

# THE DOSSIER

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

March 2016

Issue 23



## 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 Carol J. Thiele, Ph.D. An update is also included on the SSSC New Hire Handbook by Christophe Marchand, Ph.D., along with information about the upcoming SSSC Retreat by our Retreat Co-Chairs, Christina Stuelten, M.D., Ph.D., and Gabriella Andreotti,

M.P.H., Ph.D. The published work of Monica Vaccari,

Ph.D., is highlighted in our Author's Corner, while we feature Yuri Postnikov, M.D., Ph.D., in the SSSC Corner. The collaborative efforts of Shoba M. Amarnath, Ph.D., and Ulrich Baxa, Ph.D., at the Electron Microscopy Laboratory are described in our Core 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](mailto:budhua@mail.nih.gov).

**Anuradha Budhu, Ph.D. (SS)  
Editor-in-Chief**

*Laboratory of Human Carcinogenesis*

## In This Issue

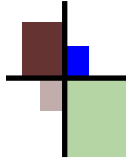
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## From the Office of the Director

Staff Scientists and Staff Clinicians play a significant role in our basic and clinical research, so I am pleased to update you on some exciting activities and resources in CCR. This is an exciting and promising time in the field of cancer research.

We continue to improve our structural biology capabilities and have recently established a small ange X-ray scattering (SAXS) Core Facility in Frederick. This facility houses a state-of-the-art BioSAXS-2000 camera with routine access to beamline time. Yun-Xing Wang, Ph.D., and Lixin Fan, Ph.D. lead this Core and will offer support in experimental design, data collection, processing, analysis, and interpretation for determining structure of bio-macromolecules and their complexes in solution.

As many of you have heard, NCI is investing tens of millions of dollars to upgrade and refurbish multiple buildings and facilities on the NCI-Frederick campus. CCR occupies a fair number of these structures and the renovation projects include complete refurbishment to Buildings 469, 538, 539, 560, and 433. Many of these buildings were constructed in the World War II era. Once completed, these new laboratories will allow for consolidation of programs, provide expansion space for structural biology and chemistry initiatives, meet emerging science and technology needs, create a more collaborative environment, and modernize the building infrastructure to support state of the art laboratories. Those of you affected by these renovations will benefit, but I do understand that such activities can be disruptive and I appreciate your patience and flexibility as we make these major improvements.

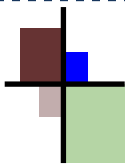
I would like to highlight CCR's ongoing efforts in liver cancer and to remind you of our upcoming Symposium on Integrative Cancer Biology and Genomics with a special focus on liver cancer on March 17-18. CCR has established a highly translational group focusing on this recalcitrant disease and many of our CCR investigators as well as leading extramural investigators will speak at this symposium. Liver cancer will also be a focus of this year's Annual Report to the Nation on the Status of Cancer expected to be released in late February/early March.

Lastly, I want to announce CCR's current effort to identify motivated senior staff to serve as Women Scientist Advisors (WSAs). Female scientists play a vital role in our scientific community and our collective success and it is therefore very important to re-energize this group. The WSAs represent the interest of women scientists and advise the CCR Director on the successful recruitment, retention, and promotion of female scientists at all levels and also serve on the NIH WSA committee. After soliciting nominations from the CCR community, female senior staff were invited to participate in an election. I hope many of you took the time to make your voice heard.



**Lee Helman, M.D.**  
Acting Director and  
Scientific Director for Clinical Research,  
Center for Cancer Research





# The 12th Annual SSSC Retreat

This year's Annual CCR and DCEG Staff Scientist Retreat will be held on April, 29<sup>th</sup> 2016, at NCI Shady Grove.

The retreat theme will be "The Microbiome: From The Front to The Back End" - a topic that made recent headlines in news and popular literature beyond HPV, Helicobacter and yogurt cultures. However, we will aim to put science to this subject. We invited a panel of world leaders in microbiome and cancer research to share their research and ideas, and to discuss the highlights and pitfalls of microbiome research.

Please come and join us for these exciting presentations and to share your own thoughts and research with guests and fellow Staff Scientists and Staff Clinician from CCR, DCEG and Leidos over panel discussions, lunch and poster presentations. Travel awards for best poster presentations will be provided by NCI, DCEG and Leidos.

We added brown bag lunch meetings as well as the option to register one guest to attend the retreat to this year's program. Sign up early to claim your spot as lunch meetings and guest registrations will be filled based on the registration date!



