THE DOSSIER

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

September 2018 Issue 33

From the Editor

Welcome to the September issue of The Dossier, a newsletter dedicated to the Staff Scientists and Staff Clinicians (SSSC) of CCR!

This issue contains information on CCR's Office of Research Operations and Planning from Melissa Bronez, M.P.A. and Tom Misteli, Ph.D, . In our PI Corner, Ettore Apella, M.D., discusses his research and the important role of his Staff Scientist, Sharyn Mazur, Ph.D., while we learn about the research of Hidetaka Ohnuki, Ph.D., in our SSSC Corner. In our Author's Corner, we highlight the published work of Julius Strauss, Ph.D., while in our Core Corner, Jan Wisniewski, Ph.D., describes the instruments and technology available at the Confocal Miscroscopy and Digital Imaging Facility. Meanwhile, Swati Choksi, Ph.D., informs us of the upcoming SSSC Professional Development Day and in our personal development corner, Brunilde Gril, Ph.D., overviews the new Enrichment Program for Staff Scientists. In our Clinical Corner, we obtain the viewpoints of Geraldine O'Sullivan Coyne, M.D., Ph.D., on several aspects of the Staff Clinician position. We hope to continue to provide pertinent information to aid in the success of SSSCs. Please send your contributions, suggestions and comments to budhua@mail.nih.gov.

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

In This Issue

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The Office of the Director: Guest Editorial*

*The CCR Director regularly invites senior staff members as guest columnists to expertly inform the SSSC community on diverse aspects of the CCR.

Here to Help: OD's Office of Research Operations and Planning

What do Twitter accounts, the annual reporting system, scientific symposia, patient recruitment, the 60 Second Update newsletter and the Stadtman tenure track investigator recruitment program have in common? They are all functions supported by the Office of Research Operations and Planning (OROP) within CCR's Office of the Director. OROP is here to help CCR staff members with these and many other areas.

Communications

OROP has recently developed and now implements a broad communication strategy to publicize CCR's remarkable research advances, recruit patients and staff, and to foster internal communications. The office produces original news stories and features on our most important scientific publications, new and ongoing clinical trials, our patients and our staff and these are publicized on the web, social media, the NCI electronic "Govdelivery" news feed, in 60 Second Update, CCR's internal newsletter, and on the digital screens located around the campus. With CCR's Jason Levine, Chief of IT, OROP also manages CCR's website with more than 3,500 individual pages. In June 2018 alone, the CCR website had ~129,000-page views and 46,000 unique visitors. These numbers have been steadily climbing as we work to continually improve the site's navigation and content. A big project currently underway is improving CCR's "for staff" intranet site to better serve as a "one stop shop" for information that CCR staff need. OROP also publishes CCR's research magazines, *Milestones* and *Landmarks*, and is currently working on a third, forward-looking publication, called *Horizons*. OROP also manages CCR's social media footprint. CCR has a growing Twitter community with 18 official Twitter accounts. OROP tweets about 100 times a month from @NCIResearchCtr to over 4,600 Twitter followers. We also push content to NCI's Facebook and Instagram accounts. Did you know that we tweet job and training openings that are posted on the Careers website? We also work closely with the NCI Press Office on media inquiries about CCR's research and expertise. Remember, if you are contacted by the media, always be sure to obtain clearance from the Press Office. Not sure? Contact: Li Gwatkin, Communications Manager.

Scientific Meetings & Conferences

Last year, OROP managed 14 major meetings and it organizes the near weekly CCR Grand Rounds bringing together thousands of scientists every year. OROP oversees planning, logistics, registration, onsite management and publicity and coordinates the review of requests for large meeting support submitted by PIs through CCR's Resource Request System (RRS). The office also provides guidance to our local lab meeting organizers. Meeting-related questions may be directed to Julia Lam, Scientific Meeting Manager.

Research Reporting

Each year CCR receives requests for information about our research activities. These come from other NCI or NIH offices, such as the Center for Global Health, from Congress and from the public, as for example under the Freedom of Information Act (FOIA). We typically report each year on our clinical trials, use of stem cells and fetal tissue, human data sharing, research in women's health, minority/ health disparities issues, AIDS, specific cancer types, and our collaborations (international, trans-NIH, and within DHHS.) Much of our reporting is done using the Annual Reporting System (ARS), which contains information on ~750 projects and collects input from more than 350 users, twenty-one percent of whom are staff scientists or staff clinicians. CCR's Planning Contact & ARS Administrator is Brenda Boersma.

Clinical Program Administration

Did you know that CCR's clinical program is the largest at NIH, using over 35% of the NIH Clinical Center? We have 52 Staff Clinicians and 82 Staff Scientists working in CCR clinical branches. The clinical program offers additional administrative complexity in areas such as accreditation, clinical trial development, patient recruitment, patient care, medical licensure, subspecialty training, nursing, CRADAs, and specialized clinical programs and partnerships, such as multi-institute collaborations, the UO1 program, and, most recently, CCR Moonshot projects. OROP provides administrative coordination and expertise in support of these areas. If you have a question about Staff Clinician professional titling, patient recruitment,

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the Clinical Investigator Development Program, the Lasker Clinical Research Scholar program, CRADA budgeting, or other clinical administrative issues contact: Aubrey Wachter, Clinical Program Specialist.

