

THE DOSSIER

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

From the Editor's Desk

Dear Colleagues,

As the Thanksgiving holiday is approaching soon and most of us are eagerly looking forward to it, I'd like to thank each of you for your unwavering commitment and the hard work you do every day to profoundly contribute to cancer research that improves health and saves lives. I am grateful for the opportunity to work with such a dedicated and talented group of people at the Center for Cancer Research (CCR), National Cancer Institute (NCI).

I sincerely appreciate the hard work and enthusiasm of all contributing writers, editors, and editorial board members for putting the 49th issue together. In this issue, we have a forward-looking note from CCR's Acting Co-Directors Dr. James Gulley and Dr. Carol Thiele, the newly available resources from the Center for Clinical Cancer Metabolism (CCM) for NCI researchers in the Core Corner, highlights from the Annual Meeting of the Staff Scientists/Staff Clinicians (SS/SC) focusing on how to prepare for and navigate Staff Scientist displacement, a spotlight on a CCR Principal Investigator (PI) in the PI Corner, and highlights of a Staff Clinician and a Staff Scientist's research in the Author Corner.

Many of us attended the 2024 Annual Professional Development Meeting that took place on October 4, 2024, at the NCI Shady Grove Campus. I thank all Professional Development Committee members for their hard work so we could enjoy networking and benefit from discussions on various topics. You can read more about the last Professional Development Meeting in the Event Report section of this issue.

On behalf of the entire Editorial Board, I wish you and your loved ones a wonderful and joyous Thanksgiving holiday filled with memory-making moments. Together, we can make this Thanksgiving truly special by helping those in need and less fortunate.



Brajendra Tripathi, Ph.D.
Editor-in-Chief

THE DOSSIER

A Message From The Acting Co-Directors, CCR

A look forward

Greetings, Staff Scientists and Staff Clinicians:

This is our first note to you as Acting Co-Directors of CCR. Carol Thiele, Ph.D. succeeds Glenn Merlino, Ph.D., who retired in June 2024 and James Gulley, M.D., Ph.D. continues in his role. We have a long history of working together as CCR colleagues, Investigators and Deputy Directors, and we look forward to leading CCR through this challenging and scientifically exciting time.

A quick word on the budget

Just a quick word on the budget. The last few years have been difficult to navigate. We have been assured by NCI leadership that it is a money problem as opposed to an issue with the quality of our science. The budget and hiring controls we've put into place are starting to make a difference. For FY25, the budget remains tight. However, on the positive side, we have a realistic budget for the first time in many years so that everyone can be confident that they will be able to spend all allocated funds. In addition, the budget and hiring controls we've put into place are starting to make a difference.

A goal for valued and well-resourced people

Our people are the most valuable resource, and you, our Staff Scientists and Staff Clinicians, are the engine of scientific and clinical research at the CCR. We can't do it without you. At the same time, CCR will need to become a smaller organization, with fewer PIs and staff. While these two thoughts may seem inconsistent, they drive our strategy to ensure that while CCR becomes smaller, the personnel we retain are fully resourced and able to not only succeed but flourish.

Planning for the future

We have several efforts underway to make sure we reach this goal and to help us move forward strategically.

Scientific Strategic Planning Working Group

A strategic planning working group, co-chaired by

[Deb Citrin, M.D.](#), CCR Scientific Director for Clinical Research and [Bev Mock, Ph.D.](#), CCR Deputy Director, is examining CCR's organizational makeup, scientific portfolio and best practices across peer research institutions. They will recommend approaches to leverage CCR strengths and improve resource utilization.

We are delighted to welcome two extramural members to this group: [Patricia LoRusso, D.O.](#), Smilow Cancer Hospital/Yale School of Medicine and [Martin McMahon, Ph.D.](#), Huntsman Cancer Institute/University of Utah School of Medicine. Both are respected cancer research leaders, who have years of experience on CCR's Board of Scientific Counselors. Other workgroup members represent a cross-section of CCR PIs.

Scientific Cores Working Group

Another working group, co-chaired by [Dan McVicar, Ph.D.](#), and [Tim Greten, M.D.](#), both CCR Deputy Directors, is reviewing CCR scientific cores. This group, which is primarily made up of PIs with deep knowledge of CCR cores and contracts, will make recommendations aimed at ensuring that the most scientifically important cores are funded appropriately, that access is equitable, and operations are efficient. The review will go beyond a simple funding analysis. Some questions to be addressed are whether CCR is supporting the best, most cutting-edge technologies, whether the technologies or approaches are available elsewhere in CCR or NIH and whether CCR has too much capacity or not enough.

CCR Scientific Board Reviews

We have also asked the CCR Science Board, chaired by [Natasha Caplen, Ph.D.](#), to engage in reviews of multiple CCR non-PI-based supplemental programs for scientific productivity and return on investment. We expect at least six reviews in FY 25. In addition to these three efforts, we are analyzing other areas of CCR's spending including the Office of the Director and Office of the Clinical Director. While significant cuts have already been made within these groups, we continue our detailed analysis to identify further

THE DOSSIER

efficiencies and prioritize needs. And we welcome creative ideas on opportunities to cut costs.

Moving forward

We are looking at a future of more stability and opportunity at the CCR. The field has never had more opportunities in biomedical science in cancer and we look forward to working with you on future discoveries.

Thank you for your patience, dedication and hard work.



Dr. James Gulley
Acting Co-Director



Dr. Carol Thiele
Acting Co-Director

Getting to Know Our New SS/SC

Section Editor: Yoshimi Greer, M.D. Ph.D. (SS)



Najla El Jurdi, M.D., SC

Immune Deficiency Cellular Therapy program (ID-CTP)

Research focus:

I am a hematopoietic cell transplantation and cellular therapy physician focused on clinical and translational investigations to better understand, prevent, and treat Graft-versus-Host Disease (GVHD), with a particular emphasis on chronic GVHD.