**Christina Stuelten, M.D., Ph.D., & Gabriella Andreotti, M.P.H., Ph.D.**  
**2016 SSSC Retreat Co-Chairs**



## Retreat Agenda

8:30 - 9:00 **Registration**

9:00 - 9:15 **Opening Remarks**  
(Stephen Chanock, M.D.)

9:15 – 10:45 **MORNING SESSION**  
**"THE MICROBIOME: FROM THE FRONT TO THE BACK END"** (Moderator: *Romina Goldszmid, Ph.D.*)

**Christian Jobin, Ph.D.** (Professor of Medicine, University of Florida College of Medicine)

**Curtis Huttenhower, Ph.D.** (Associate Professor, Harvard School of Public Health)

**Giorgio Trinchieri, M.D.** (Director, Cancer and Inflammation Program, NCI)

10:45 – 11:00 **Break**

11:00 – 12:00 **Panel Discussion** with speakers and panelists

12:00 – 1:00 **Brown Bag Lunch Sessions**

1:00 – 1:45 **Poster Session 1**

1:45 – 2:30 **Poster Session 2**

2:30 – 3:30 **AFTERNOON SESSION** (Moderator: *Gwen Murphy, Ph.D.*)

**Heidi Kong M.D., MHSc** (Principal Investigator, Dermatology Branch, NCI)

**Rashmi Sinha, Ph.D.** (Principal Investigator, Metabolic Epidemiology Branch, DCEG)

3:30 – 4:00 **Awards and Closing Remarks**  
(Jonathan Wiest, Ph.D., and Glenn Merlino, Ph.D.)

4:00 – 4:30 **Adjourn**

## From the Professional Development Committee



### NCI-CCR Staff Scientist/Staff Clinician

#### Handbook

V 2.0

*Professional Development Committee*

*NCI-CCR SSSC Organization*

Staff Scientists and Staff Clinicians at NCI:

Congratulations on becoming a Staff Scientist/ Clinician (SS/SC) at the National Institutes of Health. You are an important force behind successful research at NIH.

*Reviewed by the CCR Senior Leadership*

The Professional Development Committee has updated its original SSSC New Hire Handbook to reflect the recent changes affecting Staff Scientist and Staff Clinician positions including, but not limited to, new title-42 specifics, new CCR designations and a brand new displacement checklist. The new SSSC Handbook v2.0 is the result of a close collaboration between the Professional Development Committee and the CCR Senior Leadership. The original document has been updated extensively for content and links and has been approved by the CCR Senior Leadership. The new SSSC Handbook v2.0 is available immediately for download from the SSSC website and will be sent in a welcome email from the Professional Development Committee to any newly hired SSSC. This document is the first of its kind and represents an invaluable tool to develop awareness and promote professional development within the SSSC workforce.

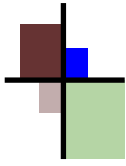


**Christophe Marchand, Ph.D. (SS)**  
Laboratory of Molecular Pharmacology



Please share this newsletter with your colleagues and visit the SSSC website at [sssc.nci.nih.gov](http://sssc.nci.nih.gov)





### Regulatory and Helper Follicular T Cells and Antibody Avidity to Simian Immunodeficiency Virus Glycoprotein 120

[Blackburn MJ, Zhong-Min M, Caccuri F, McKinnon K, Schifanella L, Guan Y, Gorini G, Venzon D, Fenizia C, Binello N, Gordon SN, Miller CJ, Franchini G, Vaccari M. J Immunol. 2015 Oct 1;195\(7\):3227-36.](#)

CD4<sup>+</sup> T cells are a T-cell population with an unexpected degree of phenotypic and functional heterogeneity that play a crucial role in achieving a regulated effective immune response to pathogens<sup>1</sup>. Since the 1980s, when the first two subsets of CD4<sup>+</sup> T cells were discovered, called T-helper cells 1 and 2 (Th1/Th2 dichotomy)<sup>2</sup>, many other subpopulations have been identified. It is now known that CD4<sup>+</sup> T cells carry out multiple functions ranging from activation (T-helper cells) to suppression (T-regulatory cells) of immune reactions. The many subsets identified so far differ in location within the immune system organs, the cytokines they release and the type of immune responses they regulate.

