THE DOSSIER

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

September 2012 **Issue 10**

From the Editor

Welcome to the September 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 Glenn Merlino, Ph.D. Our SSSC Bethesda Co-Chair, Christophe Marchand, Ph.D., announces the Second Biennial SSSC Professional Development Day and we highlight the Microscopy Core Facility headed by Valarie Barr, Ph.D. Peter Fitzgerald, Ph.D., introduces the SSSC community to NCI's Bioinformatics Training and Education Program and we welcome Lakshmi Balagopalan, Ph.D., our new Section Editor for the PI Corner. 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
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In This Issue

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From the Office of the Director

The cGVHD Clinical Program: A Collaborative Model of Success

Chronic graft-versus-host disease (cGVHD) is a serious illness that develops in about 50 percent of patients who receive bone marrow or hematopoietic stem cell transplantation. This potentially fatal disorder is a limitation of transplantation as a therapy for cancer. It can affect multiple organ systems, decrease patient survival and adversely affect quality of life. Many of the complications of treatment for cGVHD occur because of side effects of medications. These medications are commonly broadly immunosuppressive because the pathogenesis of cGVHD, beyond being immune-mediated, remains uncharacterized.

CCR Staff Clinicians have played a major role in NIH's efforts to study cGVHD. They were instrumental in the establishment of a multidisciplinary clinical research program that brings together researchers from ten NIH institutes and from across the Clinical Center. The NCI cGVHD clinic serves as a foundation for providing better care of patients suffering from this disorder and seeks to address the urgent need to develop effective treatments. The clinic integrates the skills of specialists across a wide spectrum, such as hematology, ophthalmology, pain management, and palliative care. This multidisciplinary effort has also included Staff Scientists studying the biology and pathogenesis of cGVHD laying the foundation for translation into the clinic.

The success of the cGVHD clinical program is an example of the important role that Staff Clinicians and Staff Scientists have working within NCI, across the NIH, and with extramural researchers to make progress against an important health problem. Thanks to all of you in our important Staff Scientist/Clinician community for contributing so significantly to the success of the CCR clinical program.

" CCR Staff Clinicians have played a major role in NIH's efforts to study cGVHD….This multidisciplinary effort has also included Staff Scientists studying the biology and pathogenesis of cGVHD laying the foundation for translation into the clinic."

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 SSSC Professional Development Corner

The Second Biennial NCI SSSC Professional Development Day

September 13, 2012, Natcher Building, Balcony B

The SSSC Professional Development Committee is proud to announce the Second Biennial NCI SSSC Professional Development Day to be held in the Natcher Building on September 13, 2012 from 8:30am to 4:00pm. This year's program will cover the following topics:

Time	Topic
8:30	**Registration**
9:00 – 10:15	**Dos and Don'ts of Grant Submissions** *Erika Ginsburg, MA, Center for Cancer Training*
10:15 – 10:45	**Break**
10:45 – 12:00	**Licensing and Patenting at the NIH** *Tara Kirby, PhD, Office of Technology Transfer*
12:00 – 12:45	**Lunch on our own**
12:45 – 2:15	**Leading from any Level** *Shannon Connolly, MSW, MPA, Office of Workforce Management and Development*
2:15 – 2:30	**Break**
2:30 – 4:00	**Panel Discussion with SSSC Alumni**

We are counting on your active participation. Please register today at:

http://ncifrederick.cancer.gov/Events/NCISSSC/register.asp

Registration deadline: September 7, 2012

The Core Corner

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

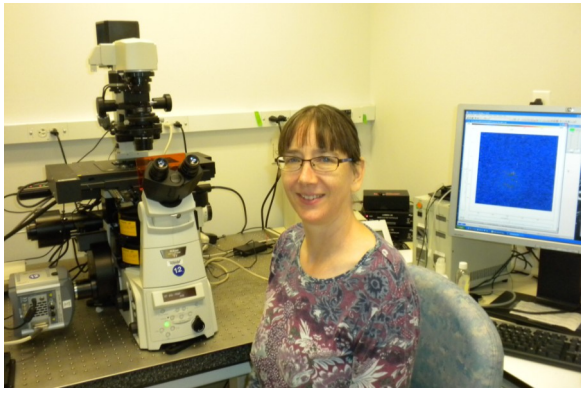
Super-Resolution Microscopy Reveals Nanoscale Organization of T Cell Signaling Complexes

The Laboratory of Cellular and Molecular Biology (LCMB), Center for Cancer Research, investigates normal cellular signal transduction and aberrance in signaling pathways that are associated with neoplasias in humans and model systems. Particular emphasis has been placed on understanding signal transduction pathways mediated by activation of growth factors, cytokines and T cell antigen receptors (TCR).

