receives a monthly report with a list of newly promoted SSSCs and a list of SSSCs leaving the position. The committee is greeting the newly appointed SSSCs via a welcome email in which we describe our association and attach our SSSC New Hiring Handbook (also available for download from the SSSC website <http://sssc.nci.nih.gov>). The committee is also contacting SSSCs leaving their position to ask them if they wish to join our NCI SSSC Alumni database. This enrollment is of course on a voluntary basis. The database will help to develop networking among the SSSC community past and present. An example of what a SSSC Alumni group can offer to the SSSC community was demonstrated during our afternoon discussion with former SSSCs during the Second Biennial NCI SSSC

Professional Development Day in September 2012. Statistical analysis performed on this database should also help increase self-awareness inside our own community.



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



Introducing our New Section Editor

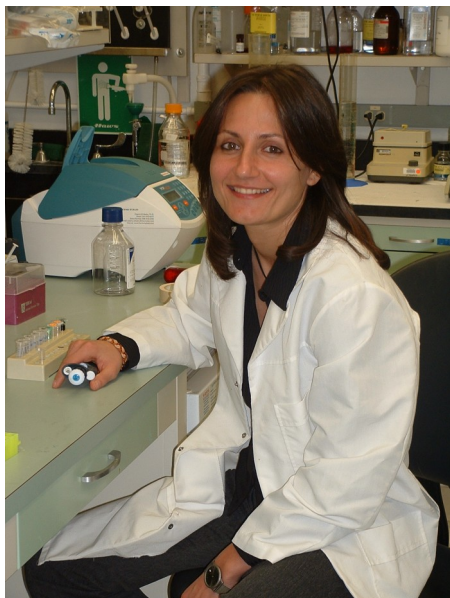
Please welcome **Takashi Furusawa, Ph.D.**, our new Section Editor for the SSSC Corner of The Dossier. Dr. Furusawa received his Ph.D. in Molecular Biology from Osaka University, Japan, in 2001 where he studied transcriptional regulation by transcriptional repressors and corepressors in mouse development. He then joined Dr. Michael Bustin's laboratory (Laboratory of Metabolism) at NCI as a visiting fellow. In 2006, he became a Research Fellow and in 2009, he was hired as a Staff Scientist. Dr. Bustin's laboratory is focusing on the biological function of chromatin structure by studying the High Mobility Group Nucleosome (HMGN) protein family, which specifically bind to nucleosomes and alters the chromatin structure. We encourage SSSCs to share their work and fun activities in The SSSC Corner of The Dossier. If

you would like to write an article for The SSSC Corner, please email: furusawt@mail.nih.gov with subject title "The SSSC Corner."



The SSSC Corner

Section Editor: Takashi Furusawa, Ph.D. (SS)



I first visited NCI while I was a graduate student, when I worked in Dr. Tom Misteli's group for a short collaboration. Since the first day there, I just knew that was the place I wanted to carry out my future research. Here I am, 11 years

later, working as a Staff Scientist in the same laboratory. Working at NCI over all these years has been a very rewarding experience, both at the scientific and personal level. As a post-doctoral fellow, my work mainly focused on the study of the cell biological basis of a childhood premature aging disorder, Hutchinson-Gilford Progeria Syndrome, and the relationship between the disease and the normal process of aging. As a Staff Scientist, I initiated a new area of investigation focused on elucidating how epigenetic mechanisms and interference with differentiation programs affect initiation and maintenance of solid tumors, by promoting cancer stem cell formation and regulating their function.

Changing the focus of my research has been challenging, since I had to start from scratch, but has, at the same time, been stimulating. Dr. Misteli gave me the freedom to work on something that interested me, although it was quite far away from the main focus of the group and that meant diving into a field that was new for both of us. This has been a great opportunity for me and opened new areas of research in the group. That is, I think, the beauty of being a Staff Scientist. You can undertake challenging projects and take risks you could not afford if you were either a postdoctoral fellow or a young Principal Investigator. On the other hand, not having independent financial support often makes it difficult for Staff Scientists to

develop new lines of investigation, complementary to the laboratory's main research. I think having even a small budget is a good way to feel more "free" and dare to explore new directions, compatible with the needs of the laboratory. Funding opportunities for Staff Scientists are not endless, but we should keep in mind they exist.