How did you choose your career?

I have been intrigued by human biology and the understanding of pathogenesis and disease since a very young age. I was fascinated with hematopoietic cell transplantation and cellular therapy as a platform to deliver immunotherapies and decided that this is the exact subspecialty I want to dedicate my career early in my medical training.

What could be the impact of your research?

My goal is to leverage the expertise of the NIH GVHD multidisciplinary team and intramural program to bring forth novel clinical trials and therapeutic approaches for highly morbid forms of GVHD. I am additionally strongly committed to research aimed at understanding accelerated aging after transplantation, preventing late effects, and improving quality of life for transplant patients and survivors.



Gil Kanfer, Ph.D., SS

CCR High-Throughput Imaging Facility (HiTIF), Laboratory of Receptor Biology and Gene Expressing (LRBGE)

Research focus:

As a computational Staff Scientist at the HiTIF, I develop and apply spatial omics computational tools that bridge cutting-edge open-source analysis frameworks with custom developed spatial statistics algorithms. These will be used by HiTIF collaborators that need downstream spatial statistics analysis to extract biological insights from spatial transcriptomics and spatial proteomics datasets generated in collaboration with other CCR Cores.

How did you wind up in your field?

During my PhD, I developed a fascination with functional genomics, which led me to join the Youle Lab at NINDS-NIH in 2016. My focus shifted from wet lab work to computational biology, emphasizing image analysis and statistical modeling. I'm drawn to the challenges of managing large imaging and NGS datasets, which are crucial in modern biomedical research.

What could be the impact of your research?

With training in both cell and computational biology, I bridge the gap between these fields, understanding their challenges. This dual expertise helps me apply the best computational and statistical tools to answer biological questions relevant to human disease. My goal is to use my quantitative skills and passion to help collaborators solve spatial biology problems.



Francisco Pereira Lobo, Ph.D., SS

Cancer and Developmental Biology Laboratory (CDBL)

Research focus:

I am a bioinformatician that develops and uses computational tools to integrate omics data aiming at generating statistically sound and biologically meaningful knowledge. Currently, I provide bioinformatics support for various research projects at CDBL, ranging from the description of single-cell atlas of non-model metazoan species to the study of organ development in vertebrates.

How did you choose your career?

I began my career in biochemistry, a field that integrates data to study life at the molecular level. This led me to bioinformatics, where I've spent the past 20 years working in evolutionary comparative genomics. As I analyzed genomic data across organisms, I recognized the need for computational strategies that can integrate heterogeneous biological data to extract meaningful insights, particularly to identify genes contributing to complex phenotypes, such as developmental disorders and cancer.

What could be the impact of your research?

The biological sciences are rapidly shifting towards data-driven hypotheses, thanks to the genomic revolution and decreasing sequencing costs. Genomic data, inherently digital, requires data science to uncover biologically meaningful insights. I expect data-driven approaches will dominate biology even more, with a growing demand for data scientists with a strong background in biology. This will provide large-scale functional insights from uncharacterized sequence data, impacting many aspects of human health and leading to many actionable genes/variants associated with complex disease phenotypes.



Ayush Raman, Ph.D., SS

Laboratory of Receptor Biology and Gene Expression (LRBGE)

Research focus:

I am a trained Computational Biologist, interested in understanding the role of RNA modifications and splicing factors in gene expression in both development and diseases, including cancer and neurological diseases.

How did you choose your career?

I have been working in the field of epigenetics since 2010. I was interested in making a transition from analyzing microarrays to next-gen sequencing datasets. I got the opportunity to work in this field during my tenure as a Bioinformatics Scientist at the Institute for Systems Biology, Seattle. I co-authored a paper where we used a systems approach to predict the role of FOXO3 as a negative regulator of a subset of antiviral genes. This prediction was later validated in the wet lab. I was fascinated as it was the first time I experienced my computational predictions getting validated. The paper was published in Nature. I later pursued my doctoral studies in the area of computational epigenetics.

Would you like to tell us something else about yourself?

I was born in a small city in the eastern part of India and grew up in a suburb of Delhi. During high school, I never liked Biology. I didn't take the biology track courses in Grades 11 and 12, which is a norm for students who are interested in pursuing a career in medicine. I became interested in this field through a chapter about molecular biology in my chemistry book and later read a mesmerizing article about the Human Genome Project in the national newspaper in India, which got me interested in pursuing my undergrad in Biotechnology and Bioinformatics.



Sarah J. Shin, M.D., M.P.H., SC

Developmental Therapeutics Clinic (DTC)/Division of Cancer Treatment and Diagnosis (DCTD)

Research focus:

Early phase clinical trials. Novel cancer therapeutics (DNA damage response, Antibody drug-conjugates, Immunotherapy).

How did you wind up in your current field?

Research has been an integral aspect of my medical training and I strongly believe it is essential in advancing treatment and patient outcomes. During my hematology/oncology fellowship, I became particularly interested in early drug development and furthered my training as an advanced fellow in the Advanced Developmental Therapeutics Training Program (ADTTP) at the Developmental Therapeutics Clinic (DTC) in the Division of Cancer Treatment and Diagnosis (DCTD) at the NCI. At the DTC, I collaborated with many translational investigators to integrate a wide variety of cutting-edge strategies to inform rational development of novel early phase clinical trials with comprehensive correlative assays to better understand the underlying involved mechanisms. After completion of the fellowship, I remained at the DTC as a Staff Clinician to continue conducting innovative, biomarker-driven early phase clinical trials to bring promising new therapeutic options to cancer patients.