In secondary lymphoid tissues the majority of CD4<sup>+</sup> T cells express the chemokine (C-C motif) receptor 7 (CCR7), hence are found in areas within the deeper cortex, called the T-cell zone, that are enriched in CCR7-ligands, the (C-C motif) ligand 19 (CCL19) and CCL21. CD4<sup>+</sup> T cells homing to the T-zones efficiently stimulate dendritic cells to regulate cell-mediated responses. More recently, two new subsets of CD4<sup>+</sup> T cells have been described with the unique ability to exit the T-zones by down-regulating the CCR7 and to migrate to the follicles where they co-localize with B-cells. Indeed these CD4<sup>+</sup> T cell subsets express CXCR5, the receptor for CXCL13, which is selectively expressed within the outer cortex areas<sup>3-5</sup>. These highly specialized CD4<sup>+</sup> T cell populations are called T follicular helper (T<sub>FH</sub>) cells and T follicular regulatory (T<sub>FR</sub>) cells, and they are key regulators of the development of antigen-specific B cell immunity<sup>6-8</sup>. In response to antigen challenge, mature B cells proliferate, differentiate and undergo somatic hypermutation and class switching in the germinal centers (GCs). T<sub>FH</sub> cells are a key cell type in each of these steps and they are required for the formation of germinal centers (GCs) and the generation of long-lasting antibody responses<sup>9</sup>. T<sub>FH</sub> cells also provide signals for B-cell survival and differentiation<sup>3-4</sup>, and they promote the generation of antibodies with high

affinity<sup>9,10</sup>. Inducing the correct number of T<sub>FH</sub> is crucial to promote an efficient response to pathogens while avoiding excessive GCs reactions<sup>11</sup>. Indeed, studies in mice showed that the maintenance of the appropriate number of T<sub>FH</sub> cells is crucial to avoid uncontrolled germinal center reactions and the onset of some autoimmune diseases<sup>8,11</sup>. The second subset capable of migrating to the follicles, T follicular regulatory cells (T<sub>FR</sub>), co-localize with T<sub>FH</sub> cells and exert an opposite effect on GCs reactions. T<sub>FR</sub> cells control T<sub>FH</sub> cell expansion and modulate T<sub>FH</sub> cells-driven B-cell maturation, antibody class switching and affinity maturation<sup>12-14</sup>.

The role of T<sub>FH</sub> cells in the pathogenesis of HIV/SIV has been recently studied. HIV and SIV infection leads to CD4<sup>+</sup> T cell depletion and to the dysfunction of humoral responses characterized by the loss of memory B cells and hypergammaglobulinemia<sup>15,16</sup>. Many groups have reported that chronic HIV/SIV infection promotes T<sub>FH</sub> cell accumulation in the germinal centers, which in turn may drive B cell dysregulation<sup>17-19</sup>. The finding that T<sub>FH</sub> cells, which are susceptible to HIV infection, accumulate in lymph nodes rather than being depleted, suggests these cells may also constitute privileged latent viral reservoirs. However, it was not yet clear what drives the aberrant T<sub>FH</sub> cell expansion in HIV/SIV. In a recent study lead by Monica Vaccari, Ph.D., a Staff Scientist in Genoveffa Franchini's, M.D., laboratory, in the Animal Models and Retroviral Vaccines Section of the Vaccine Branch, it was shown that macaques T<sub>FR</sub> cells are susceptible to infection by SIV<sub>mac251</sub>, a CCR5-tropic highly pathogenic viral strain, and there was a significant decrease in the frequency and numbers of T<sub>FR</sub> cells in lymph nodes of chronically infected macaques. A direct association was found between T<sub>FH</sub> and T<sub>FR</sub> cell frequencies (**Figure 1**). These findings were corroborated by a parallel independent study by Chowdhury and colleagues reporting similar findings in macaques chronically infected with a different SIV strain (SIV<sub>smE660</sub>)<sup>20</sup>. Taken together these data suggest that

# The Author's Corner Con't

Section Editor: Cristina Bergamaschi, Ph.D. (SS)

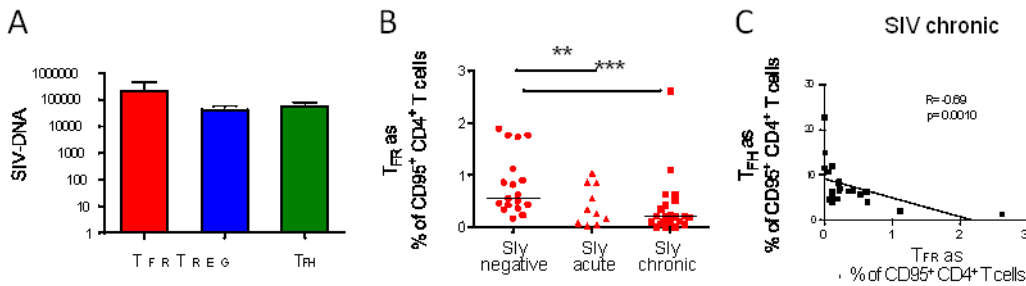


Figure 1. TFR susceptibility and dynamic during SIV infection.