Outside the lab, my favorite "hobby" is my family, and particularly my 4-year-old daughter. She actually enjoys coming to the lab and we often do "experiments" together – dry ice can do very cool things! She has taught her friends and teachers that bacteria are not just germs, but can also be very useful. Outdoor activities are our favorites: skiing and ice-skating in winter, and going to the beach or the pool in summer. If NCI was

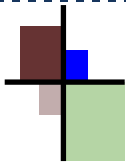
in California, it would be really perfect - but I guess you cannot have everything....



Paola and her daughter Alessia skating at the Rockville Town Center ice rink

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





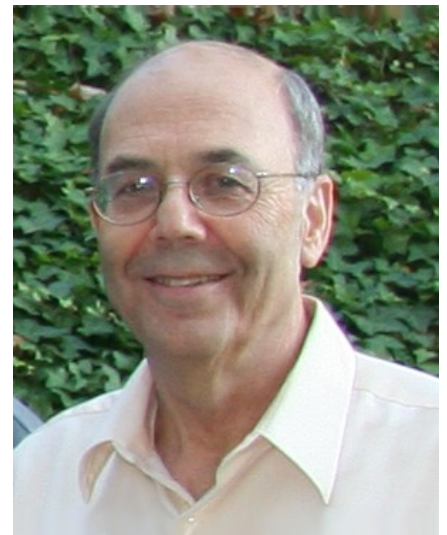
The PI Corner

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

The rapidly advancing pace of research in biological sciences is increasingly based on collaborative efforts between scientists in diverse fields. Research in our laboratory centers on chromatin and epigenetic regulation, and we are particularly fortunate in having two experienced and motivated Staff Scientists, each expert in a unique aspect of chromatin biology, as part of the research team. Dr. Yuri Postnikov is highly experienced in the field of chromatin structure and very familiar with the literature and experimental approaches used to study biochemical and molecular biology aspects of chromatin, chromosomal proteins, and epigenetic regulation. Dr. Takashi Furusawa is highly familiar with mouse genetics and experimental approaches used in cell and developmental biology studies. Their combined theoretical knowledge and experimental skills enables the laboratory to use a multidisciplinary approach to perform experiments involving a relatively wide range of techniques, and to continuously expand the repertoire of experiments that the laboratory can perform. Their expertise and knowledge facilitates the research of less experienced postdoctoral fellows, especially in the initial phases of their projects, and enables the laboratory to establish productive collaborations with researchers in, and outside the NIH campus. In addition, our research program benefits greatly from the support of Staff Scientists that manage core facilities. I view the Staff Scientist as a pivotal position of a research team, and crucial to efficiently perform research at

"I view the Staff Scientist as a pivotal position of a research team, and crucial to efficiently perform research at the NIH."

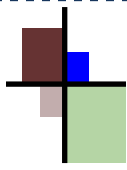
NIH. It is therefore important that we encourage and support the professional development of Staff Scientists in our research groups and in our core facilities.



Michael Bustin, Ph.D.
Head, Protein Section,
Laboratory of Metabolism



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visit the SSSC website at sssc.nci.nih.gov



Looking at the thymus with many eyes: polychromatic flow cytometry facilitates dissection of T cell differentiation.

Dr. Remy Bosselut's research group, part of the Laboratory of Immune Cell Biology, investigates the differentiation of T lymphocytes to the CD4 lineage. Dissecting the formative steps that give rise to CD4 and CD8 T cells is critical to understanding how the immune system functions, and ultimately to the development of immune-based therapeutics for cancer treatment, and immune reconstitution strategies after myeloablative chemotherapies.

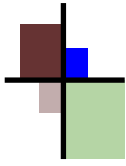
CD4 T cells are required for the proper function of the immune system, as illustrated by the dire opportunistic infections and tumor development that follow CD4 T cell deficiency post-HIV infection or post-chemotherapy. CD4 T cells provide helper function, cooperating with B cells to facilitate development of protective antibodies, assisting cytolytic CD8 T cells, as well as performing their own antimicrobial functions. T cells differentiate in the thymus proceeding from early thymic precursors to the immature thymocytes that express both CD4 and CD8 (double positive, DP) along with various immature cell surface markers. DP thymocytes must express a functional T cell receptor (TCR) before differentiating further into either CD4 or CD8 thymocytes. Commitment to either the CD4 or CD8 lineage is ultimately dependent on the specificity of the TCR and is enforced by expression of specific transcription factors. This differentiation process can be followed by changes in expression of numerous surface markers.