Would you like to tell us something else about yourself?

As an Asian woman in science and having trained in hospitals treating many from underserved populations, I strive for opportunities to learn, research, and incorporate measures for diversity, equity, and inclusion in early phase clinical trials.



Bhagawat C. Subramanian, Ph.D., SS

Laboratory of Cellular and Molecular Biology (LCMB), CCR Intravital Microscopy Core

Research focus:

As part of the intravital microscopy core, I assist CCR/NCI investigators in developing multiphoton microscopy-based approaches to directly investigate cellular and molecular dynamics underlying tumor progression in live animal models. Additionally, I investigate the molecular mechanisms driving immune cell dynamics in physiological and pathological responses using multiphoton intravital microscopy.

How did you wind up in your current field?

My interest in immune cell dynamics led me to a postdoctoral fellowship with Dr. Carole Parent, then at CCR, to study the role of 'signal-relay' mechanism in directed neutrophil migration. Subsequently, I worked with Dr. Roberto Weigert at CCR to develop multiphoton microscopy-based approach to study neutrophil extravasation at sub-cellular resolution in live mice. Thereafter, I worked with Dr. James Bear, Lineberger Cancer Center at the UNC Chapel Hill, to explore the roles of actin debranching regulators during tumor progression. All the above experiences have shaped my current and future research endeavors.

What could be the impact of your research?

Our objective is to enable investigators to visualize specific molecular and cellular dynamics directly within tumors in live mice over multiple days and weeks. This approach will not only identify dynamic processes that occur within the tumor tissue in vivo but will aid in precise design and spatiotemporal targeting of such processes during tumor progression.



Francesco Tomassoni-Ardori, Ph.D., SS
Mouse Cancer Genetics Program
(MCGP)

Research focus:

My research currently focuses on in vivo modeling of rare tumors through the generation and characterization of new genetically engineered animals harboring genetic alterations found in human patients.

How did you choose your career?

I was fortunate to be part of the Gene Targeting Facility within the MCGP and to have the opportunity to collaborate with various laboratories seeking genetic engineering expertise. This experience significantly enhanced my skills in gene editing. The recent collaboration between the MCGP and the Pediatric and Adult Rare Tumor Network (MyPART) has paved the way for an exciting and challenging research project on modeling rare “wild-type” gastrointestinal stromal tumors (WT-GISTs).

What could be the impact of your research?

Currently, there are no standard therapies for wild-type gastrointestinal stromal tumors (WT-GISTs), and they lack preclinical models. Our goal is to develop animal models that can faithfully recapitulate the molecular alterations and phenotypes observed in human WT-GISTs. These models could ultimately serve as valuable tools for uncovering new molecular mechanisms involved in the pathogenesis of these rare tumors and for developing new therapeutic approaches.



Mingming Zhao, M.D., Ph.D., SS
Thoracic and GI Malignancies Branch
(TGMB)

Research focus:

The transcriptional regulation of immune cells to unravel the complex mechanisms underlying immune responses and their regulation by various factors.

How did you choose your career?

I chose to pursue bioinformatics because I became fascinated by the role of data in advancing our understanding of complex biological systems. While working in the field of immunology, I encountered vast amounts of experimental data that held the potential for deeper insights into immune responses. The growing importance of big data in biology and the potential for bioinformatics to drive discoveries in immunology inspired me to acquire new skills in data analysis, programming, and machine learning. This transition allows me to merge my passion for immunology with computational, contributing to a comprehensive understanding of immune mechanisms and development of therapeutic strategies.

Would you like to tell us something else about yourself?

I have a passion for exploring diverse fields of study, which mirrors my adventurous approach to life. My journey into bioinformatics has been particularly exciting, as it allows me to delve into the intersection of biology and data science. Each project is a new adventure, presenting unique challenges and opportunities to uncover insights. This blend of curiosity and exploration drives my commitment to continuous learning and growth in my research.

THE DOSSIER

Event Report: Highlights from the 2024 Annual Professional Development Day Meeting



The Professional Development Committee at the CCR/DCEG, NCI, works towards the goals of identifying and establishing opportunities for the professional development and career advancement of Staff Scientists and Staff Clinicians (SS/SC). Each year, the committee organizes a one-day workshop with a theme focused on SS/SC to further enhance their knowledge and expertise. This year's Professional Development Day was held as a hybrid meeting on October 4, 2024, at NCI Shady Grove, with a theme: "Boosting Collaboration to Achieve Your Career Goals".

The morning session began with the welcome address by Dr. Balamurugan Kuppasamy, Chair of the Professional Development Committee, followed by stimulating opening remarks from Dr. James Gulley, Acting Co-Director and Clinical Director, CCR, NCI. This was followed by presentations from Core facility heads on collaboration opportunities, with contributions from Dr. Stephen Lockett, Director, Optical Microscopy and Analysis Laboratory (FNLCR); Dr. Thorkell Andresson, Director, Protein Characterization Laboratory (FNLCR); Dr. Ferenc Livak, Staff Scientist, Flow Cytometry Core; and Dr. Madeline Wong, Scientist, Cancer Genomics Core. These presentations highlighted the services offered by the cores and encouraged the SS/SC community to come up with innovative ideas and questions that could be addressed with state-of-art facility services. To enhance communication skills, a sixty-second Elevator Pitch session was organized, which was well received. Dr. Swati Choksi, Staff Scientist, highlighted the SCEP program to the SS/SC community.