A. SIV-DNA levels in sorted TFR CCR7<sup>+</sup>-TREG and TFH by PCR.

B. Frequency of TFR within memory CD4<sup>+</sup> T cells in lymph nodes of naïve, acutely and chronically SIV infected macaques.

C. Correlation between the percentage of TFR and TFH on memory CD4<sup>+</sup> T cells in chronic infection.

a reduction or lack of expansion of T<sub>FR</sub> cells may contribute to the aberrant T<sub>FH</sub> cell accumulation in chronic HIV/SIV infection.

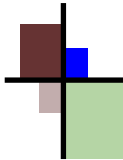
The increase frequencies of T<sub>FH</sub> cells in chronic SIV infection has been previously associated with an increase in titers of high avidity SIV-specific immunoglobulins<sup>17</sup>. Interestingly, in this study, we observed an antithetic role of T<sub>FR</sub> and T<sub>FH</sub> cells in the avidity of antibodies to the SIV-gp120 protein throughout the infection. T<sub>FR</sub> levels were associated with a reduction of binding high avidity antibodies to SIV-gp120 in all the infected animals. The role of T<sub>FR</sub> cells in the impairment in B-cell selection during HIV infection remains to be determined. Nonetheless this study reveals potential new mechanisms for the complex perturbation of B cell responses observed during HIV/SIV infection, and for the accumulation of infected T<sub>FH</sub> cells, a relevant cellular reservoir in secondary lymphoid tissues. Undoubtedly a fuller appreciation for the range of cells participating in meaningful cellular reservoirs could result in a rational attack on latent HIV-1. Finally, insights into T<sub>FH</sub>/T<sub>FR</sub> immunobiology may provide inroads into effective vaccine design.

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Section Editor: Cristina Bergamaschi, Ph.D. (SS)

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Monica is a Staff Scientist and a vital part of Dr. Franchini's team, where she leads multiple interdisciplinary projects using non-human primate models of HIV infection to test preventive and therapeutic strategies against HIV. She regularly assists and mentors numerous postdoctoral fellows, undergraduate and graduate students. One of her deepest interests has been on the pathogenesis of HIV infection and on the role of T-regulatory cells in the HIV-triggered immune deregulation. On this topic, Monica has generated her own line of research by conducting a study, described in this section, on T-follicular regulatory cells. Her findings have revealed potential new mechanisms for the complex perturbation of T follicular helper cells dynamic and humoral immune responses during HIV and SIV infections and have created collaborative efforts with other extramural and intramural laboratories.



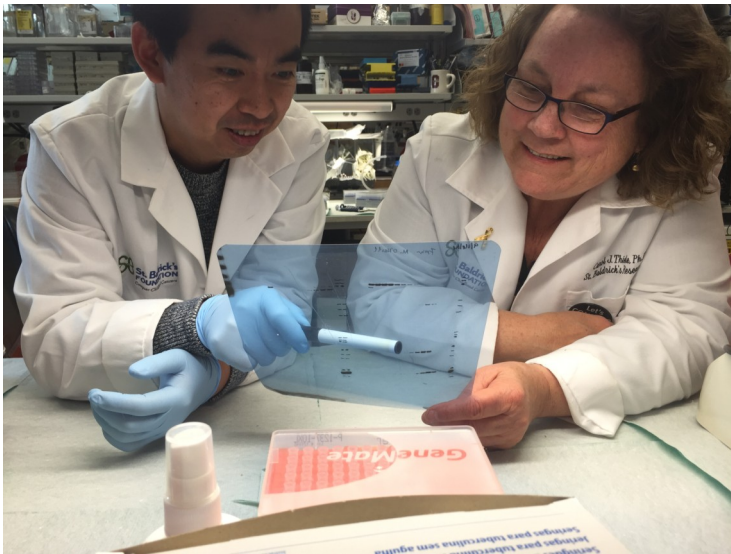
**Monica Vaccari, Ph.D. (SS)**  
Animal Models and Retroviral Vaccines  
Section  
Vaccine Branch





## The PI Corner

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



Dr. Thiele is pictured with her Staff Scientist, Dr. Zhihui Liu.