T cell activation is an essential component of the adaptive immune response, mediating cytokine and antibody production, killing of infected or transformed cells and tolerance to self-antigens. Loss of T cell function results in severe immunodeficiency, while inappropriate activation can lead to autoimmune diseases. Proper T cell activation depends in turn on cellular responses initiated by the T cell antigen receptor. One of the first responses to TCR activation is the formation of micron-sized microclusters that have been visualized by diffraction-limited optical microscopy. Microclusters form around the activated receptors, contain a large number of scaffolding and effector molecules and are essential for proper signal transduction. Recently, Dr. Eilon Sherman, a postdoctoral fellow working with Dr. Lawrence Samelson, began using super-resolution microscopy to study the microclusters involved in T cell activation at the molecular level.

These studies used single and two-color photoactivated-localization microscopy (PALM) to image microclusters in single molecule detail at the plasma membrane of intact T cells. Dr. Sherman decided to focus on the organization of several critical molecules within the microclusters: the TCR receptor, the proximal kinase ZAP-70 and two important substrates of ZAP-70, Linker of Activation in T cells (LAT) and an adapter protein that binds to phosphorylated LAT, SH2 domain-containing leukocyte protein of 76kD (SLP-76). These proteins are all required to generate a T cell response. Analysis of super-resolution images from either resting or activated cells showed that LAT resided in small nanoscale clusters, mainly dimers and trimers, whose formation depended on protein-protein and protein-lipid interactions. Following TCR stimulation, ZAP-70 mixed randomly and completely with the TCRz chain. Both ZAP-70 and TCRz partially mixed with LAT in activated cells, thus showing localized activation of LAT by TCR-coupled ZAP-70. Surprisingly, SLP-76 localized to the periphery of LAT clusters. This structure depended on polymerized actin and disruption of the structure affected TCR-dependent cell function. These results, which were published recently (Sherman et al., 2011; Immunity 35: 705–720), introduce a new concept of nanoscale organization that is required for the proper formation and function of TCR-mediated signaling complexes. Moreover, nanoscale organization of molecules within signaling complexes is likely to be relevant to other receptor systems.

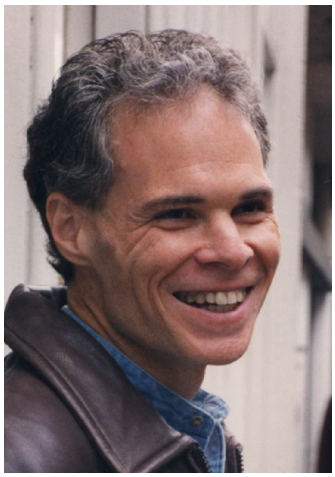
Dr. Sherman performed his experiments in collaboration with the LCMB Microscopy Core Facility. Dr. Valarie Barr, a Staff Scientist, is the head of the Core. The facility houses two confocal microscopes and a system for Total Internal Reflection Fluorescence (TIRF) that is capable of single molecule imaging. These instruments can collect TIRF, PALM, laser scanning confocal and spinning disk confocal images as well as epifluorescence, histology and differential contrast brightfield images. The facility also has stations for processing images, including 4D sequences, for analysis, presentation and publication. Dedicated software is available for volume reconstruction, quantification of fluorescent and brightfield images, colocalization, identification of super-resolution peaks and particle tracking. The TIRF system with single molecule sensitivity was used for high-resolution PALM imaging.



Valarie Barr, Ph.D. (SS)
Head, Microscopy Core Facility,
Laboratory of Cellular and
Molecular Biology

The PI Corner

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



I was here at the inception of the CCR Staff Scientist position, and I have watched it evolve over the years. As with any laboratory job, the Staff Scientist position has advantages and disadvantages. What stands out is the broad variety of responsibilities and duties found associated with this position throughout the CCR. Staff Scientists can function as de facto Principal Investigators in some labs, working on research projects of their own interest and choosing. In others they act as scientific lab managers, instructing junior members and allowing the rest of the lab to run more efficiently and productively. Yet in others they serve as managers of core facilities, where their expertise facilitates science in the larger Lab or Branch, and even the entire CCR. Of course, individuals in the related Staff Clinician position contribute mightily to CCR patient care. In many cases the role of the Staff Scientists falls somewhere in between these various categories. And in all these capacities Staff Scientists are performing admirably, serving as invaluable members of Labs and Branches as they drive toward achieving their basic, translational and/or clinical goals.