Additionally, the current co-chairs of the SS/SC organization announced the co-chair election, to be held in November 2024. In the afternoon session, Scott Morgan, President, The Morgan Group, delivered a keynote presentation addressing the importance of

mindful career goals. This was followed by updates on the quadrennial review process presented by Dr. Cynthia Masison and Mrs. Rena Rodriguez. Aligned with career goal theme, a panel discussion with former SS/SC alumni, Dr. Evan Walseng, Dr. Cristina Bergamaschi and Dr. Anita Tandle was held, where they shared their experience transitioning to extramural and industry jobs. The workshop concluded with remarks from Dr. Stephen J. Chanock, Director, Division of Cancer Epidemiology & Genetics (DCEG), NCI. The committee also arranged refreshments and coffee to all the attendees. Overall, the Professional Development Day was filled with numerous presentations and discussions focused on enriching the SS/SC community's professional growth and career development. Moreover, the forum provided a space to discuss the exciting opportunities and resources available to the SS/SC community. We thank the NCI/CCR leaderships, OITE team-- Ms. Angela Jones, Ms. Maria Moten, Ms. Erika Ginsburg, Mr. Kevin Ferrel, and Ms. Alex Stewart – along with the NCI conference center and AV team staffs for their enormous support.

(The Professional Development Committee)

Balamurugan Kuppasamy, Chair
 Acong Yang
 Brajendra Tripathi
 Cynthia Masison
 Dale Lewis
 David Davis
 Haydar Bulut
 Imran Khan
 Nicolas Cuburu
 Sabina Kaczanowska
 Snehal Gaikwad
 Sudheer Kumar Gara
 Sukhbir Kaur
 Xiyuan Zhang
 Xue Zhi Zhao

THE DOSSIER

The CCR SS/SC Organization Annual Meeting 2024

The CCR SS/SC Organization held its Annual Meeting on September 27, 2024. The mission of the organization is to advance the professional goals and scientific careers of the CCR SS/SC. The Annual Meeting typically serves to update the SS/SC community on organizational activities, policy changes, upcoming elections, and other relevant matters.

This year, the co-chairs identified Staff Scientist displacement as a critical issue, which led to the development of an updated Standard Operating Procedure (SOP) on displacement policy. Over the past few months, the co-chairs collaborated with the Administrative Resource Center (ARC) and CCR leadership to establish a clear and equitable SOP for the displacement policy. As a result, this year's meeting focused on addressing how to prepare for and navigate staff displacement. It also provided an opportunity for open dialogue, including a Q&A session where attendees could discuss the new policy with NCI leadership and ARC representatives. NCI leadership, represented by Dr. James Gulley (Acting CCR Director) and CCR Deputy Directors Dr. Mary Kearney, Dr. Dan McVicar, and Dr. Ramaprasad Srinivasan, emphasized their commitment to supporting Staff Scientists through the transition and highlighted available resources for those affected. Ms. Rena Rodriguez, Deputy Director of the ARC, Center for Cancer Research (CCR), presented the updated displacement policy and the newly established SOP. The meeting was opened by Bethesda SS Co-chair, Dr. Swati Choksi, who detailed the issue of Staff Scientist displacement. Dr. Choksi then introduced Dr. James Gulley, the current CCR Acting Co-Director, who acknowledged the financial challenges facing NCI but emphasized the crucial role that Staff Scientists play in advancing NCI's mission. Dr. Gulley expressed his gratitude to the SS community for their contribution in achieving the mission of the NCI. Thank you, Dr. Gulley!

Considering the current budget constraints, the focus on displacement policy during this meeting was especially timely. Dr. Nicolas Cuburu, Bethesda SS Co-Chair, introduced CCR ARC Deputy Director,

Rena Rodriguez, who provided a detailed account of the newly drafted Displacement SOP. This policy was a collaborative effort involving the SS/SC Organization Co-chairs, CCR leadership, and Ms. Rodriguez's office. Ms. Rodriguez outlined the key features of the Displacement policy. It was pointed out that while CCR has developed an SOP to help during the displacement, ultimately, the SS is responsible for finding a new position and making it a priority from the official notification of displacement before the final appointment not-to-exceed (NTE) date.

This SOP aims to address this issue by providing a structured approach to support displaced SSs and preserve their expertise within the IRP. Briefly, once the PI notifies CCR leadership, the Administrative Officer (AO) or designee of lab transition regarding lab closure, the ARC Manager will schedule a transition meeting with the transitioning PI, Chief, CCR Deputy, and the administrative staff to discuss all required transition requirements, including current staffing. It is at this meeting that a lab closure date is decided. The SS will receive an official notification letter stating the NTE date of the SS, new temporary mentor if applicable, instructions to the SS if being added to the CCR displaced list, and career counseling resources. This is what, we, the SS are most concerned with. What is the new NTE date??? We found it very comforting to find out that the current appointment NTE date is typically honored or may be renewed to coincide with the lab closure date. But we are assured that Staff Scientists are typically given at least a 12-month notice of the NTE date. Staff Scientists will be placed on the CCR displaced list and the assigned CCR Deputy Director, transitioning PI, and Laboratory Chief will make a concerted effort to place productive Staff Scientists in another laboratory. The CCR will clearly communicate the displacement trajectory to the SS. This includes the duration of the displacement grace period and the mechanism and possibilities of transition to a new lab in the IC. CCR will assist in facilitating the transition to a new lab/position; however, it was emphasized that while CCR may provide support during this process, it is not responsible for securing a new position for the displaced Staff Scientist.