*What makes a successful researcher?* Over my 25 years as a PI and Head of the Cell & Molecular Biology Section in the Pediatric Oncology Branch (POB) at the NCI, I am frequently asked this question whether speaking with high school, graduate or medical students, postdoctoral fellows or clinical fellows. Common elements usually included in my answer are *“intellectual curiosity and not being afraid to go outside your comfort zone”*. These clearly are qualities that are emblematic of the Staff Scientists and Staff Clinicians I have had the opportunity to work with in POB and the CCR in general.

I know the progress we have made on understanding the pathogenesis of neuroblastoma, a childhood tumor of neural crest-derived sympathoadrenal neuroblasts, emanates from these qualities found in my Staff Scientist, Zhihui Liu, Ph.D.. He came to my lab as a postdoctoral fellow after receiving his Ph.D. from the Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences in Shanghai to work on the human homolog of a well-known *Drosophila* neural developmental gene *cas* that mapped to Chr1p36 the location of the putative neuroblastoma tumor suppressor gene. Dr. Liu's early publications, characterized the *CASZ1* gene, provided evidence for its tumor suppressor function and identified it as a prognostic marker in primary tumors from neuroblastoma patients<sup>1</sup>. More recent studies<sup>2</sup> demonstrated a functional interaction with another neuroblastoma 1p36 tumor suppressor gene, *CHD*, which led to the evolu-

ing concept that it is haploinsufficiency of a number of genes on 1p36 with tumor suppressor properties that contributes to the pathogenesis of neuroblastoma.

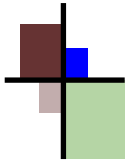
When the *Casz1* KO mouse we generated with the lab of Lino Tessarollo, Ph.D., was embryonic lethal due to a heart defect, Dr. Liu had the *“intellectual curiosity”* to wonder how this neural gene was affecting cardiac muscle cell development. Even though his skillset was in the area of biochemistry and molecular biology, he was not afraid to *“go outside his comfort zone”* to learn embryology, heart development and cardiac cell culture from Wenling Li, Ph.D., and Xuefei Ma, Ph.D., Staff Scientists in the Yoh-suke Mukoyama, Ph.D., and Robert S. Adelstein, M.D., labs at NHLBI. The resulting study was the first identification of *Casz1*'s role in mammalian heart development<sup>3</sup>. Subsequently this led to the identification of *CASZ1* as a key gene in the *“proximal critical region”* of 1p36 deletion syndrome, a complex pathology marked by developmental delays, cognitive issues and congenital heart defects and occurs in 1/5000 newborns<sup>4</sup>. From cancer biology to heart development quite a jump!

As some areas of research have been facilitated due to large databases such as the Human Genome and Encode projects, successful research in the 21<sup>st</sup> century requires a wide network, involving not only scientists at your own institute but those in the NIH community and beyond as well. How do we develop a network that enables one to *“go outside their comfort zone”*? One needs to balance a busy lab schedule with taking some time to attend/or participate in events such as the NIH Research Festival, topic-driven Research Interest Groups, the WALS lectures and the CCR Staff Scientist and Clinician Retreat. All these events give scientists the opportunity to learn and engage other scientist/clinicians. Such networking then makes it easy for those with intellectual curiosity to *go outside their comfort zone*.