Our general approach to dissect the mechanisms of CD4 T cell lineage commitment is to generate mice either deficient or overexpressing proteins of interest during thymocyte development. Thymocytes can then be evaluated for alterations in T cell differentiation using analytical flow cytometry. Dr. Yumei Xiong, a postdoctoral fellow in the Bosselut lab, recently took this approach to dissect the complex interplay of three transcription factors crucial for normal thymic differentiation: Thpok, Gata3 and Runx3. Analysis was performed using analytical flow cytometers available in the NCI Laboratory of Cancer Biology and Genetics FACS Core Facility. Characterization of thymocyte subsets routinely analyzes expression of 10 markers at the single cell level, including cell surface molecules, intracellular transcription factors and cyto-

kines. The BD LSR Fortessa and LSR II analyzers in the core facility are equipped with 4 and 5 lasers, respectively, that can accommodate this type of complex analysis.

An additional strategy that we take to assess transcriptional control of gene expression utilizes mice expressing fluorescent reporter molecules. In this approach, genes encoding reporters such as yellow (YFP) or green fluorescent proteins (GFP) are placed under transcriptional control of the gene of interest and subsequent expression can then be visualized by flow cytometry. Both GFP and YFP can be detected on the LSR Fortessa and LSR II analyzers. The LSR II analyzer has an additional yellow laser that is used to detect the various red fluorescent proteins (RFP). Dr. Xiong generated a reporter line using 'tandem-dimer' tomato red fluorescent protein (tRFP), an especially bright RFP particularly suited for flow cytometry that has little or no overlap with GFP or YFP fluorescence. In this reporter line, tRFP is encoded from the Runx3 promoter, and can be used in mouse lines that also express a Thpok-GFP reporter, permitting visualization of cells that express either or both of these transcription factors during thymic development. This strategy, taking maximal advantage of the flow core equipment, allowed Dr. Xiong to characterize a novel function of Gata3, namely repression of Runx3 during thymocyte differentiation, thereby establishing a previously unknown relationship between Gata3 and Runx3 (Xiong, Y et al, Eur J Immunol 2013). The FACS Core Facility recently acquired a new cell sorter, notably equipped with a yellow laser that will, in the future, allow purification of cells expressing either or both reporters for further analyses of protein and gene expression.

The FACS Core Facility, located in Building 37, was opened in December 2000 to serve as a core flow cytometry and cell sorting facility for CCR investigators. The facility, equipped with state-of-the-art instruments, provides technical expertise and protocol design consultation to meet the research needs of investigators like Dr. Remy Bosselut's group. The facility houses four flow cytometry cell analyzers; two BD FACSCalibur flow cytometers (2 lasers, 6 param-



The Core Corner Con't

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

-ters), a BD LSRII flow cytometer (5 lasers, 14 parameters) and a BD LSRFortessa (4 lasers, 16 parameters). There are four flow cytometry cell sorters; a standard BD FACSAria (3 lasers, 11 parameters), two special order BD FACSArias (3 lasers, 13 parameters) each configured with a UV laser and a Beckman-Coulter MoFlo Astrios cell sorter (5 lasers, 20 parameters). These instruments have been specially configured with various combinations of the following lasers, 355nm, 407nm, 488nm, 561nm, and

633nm, as well as a myriad of optical filters and detectors to facilitate cutting edge research. FACS Core staff are available to train investigators to independently operate these instruments, assist in multi-color data acquisition and analysis using BD FACSDiva, BD CellQuest Pro, Summit and FlowJo software. DNA cell cycle analysis is done using ModFit software.



Karen M. Wolcott
Head, FACS Flow Core Facility
Laboratory of Cell Biology and Genetics



Melanie S. Vacchio, Ph.D.
Senior Research Assistant
Laboratory of Immune Cell Biology

References:

1. Xiong Y, Castro E, Yagi R, Zhu J, Lesourne R, Love PE, Feigenbaum L, Bosselut R. "Thpok-independent repression of Runx3 by Gata3 during CD4(+) T-cell differentiation in the thymus". *Eur J Immunol.* Jan 11, 2013.



Congratulations!

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

Natalay Y. Kouprina, Ph.D., Laboratory of Molecular Pathology

Ty C. Voss, Ph.D., Laboratory of Receptor Biology and Gene Expression



Introducing our new SSSC Co-Chairs and Secretaries

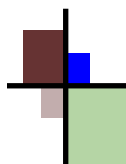
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Frederick Co-Chair: Sergey Tarasov, Ph.D.

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Frederick Secretary: Krista Frankenberry, Ph.D.



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 matter and we will do our utmost to include your material in upcoming issues.

Join one of these SSSC Committees

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SSSC Website: Contact [Sharon Moore, Ph.D.](#)

The Dossier: Contact [Anuradha Budhu, Ph.D.](#)

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