Resources and contacts are listed in the official notification letter. Details can be found at:

CCR Central: <https://ccr.cancer.gov/ccr-central/staffscientists-staffclinicians>

Frederick SS Co-chair Dr. Acong Yang presented a chart of the current Deputy Directors and their portfolios, explaining the importance of knowing one's Deputy Director, particularly in the context of the new displacement SOP. It was made clear that the Deputy Directors would be playing a bigger role in SS displacement. Dr. Yang introduced three Deputies present at the meeting: Dr. Mary Kearney, Dr. Dan McVicar, and Dr. Ramaprasad Srinivasan. Each provided their vision and described their role in the displacement process, answering numerous questions during the Q&A session. They emphasized the importance of maintaining strong scientific expertise, developing new skillsets (notably in bioinformatics), sustaining scientific visibility, and fostering collaborations and networks both within and outside the NIH.

A recording of the meeting is available for those who were unable to attend.

CCR SS/SC organization:

<https://ccrod.cancer.gov/confluence/display/CCRSSS>
[CArchive/Home](#)

Co-Chairs, CCR SS/SC Organization

Swati Choksi
Ravi Chalamalasetty
Nicolas Cuburu
Esther Mena
Acong Yang

A brief history of the Staff Scientist position will help us to better understand how and why displacement has become such a big issue. The Staff Scientist position was created to enable faculty-level doctoral scientists to work with Principal Investigators (PIs) to further the NCI's research mission. Staff Scientists are generally appointed for a time-limited, renewable period to support the work of a PI or core facility. However, due to various reasons, such as lab or core closure, Staff Scientists may face displacement regardless of their performance. When displacement occurs, Staff Scientists --many of whom are mid-career or beyond--may find it challenging to secure a new position, given their extensive experience and government employment. Currently, Staff Scientists receive lab closure notifications following a lab transition meeting. There are unexpected circumstances that occur, such as the sudden retirement or death of a PI, that requires a different timeline to notify lab staff. This career-disrupting event is extremely stressful for Staff Scientists. Several surveys for Staff Scientists have indicated that becoming displaced is a great concern for them. This concern has deepened as the number of Staff Scientists has started to outpace the number of PIs in recent years. This trend predicts that it will become increasingly difficult for those displaced Staff Scientists to find another lab or core facility to work within NIH. Given the significant investment of time and taxpayer dollars in training Staff Scientists, it benefits NCI to make every effort to retain and transfer the expertise of these scientists within the Intramural Research Program (IRP). Ultimately, the Staff Scientist is responsible for finding a new position before the final appointment not-to-exceed (NTE) date.

THE DOSSIER

Core Corner

Section Editor: Lisa Jenkins, Ph.D. (SS)

The CCR Center for Clinical Cancer Metabolism

Although we all appreciate that alterations in metabolism are central to supporting tumor growth, performing experiments to characterize these changes can be challenging. Would you like to identify the metabolic alterations in a human tumor? Would understanding the effects of inhibitors on metabolism in tumor cells help you study their therapeutic effects?

The CCR Center for Clinical Cancer Metabolism (CCM), housed within Building 10, conducts metabolomics studies and performs metabolic imaging with a focus on isotope-resolved analysis of clinical samples and patient-based studies and clinical studies. Within the CCM, the Mass Spectrometry and Sample Preparation Core Facility focuses on targeted, ultra-high resolution stable isotope-resolved metabolomics by mass spectrometry and the Clinical NMR Metabolomics Facility uses NMR for targeted, isotope-resolved studies of polar and non-polar metabolite and lipid extracts. Pre-clinical metabolic imaging resources are available for small animal metabolic imaging via Dynamic Nuclear Polarization (hyperpolarization) as well as non-hyperpolarized deuterium and ^{13}C metabolic imaging using image deconvolution algorithms developed by facility staff members. In vivo non-invasive tissue oxygen imaging can be performed using a custom-made low field MRI and resonator assembly. Finally, clinical ^{13}C -hyperpolarized metabolic imaging is also available on a specialized ^{13}C MRI scanner.

The CCM is highly collaborative, working on projects in which investigators and their trainees participate directly with the facility staff in experimental design, sample preparation and extraction, data analysis, informatics, and biological interpretation. Trainees from Collaborators' labs come to the facility to prepare and extract their own tissues or cell samples under the guidance of facility staff. Computer workstations are available within the facility for analysis of NMR and mass spectrometry data, with

guidance and training provided by the facility staff. So, in addition to collecting useful data, users can acquire new technical experience by performing the experiments and analyzing the data.

One memorable project for Acting Facility Manager Dr. Dan Crooks was performed by a postdoctoral fellow in the lab of Christina Annunziata (Women's Malignancy Branch). The group was interested in understanding the mechanism of action of two clinically relevant therapeutic agents using 2D and 3D organoid cultures of human ovarian cancer cell lines. With the CCM, they performed a glucose tracer experiment which elucidated striking differences in the activity of central metabolic pathways in 2D vs. 3D cultures. Further, their work also uncovered an entirely novel mechanism of action of one for the therapeutic agents which has been in clinical use since the 1950's!

To start a new project, contact Dr. Dan Crooks (crooksda@mail.nih.gov), and/or Dr. W. Marston Linehan (linehanm@mail.nih.gov) to discuss whether the experiments are a good fit with their capabilities.

All new projects require a proposal that is reviewed by the CCM Steering Committee. General criteria that are evaluated include whether the project fits within the capabilities of the facility; if there are sufficient preliminary experiments to support the experimental approach; and how the project could translate to patients at the Clinical Center.

Facility staff typically work together with the PI and their trainee to help develop that proposal prior to submission.