**Carol J. Thiele, Ph.D.**

Senior Investigator, Pediatric Oncology Branch



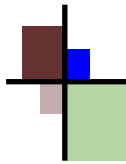


## The PI Corner Con't

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

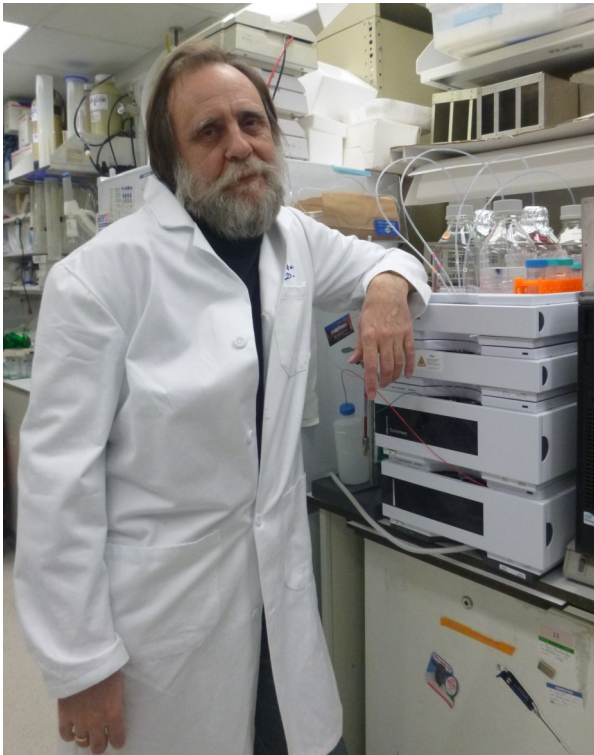
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## The SSSC Corner

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

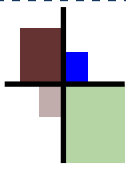


My story at the NIH started with the fall of the Iron Curtain. Following the USSR dissolution in 1992, many scientists obtained the opportunity to work in Western Europe and the USA. I left the Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, where I had been in the Laboratory of Molecular Organization of Chromatin, and moved my research to the NIH since this was a capital for the leading scientists in chromatin field.

For almost a quarter of a century I was lucky enough to experience all the wonderful things that happened in the biological sciences in general, and to the chromatin field, in particular. The life sciences became more technically and intellectually advanced, shifting observational science towards experimental and social-oriented science. Innovative research strategies led to fundamental creative discoveries that eventually helped to expand our knowledge in medical sciences. Back then, in the 20th century, we addressed simple questions such as “Can RNA polymerase transcribe through the nucleosome in vitro without



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help from other proteins?’ or “What does it take to maintain gene activity through cell mitosis?”. Now, we have turned to amazing global genome-era ambitious projects such as “What is the human DNA sequence?” or “What does the epigenetic profile of all possible histone modifications look like across the whole genome?” The good news is that science still wants us to be innovative, creative and expand our knowledge.

Now I am a Staff Scientist in CCR, working in the laboratory headed by Michael Bustin, Ph.D., who is the most persistent and productive Investigator studying small non-histone nucleosome binding proteins – called HMG proteins. Working in his lab, I was able to publish over 30 papers in top journals, giving interesting insights into chromatin structure, function and the biological consequences of the alterations in chromatin. The NIH offers an unprecedented opportunity to be the frontrunners at any branch of research, and chromatin biology is not an exception. I am proud to be a member of the NCI Center of Excellence in Chromosome Biology. It brings together experts from various fields of chromatin structure and function; epigenetics, gene expression, replication, repair, and recombination; chromosome organization and gene localization.

In our lab, we learned that HMGN binds to nucleosomes and changes the properties of chromatin fibers, such as the ability of various factors (including histone modifying enzymes) to access chromatin. We believe that HMGN plays a role as a fine modulator of the nuclear processes occurring in chromatin. We are using a multidisciplinary approach that includes the generation and analysis of genetically altered mice, molecular biology, cell biology and biochemistry, to study the structure of these proteins, their precise location on nucleosomes, their genome-wide distribution in chromatin, their expression during the cell cycle and differentiation, the manner in which they assemble into the chromatin fiber, their role in transcription regulation, and their biological function. Now we face a challenging hypothesis of determining how architectural proteins (including HMGN proteins), with

the assistance from other factors, establish and maintain the structure of various epigenetically defined chromatin domains.

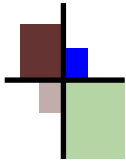


*Outside of work: Yuri stands in front of William Shakespeare's birthplace in Stratford-upon-Avon, Warwickshire, UK.*

Outside the lab, I prefer to do relaxing things of late: reading, watching movies, surfing the net. When I first came to the NIH, I played soccer and tennis. Then I switched to skiing and biking. For the last few years, I go on a safer side: swimming, hiking. On vacation, I love to travel to historic sites and natural wonders. Our (my wife and I) favorite is Western Europe – the cradle of Western civilization. We have been to Spain, France, Monaco, Italy, Switzerland, France, Germany, three times to the UK, etc. We are looking forward to going to Scandinavia to view the Norwegian fjords. The latter decision was partially inspired by our 2015 journey to Misty Fjords near Ketchikan, Alaska.