"Staff Scientists are performing admirably, serving as invaluable members of Labs and Branches as they drive toward achieving their basic, translational and/or clinical goals. "

I find myself in the most enviable position of having two Staff Scientists, and these talented individuals serve as excellent examples of the potential of this position. Dr. Yanlin Yu is the senior member of my lab, interested in studying melanoma and its metastatic propensity. He independently designs and performs creative experiments, serves as supervisor and mentor to Post-Baccalaureate fellows as well as summer interns, and is the technical guru of the lab. Dr. Chi-Ping Day is a recently promoted Staff Scientist, spearheading a highly ambitious preclinical melanoma program that requires constant vigilance, effective communication skills and yes, a great deal of patience. There is no doubt that both of these outstanding scientists would have been successful Principal Investigators if they had so chosen, and I am humbled by their decision to work with me as Staff Scientists. Passion drives these individuals - passion for their science, and the desire to make discoveries that will someday help other people. There are many ways to achieve this goal in life, and everyone has to find their own special path. To me, passion is what the CCR Staff Scientist is all about.

Glenn Merlino, Ph.D.
Chief, Laboratory of Cancer Biology and Genetics

Introducing our new Dossier Section Editor

Please welcome ***Lakshmi Balagopalan, Ph.D.,*** our new Section Editor for the PI Corner of The Dossier. Dr. Balagopalan received her Ph.D. in Genetics from The Pennsylvania Sate University in 2003 where she studied the genetic program that directs muscle development and myoblast fusion events in fruit flies. She then joined Dr. Lawrence Samelson's laboratory (Laboratory of Cellular and Molecular Biology) at the NCI as a postdoctoral fellow. In 2006 she became a research fellow and in 2011 she was hired as a Staff Scientist. Dr. Balagopalan's research program focuses on the role of ubiquitylation in the regulation of the essential adapter protein LAT in T cell signaling. If you would like to write an article for The PI Corner, please email: balagopl@mail.nih.gov with subject title "The PI Corner".

The Bioinformatics Corner

The Bioinformatics Training and Education Program (BTEP) is here to help you

The exponential growth in the use of high throughput technologies, such as "next-generation" DNA sequencing, has dictated that competency in the computational aspects of data analysis is a necessary skill for success in modern biomedical research. These new technologies have not only introduced new challenges for data-analysis, data storage and retrieval, but have frequently necessitated a rethinking of experimental design. Unfortunately, many current researchers have had little formal training in computational biology and frequently lack the necessary skills to correctly interpret and/or make optimal use of the data they acquire. Thus, with constant changes in research and analytical technologies there is a need to educate and train the diverse CCR research community in order to keep up with growing demands of computational biology. With this in mind, the Office of Science and Technology Partnerships (OSTP) established the Bioinformatics Training and Education Program (BTEP) in March 2012. The goal of this program is to increase the awareness and understanding of Bioinformatics techniques and processes among CCR scientists, and to empower postdocs/staff scientists to perform a basic, informed set of analyses on their own behalf.

During the spring of 2012, BTEP presented a series of lectures and hands-on training sessions provided by private sector experts focusing on the operational aspects and capabilities of several commercial software packages. Attended by over 100 CCR researchers, these classes provided an introduction to the various analytical software packages, currently available to CCR researchers through site licensing, highlighting the strengths and unique capabilities of many of these packages.

In the coming months BTEP will present a series of coordinated lectures and training sessions, presented by subject-matter experts, focusing on select topics of data analysis. These classes will underscore the practical aspects of acquiring, representing, and analyzing complex biomedical data sets. Relevant theory and experimental design will also be discussed where appropriate. The goal here is to not just provide analytic recipes but to ensure a better understanding of the theoretical and practical aspects of sound analytical technique. While concentrating on various methods of analysis of high throughput sequencing and microarray data, the program will also include topics such as genome browsers, sequence databases and repositories, regulatory elements and pathways. In conclusion, the ultimate goal of this training program is to empower the bench scientist to be able to perform the first line of analyses on their high throughput data, thus allowing them to sharpen the focus of their research and thinking, either as an end unto itself, or prior to engaging a computational collaborator to perform additional, more sophisticated bioinformatics analyses.

For more information, please visit the BTEP wiki page http://genome.nci.nih.gov/btep/. Questions/ Comments and/or suggestions may be directed to David Goldstein, Ph.D., at 301-496-4357 or goldsted@mail.nih.gov, or Peter FitzGerald, Ph.D., at 301 -402-3044 or fitzgePe@mail.nih.gov.

Peter C. Fitzgerald, Ph.D.
Head, Genome Analysis Unit
Office of Science and Technology Partnerships

Announcements

Attend!

The Second Biennial NCI SSSC

Professional Development Day

September 13, 2012, 8:30am-4:00pm

Natcher (Bldg 45), Balcony B

Attend!

SSSC Fall Social

October 11, 2012, 1:30-2:30pm

Bethesda campus
Bldg 37, Rm. 2107/2041

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 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: Rimas Orentas, Ph.D.
Aleksandra Michalowski, Ph.D.

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