In the Tissue Sample Preparation Lab: Trainees from two different collaborative NCI labs work with CCM staff to extract metabolites from human tumor tissue samples. Tissue specimens are ground under liquid nitrogen in a SPEX Freezer Mill, quenched with methanol, acetonitrile and water, and ultimately undergo a three-phase extraction procedure yielding: 1. polar metabolites, 2. non-polar metabolites/lipids, 3. proteins. The polar metabolite fraction is further separated into four to six tubes and lyophilized and stored for downstream NMR analyses, Ion Chromatography-Ultra-high Resolution Mass Spectrometry analyses, and Direct Infusion Mass Spectrometry analyses.

THE DOSSIER

PI Corner

Section Editor: Andaleeb Sajid, Ph.D. (SS)



Dr. S.K. Muthuswamy
Lab Chief, LCBG

Dr. Senthil Muthuswamy began a remarkable journey in the heart of India, where a passion for plant genetics ignited a lifelong love for scientific inquiry. After earning a master's degree at the Indian Agricultural Research Institute, known as the Pusa Institute in New Delhi (India), Senthil laid the groundwork for a career that would eventually take

a bold turn into the realm of cancer biology. With a foundation in plant genetics, Senthil felt a compelling urge to explore animal physiology and biology. This curiosity led to the pursuit of a PhD at McMaster University in Canada, focusing on cancer biology, which shaped the trajectory of his career. After completing the PhD, Senthil embarked on a postdoctoral fellowship in industry, where he explored basic research with a personal project backed by his own funding. This pivotal experience was followed by another postdoctoral fellowship at the Harvard Medical School, where the focus remained steadfast on cancer research. It was during these formative years that Senthil developed a three-dimensional cell culture method using MCF-10A breast epithelial cells to study breast cancer, a technique that gained widespread recognition in the field.

In 2001, Senthil accepted a faculty position at Cold Spring Harbor Laboratory, a beacon for basic science research. Over the next eight years, he not only contributed to this lab but also began his research group in 2009 at the Princess Margaret Cancer Center in Toronto. This dual role allowed for innovative collaborations between basic scientists and clinicians, fostering an environment rich in translational research. As Senthil navigated these exciting opportunities, the research began to take shape around critical questions in cancer biology. His work on cancer cell organoids, cell polarity, and its implications for cancer offered new insights, while collaborations with clinicians

facilitated the exploration to develop personalized therapy approaches. The realization that combining laboratory findings with patient-specific data could lead to groundbreaking discoveries drove his research forward. At Harvard, the focus expanded beyond pancreatic cancer to breast cancer models. Senthil and his team developed a platform that integrated patient tumor-derived organoids with T-cells from peripheral blood, paving the way for innovative immunotherapy strategies. This research sought to identify effective T-cell receptors that could target cancer cells.

In 2022, Senthil made another significant transition, joining NIH to further his research ambitions. The move presented fresh challenges but also the opportunity to establish collaborations with clinicians who were dedicated to advancing cancer treatments. Senthil readily connected with colleagues in the clinical center, which facilitated regular access to patient samples and the creation of organoid models, possibly for personalized medicine and much more.



Members of Senthil Muthuswamy's Lab

Recognizing the crucial role of collaboration in scientific progress, Senthil hired an immunology staff scientist from the Neuro-Oncology Branch within NIH, aiming to leverage their expertise for high-risk, high-reward projects. Senthil believes that, unlike postdoctoral researchers, Staff Scientists are empowered to explore innovative ideas without the pressure of immediate success. Their secured positions allow them to engage in bold research initiatives, fostering an environment where experimentation is encouraged, even when outcomes are uncertain. As a

strong advocate for mentorship, Senthil emphasizes the importance of staff scientists in training the next generation of researchers. He believes Staff scientists can serve as intellectual leaders, facilitating knowledge transfer and building networks. One of the key strengths of staff scientists lies in their ability to sustain scientific continuity. While postdoctoral researchers may cycle in and out of labs every few years, staff scientists provide the stability necessary to maintain ongoing projects. Their long-term presence helps preserve critical knowledge and expertise, ensuring that the progress made in research is not lost when postdocs move on. Looking ahead, Senthil indicates the staff scientists should explore opportunities to make connections beyond their Lab/Branch to foster collaborative interactions across NIH and initiate a connection with patient advocates, enhancing understanding of the patient experience and integrating these insights into research. He envisions a future

where collaborations with advocacy groups become a cornerstone of cancer research, fostering a community that prioritizes patient-centered basic and translational science.

Through perseverance, innovation, and a commitment to collaboration, Senthil continues to navigate the complex landscape of cancer research, driven by a passion for discovery and a vision for personalized medicine. His journey is a testament to the transformative power of science. Senthil is recipient of several awards, including The Rita Allen Scholar Award, the V Foundation Scholar Award, the U.S. Army Era of Hope Scholar Award, the Lee K. and Margaret Lau Chair in Breast Cancer Research, and the Canadian Society of Biochemistry and Molecular & Cellular Biology Young Scientist Award for his research achievements.

THE DOSSIER

Author Corner

Section Editor: Ling Zhang, Ph.D. (SS)



Dr. Scott Norberg
Assoc. Research Physician

Q1. Where did you graduate, and what led you to pursue a career as a Staff-Clinician?

I went to medical school at the Philadelphia College of Osteopathic Medicine and did my internal medicine training at Temple

University Hospital in Philadelphia. It was at that time I met Dr. Marijo Bilusic who was a medical oncologist at Fox Chase Cancer Center. He received his Medical Oncology training at the NCI and raved about his training experience. I was interested in translational and clinical research, specifically in the field of medical oncology, so applied to the NCI Medical Oncology fellowship program and was fortunate to be accepted. During my second year of medical oncology training, I joined the lab of Dr. Christian Hinrichs and loved the clinical and translational research being performed by the group. I was fortunate to obtain a Staff Clinician position in his lab and then in the Center for Immuno-Oncology where I am today.