**Yuri Postnikov, M.D., Ph.D. (SS)**  
Protein Section  
Laboratory of Metabolism





### Development and Validation of an Electron Microscopy Method for Detecting Exosomes In Vivo

In the Laboratory of the Experimental Transplantation and Immunology Branch of the NCI, headed by Daniel Fowler, M.D., our research focus is directed towards understanding the immune regulatory mechanisms that boost regulatory T (Treg) cells. In particular, we studied the immunosuppressive potential of cellular therapeutics and chemotherapeutic agents in preventing graft versus host disease (GVHD) and graft rejection. Since Dr. Fowler was already translating rapamycin-resistant Th2 cells into NIH Clinical Center protocols as a new approach to allogeneic stem cell transplantation, our main efforts were to develop the next generation of immune modulatory cells, such as Treg cells. In order to study human Tregs in vivo, we developed a novel human-into-mouse xenogeneic GVHD model. Various aspects of this research were published in mechanistic journals such as *Autophagy* and *Science Translational Medicine (STM)*. On reading our publication in *STM*, John Barrett's, M.D., group in the Hematology Branch, NHLBI, reached out to us to collaborate on yet another type of regulatory cell called Bone Marrow Derived Mesenchymal Stromal Cells (BMSC). The NIH Department of Transfusion Medicine (DTM) had developed a method for manufacturing BMSC for use in clinical trials. Dr. Barrett had already conducted a phase I trial of BMSC in GVHD patients at the NIH and was interested in further understanding the molecular mechanisms of BMSC action.

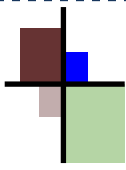
In collaboration with Dr. Barrett's group, we investigated the immune regulatory mechanism by which BMSC's inhibited inflammatory Th1 cells in our xenogeneic GVHD model. Our initial data suggested that BMSC had a profound effect both in terms of inhibition of ongoing Th1 cell-mediated inflammation and

also repair of established damage in target organs such as skin. We then sought to understand the cellular mechanism(s) by which BMSC reversed GVHD. Ultimately, we demonstrated that BMSC were exclusively embolized in the lungs of recipients but mediated their action at distal sites through the release of micro-vesicles.

We then developed methods to study the phenotype and function of exosomes in our humanized GVHD model. In order to achieve this, mice were reconstituted with human T cells and human BMSC (the same cell product used in the clinical trial) followed by serum collection at different time points. The serum samples were then subjected to exosome isolation; however, in order to confirm that the micro-vesicles were exosomes, we needed to develop assays for specific exosome staining and exosome-related electron microscopy (EM). Using the Electron Microscopy Laboratory at the Frederick National Lab, we closely collaborated with Ulrich Baxa, Ph.D., who developed a method that not only specifically identified exosomes by EM based on size but also developed a specific staining protocol for exosomes. Dr. Baxa also developed and optimized a method for quantitatively measuring size distribution of exosomes in the serum. The assays developed by this NCI core extensively helped us in elucidating a novel mechanism of human BMSC that were developed at the DTM. This exosome EM technique was key in definitively identifying in vivo exosomes as the functional component of human BMSC in our model. The work was subsequently published earlier this year in the journal *Stem Cells* ([Amarnath et al, 2015. Stem Cells, 33\(4\): 1200-12](#)).

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## The Core Corner Con't

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

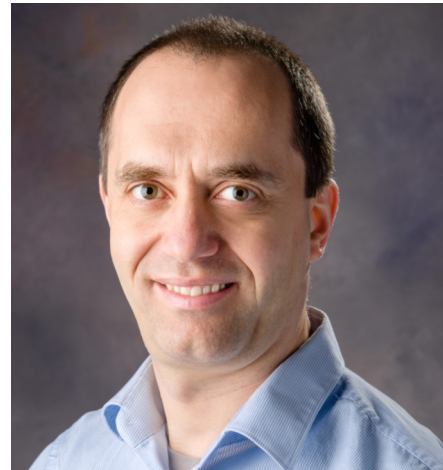
*The **Electron Microscopy Laboratory (EML)** is a CCR-subsidized core facility providing ultrastructural analysis of biological samples and nanoparticles using state-of-the-art scanning and transmission electron microscopes (SEM and TEM). Capabilities of the EML include: room-temperature processing of biological samples for thin sectioning TEM analysis or for SEM analysis including the possibility of immuno-gold labeling; negative staining analysis of protein complexes, small vesicles (e.g. exosomes) and virus particles; analysis of hard matter nanoparticles including elemental analysis using X-ray energy dispersive spectroscopy (EDS); room-temperature electron tomography of sections or nanoparticles to determine a three dimensional structure; and cryo-TEM of macromolecular structures, like protein complexes, virus particles, or liposome suspensions close to their native state.*