Q2. What is your general role as a Staff Clinician inside NIH?

My main role is to conduct clinical and translational research studies within the NCI Center for Cancer Research (CCR). I am currently the principal investigator on 4 clinical trials, 2 of which are testing TCR-engineered T cell therapy in patients with advanced cancer and 2 that are testing therapies in patients with a rare disease called recurrent respiratory papillomatosis (RRP). My job is to ensure that these clinical trials are being conducted according to established regulations and guidelines that ensure safety of the patients on the study and integrity of the study results. Fortunately, we have an outstanding team of individuals that help make sure we are doing everything necessary for this to happen. I also serve on several different committees

throughout the NCI CCR including the Scientific Review Committee (SRC) and the Safety Monitoring Committee.

Q3. What clinical studies are you currently engaged in, and what is next?

We were involved in conducting a pivotal phase 1/2 study of a novel therapeutic HPV vaccine called PRGN-2012 as adjuvant treatment for adult patients with RRP. Patients with RRP develop papillomas throughout their aerodigestive tract that can significantly affect their voice quality and breathing. There are currently no approved systemic treatments, and some patients require hundreds of lifetime surgeries to control symptoms of voice disturbance and shortness of breath. Fortunately, our clinical trial demonstrated a significant decrease in the need for surgical intervention in treated patients. Results from this study have led to PRGN-2012 being granted Breakthrough Therapy Designation by the US FDA, potentially changing the treatment landscape for patients suffering from this devastating condition. We are in the process of opening a larger, phase 3 study at the NIH clinical center testing PRGN-2012 in additional patients with RRP to determine whether these results can be replicated in a larger patient population.

Q4. Could you point out the steps and challenges of conducting a clinical study?

There are many steps involved in a study which requires an investigational new drug (IND) application, which is a common type of study performed by investigators at the NIH. The first step involves designing the study, including the measures needed to determine safety and clinical activity of the study agent(s). The study design is then reviewed by the Branch of the principal investigator (PI) where other clinicians and basic science researchers can comment on the merit of the proposal. Then, a study protocol is written. Each

protocol is then reviewed by the protocol support office (PSO) to ensure that the protocol is written clearly, and the statistical analysis section is

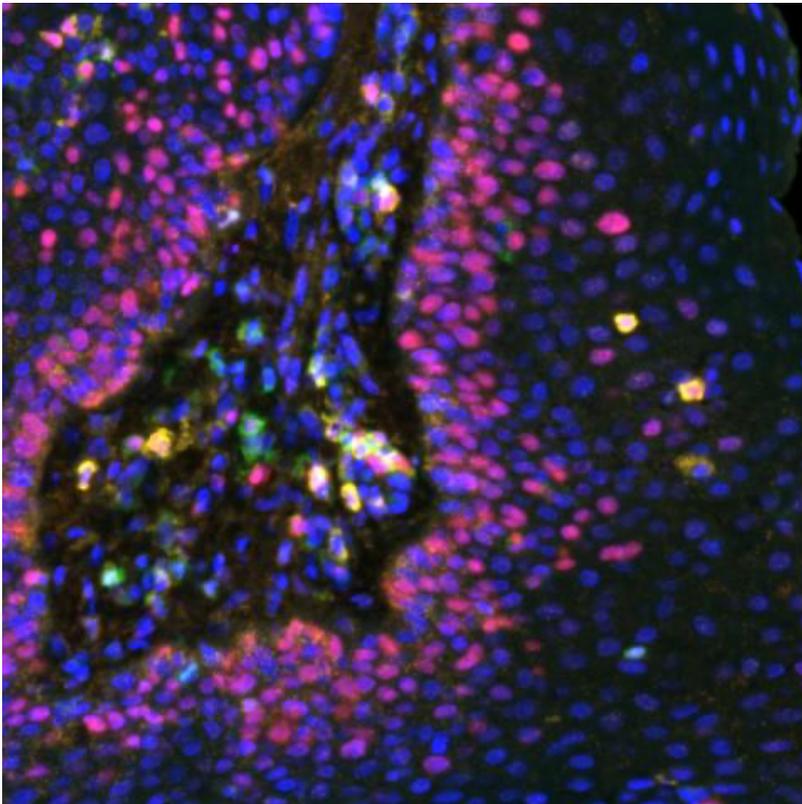
appropriate. The protocol is then reviewed by the NCI SRC to ensure scientific merit of the proposal and that it meets the strategic goals of the NCI CCR and study PI. Once the protocol is approved by the NCI SRC, it is sent to the Office of the Sponsor and Regulatory Oversight (OSRO) so that it can be prepared for submission to the US FDA. The US FDA ensures that the study abides by all federal research laws and regulations. If the US FDA does not have any stipulations or required changes, then the protocol is sent to the Institutional Review Board (IRB). The IRB ensures that the study protects research participants and follows international guidelines on participant protection. Lastly, once IRB approved, a Site Initiation Visit is conducted to train the clinical center on that trial. As you can see, there are multiple steps and groups involved in conducting clinical trials. Though this does take time, the goal is to ensure that participants are protected, and the clinical trial is designed to appropriately answer an important clinical question.

Q5. Any advice for new Staff Clinicians or about collaboration between Staff Clinicians and Staff Scientists?

Collaboration between Staff Clinicians and Staff Scientists are of utmost importance for our studies. The NIH provides an exceptional environment for collaboration between basic science researchers and clinicians. Being the largest clinical center dedicated entirely to the conduct of clinical trials, it is imperative that the clinical research we conduct not only provide information about the safety and clinical activity of a study agent(s) but also translational research studies that can lead to a better understanding of the molecular underpinnings of a disease entity or treatment effect. Staff Clinicians help bridge the gap between knowledge discovered at the bench and how it can be used to improve human health at the bedside.

Q6. What activities or hobbies do you enjoy doing outside of work?

I enjoy spending time with my 8-year-old daughter and my 10-year-old son. My daughter loves swimming, something that I am bad at, so it is fun watching her do it so well. My son loves to play basketball and collect sports cards including baseball and basketball cards. I used to collect cards when I was younger, so it has been a lot of fun doing that now with my son.



Multispectral immunofluorescence image of a respiratory papilloma stained for various biomarkers: Ki67 (red), CD8 (Gold), CD4 (green) and PDL1 (orange).

Image credit: Allen lab

THE DOSSIER

Author Corner

Section Editor: Ling Zhang, Ph.D. (SS)



Dr. Usha Acharya
Staff Scientist

Q1. When did your interest in science begin? Where did you graduate? What career would you choose if you were not a scientist?

The seeds to becoming a scientist were sown early by my parents who nurtured my curiosity, enthusiastically supported

all my home-brewed scientific experiments and encouraged me to pursue a career in STEM. My organic chemistry professor had a contagious enchantment with biochemistry that ignited me to borrow and read Lehninger Principles of Biochemistry from the library. While I could not fully comprehend the content then, I began to appreciate the field and I pursued a Master's degree followed by a Ph.D. in Biochemistry. My graduate advisors were Profs. Appaji Rao and H.S. Savithri at the Indian Institute of Science. I determined the primary structure of serine hydroxymethyltransferase, a 483 amino acid containing enzyme, by manual microsequencing! I came to the University of California, San Diego to pursue my post-doctoral work with Professor Vivek Malhotra. In his lab, I developed *in vitro* assays to understand the structural organization of the mammalian Golgi Complex. Through these efforts, I became fascinated with membrane biology. As an independent investigator at UMass Chan Medical School, I worked on sphingolipids, a class of lipids that are fundamental to membrane architecture and signaling, using fruit flies and mouse models. I moved to NCI in 2019 as a staff scientist and have continued this line of work. I am grateful for a job that excites me every day, my colleagues and the supportive environment at CDBL. Nonetheless, if I had to choose an alternate career, I would enjoy being a chef experimenting in the kitchen with different ingredients.

Q2. What project are you currently engaged in,

and what is next for you?

Our lab is interested in identifying specialized functions for sphingolipids using *Drosophila* and mouse as model organisms. Recently, we have shown that sphingolipids are required for mouse myeloid cell differentiation and T cell subset differentiation ([DOI: 10.1126/sciadv.adk104](https://doi.org/10.1126/sciadv.adk104)). Some of our interesting work in flies includes the demonstration that flies can adapt to the toxic effects of ceramide by increasing glycolysis and lipolysis. Our most recent work involves CG8093, one of the enzymes involved in lipolysis. We discovered that this lipase is synthesized in a specific region of the midgut of flies. Upon consumption of dietary fat, the lipase expression is stimulated, and it moves to the insulin producing cells (akin to mammalian pancreatic beta cells) located in the fly brain (please see figure). While glucose is the primary stimulus for insulin secretion, it is well known that lipids can amplify glucose stimulated insulin secretion (GSIS). However, the source of the lipid (whether it is dietary fat or it is endogenously synthesized), the lipid signals and the enzymes involved in GSIS have not been well established. This is challenging because of the complex inter-organ communication involved in maintaining glycemic regulation. Our study with Vaha shows that it is a molecular link between dietary fat and lipid amplified insulin secretion (<https://www.nature.com/articles/s41467-024-48851-8>). It has been wonderful interacting with talented, thoughtful, dedicated mentees in the lab. My desire is to continue to mentor the next generation of young scientists.

Q3. Do you plan to translate your fundamental discoveries into new treatments? We are still in the phase of understanding how Vaha lipase works, what its mammalian counterpart is, and how precisely results from our animal model will extrapolate to humans. It is therefore hard to predict how soon this discovery will directly benefit human health. Having said this, I am mindful of the genuine need and urgency in translating fundamental discoveries into clinical treatments. We have initiated screens in mammalian cells to test several hundred lipids in the hope of identifying novel lipids that amplify GSIS. If

THE DOSSIER

Contributors

Editor-in-Chief

Brajendra Tripathi

tripathib@mail.nih.gov

SS/SC Website

Rubén Meana Pañeda

Editorial Review Board

Melissa Bronez

Li Gwatkin

Jasmine Lee

Beverly Mock

Senior Editors

Lakshmi Balagopalan

Anuradha Budhu

Section Editors

Yoshimi Greer

Lisa Jenkins

Sabina Kaczanowska

Andaleeb Sajid

Ling Zhang

Contributing Writers

Swati Choksi (SS/SC Meeting Report)

Yoshimi Greer (Get To Know SS/SC)

James Gulley (OD)

Lisa Jenkins (Core Corner)

Bala Kuppusamy (PDD Event Report)

Andaleeb Sajid (PI Corner)

Carol Thiele (OD)

Brajendra Tripathi (Editor's Note)

Ling Zhang (Author Corner)

Current and past issues of The Dossier can be found [here](#)

Visit the [SS/SC link](#) at [CCR Central](#)

Join A [SS/SC Committee](#)

We welcome your feedback and participation. Please send any articles or comments to

tripathib@mail.nih.gov