**Shoba M. Amarnath, Ph.D.**

Previous Position: Staff Scientist  
Experimental Transplantation and  
Immunology Branch

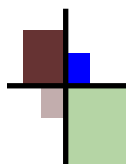
Current Position: Principal Investigator  
Laboratory of T cell Regulation,  
& Newcastle University Research Fellow  
Newcastle Upon Tyne, United Kingdom



**Ulrich Baxa, Ph.D.**

Head, Electron Microscopy Laboratory  
Frederick National Laboratory  
for Cancer Research





## Attend!

**The 12th Annual SSSC Retreat  
Friday, April 29, 2016  
NCI Shady Grove**



## Congratulations SSSCs!

### 2016 Director's Innovation Award Winners

**Songjoon Baek, Ph.D., (SS)** Laboratory of Receptor Biology and Gene Expression

**Christophe Marchand, Ph.D., (SS)** Developmental Therapeutics Branch

**Ana Robles, Ph.D., (SS)** Laboratory of Human Carcinogenesis

**Lyuba Varticovski, M.D., (AS)** Laboratory of Receptor Biology and Gene Expression

**Jonathan Weiss, Ph.D., (SS)** Cancer and Inflammation Program

Information on the Innovation Award Program, including a listing of prior year recipients can be found at <http://ccrintra.cancer.gov/news/innovation-awards.asp>.



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## CCR Monthly Publications Report

Wonder what researchers in other CCR Labs and Branches are doing? View a list of recently published papers by CCR authors [here](#). A new list will be posted each month. Archived reports are available [here](#).



## New Accepted Research Paper?

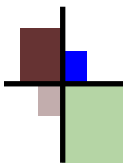
CCR's scientific community produces hundreds of high-quality published manuscripts each year. It is important that the CCR-OD be alerted when these manuscripts are accepted for publication. By knowing about publications in advance, the CCR-OD can ensure wide dissemination of the information once published to many interested parties, such as other scientists, Congress, and advocacy groups.

In order to streamline this process, the CCR-OD has set up a new online submission [form](#). We ask that some basic information be provided by authors *as soon as a manuscript has been accepted or is in the proof stage*. It should take less than two minutes. We are only collecting manuscripts accepted in journals via this form.

Don't forget that each accepted manuscript must have a purchase order (if in Bethesda). When a government purchase order is not established, an "unauthorized procurement" may occur. These take many, many months and significant staff time to resolve and can delay payment to the journal. Contact your AO or purchasing agent right away, if needed.







## Announcements from the CCR Office of the Director Con't

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[@NCILeeHelman](#) – Dr. Lee Helman, CCR Acting Director and CCR Director for Clinical Research

[@NCI\\_TGIB](#) – Thoracic and Gastrointestinal Oncology Branch

[@NCICCR\\_Lymphoma](#) – Lymphoid Malignancies Branch

[@NCI\\_CCR\\_SB](#) – Surgery Branch

[@NCICompOnc](#) – Comparative Oncology Program

[@NCICCCR\\_GMB](#) – Genitourinary Malignancies Branch

[@NCICCCR\\_MOS](#) – Medical Oncology Service

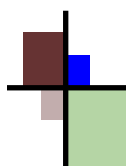
NCI Guidelines for social media are available [here](#). If your Lab/Branch or Program is interested in starting an official NCI Twitter account, contact [Kimberly Martin](#) to get the process started.



### CCR Policy for Reimbursement of Professional Medical Licensing Expenses

This is a reminder that CCR has expanded its policy for the reimbursement of professional medical licensing expenses, including professional accreditation, licenses, certifications and examinations. For example, this now includes Research Nurses, Nurse Practitioners, and Physician Assistants certifications, as well as costs related to maintenance or re-certification of subspecialty boards. For more information please contact your Administrative Officer.





# A Call for Content



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This newsletter is an avenue for you to express your ideas and thoughts on 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.

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