Faculty Recruitment

CCR is one of the most active intramural programs at NIH in terms of recruiting new faculty. For example, we recruited more than 30 new Tenure Track Investigators over the past three years. Consequently, several years ago, CCR established the new position of Faculty Recruitment Coordinator to manage our efforts with the annual NIH Stadtman tenure track investigator program, the Lasker Clinical Research Scholar program, the Clinical Investigator Development Program, and other standalone CCR leadership position searches. We are working hard to put CCR's best foot forward to recruit the best and brightest to our research community. Contact: Lori Holliday, Faculty Recruitment Coordinator.

Office of the Director

If you've visited CCR's Office of the Director suite in Building 31 recently, we hope you've liked the changes to our physical space. The CCR OD is the front door to our terrific research organization and we have tried to give it a welcoming and professional look. OROP support staff handle scheduling for CCR's scientific directors, official correspondence and support the administrative needs of some OD offices. Stop by to make an appointment, ask a question or to meet OROP staff in person.

CCR is a large, diverse and energized organization. The Office of Research Operations and Planning is here to help the Staff Scientist/Staff Clinician community. Please reach out if we can support your research activities.

Melissa Bronez, M.P.A.
Associate Director, OROP

Tom Misteli, Ph.D.
Director, CCR

The PI Corner

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

Dr. Ettore Appela (right) is pictured with his Staff Scientist, Dr. Sharyn Mazur (left).

My research group studies the effects of post-translational modifications (PTMs) of the tumor suppressor p53 following exposure to stress. These numerous modifications, which occur in all functional domains of p53, are known to affect both p53 stability and activity. We are using a combination of different methods to examine specific protein-protein interactions to understand the role of p53 PTMs in modulating complex structure or stability. A second project is an investigation of the regulation and function of Wip1, a PP2C serine/threonine protein phosphatase that was first identified in my laboratory as a gene (*PPM1D*) which is induced by wild-type p53 after DNA damage. The gene *PPM1D* is amplified and/or overexpressed in several types of human cancers. As an enzyme, Wip1 has the potential to be inactivated by low molecular weight chemical compounds. Therefore, through the combined use of rational design and screening assays, we are seeking to identify inhibitors of Wip1 phosphatase activity.

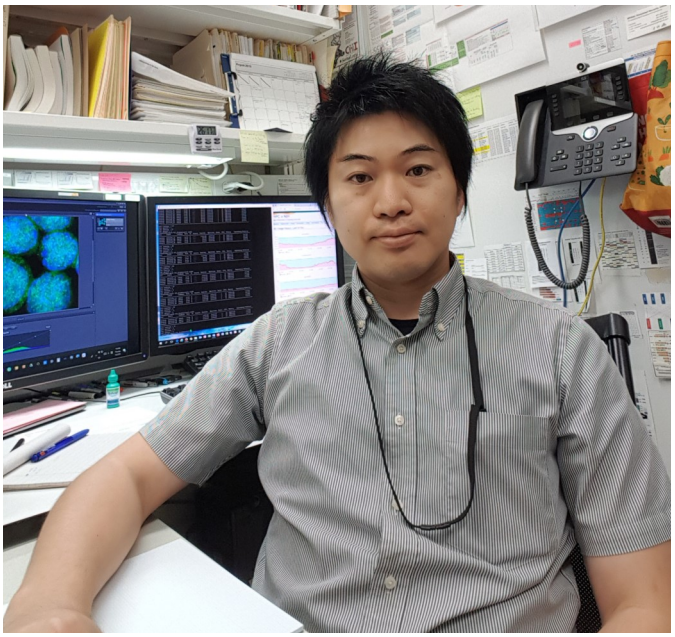
Because my research group is small, a highly trained Staff Scientist is essential for achieving the goals of these projects. Sharlyn Mazur, Ph.D., has been a Staff Scientist in my lab since 1999 and her expertise, creativity, and dedication have contributed substantially to my research program. She has provided critical skills required to master novel experimental approaches. For example, we have become interested in the technique of Hydrogen-Deuterium Exchange Mass Spectrometry (HDX-MS) and Dr. Mazur mastered the details of analyzing HDX-MS data as part of our collaborative HDX-MS projects with Jeffrey Hudgens, Ph.D. (NIST). She has also been involved in the development of a novel screening assay for activators/inhibitors of Wip1 phosphatase activity, performed in collaboration with NCATS. As we are using the same method to investigate mechanistic aspects of Wip1 inhibitors, Dr. Mazur's understanding of enzyme kinetics has been essential for planning these screens and provided us with key insights into the mechanism of Wip1 inhibition. Recently, in collaboration with Frederick Dyda, Ph.D. (NIDDK), Stewart Durell, Ph.D. (NCI), and Alexander Grishaev, Ph.D. (NIST), we used X-ray crystallography, small-angle x-ray scattering, biochemical and computational approaches to investigate how a weakly bound Mg ion and the substrate interact in the active site of PPM-family phosphatases and affect protein conformation. These results provide a physical basis for an innate mechanism regulating PPM phosphatase activity. Finally, Dr. Mazur actively mentors two post-doctoral fellows and a post-baccalaureate fellow in the laboratory. In all these areas, she provides technical expertise and diligence to solve problems and advance the research of my section.

Throughout the years, I have marveled at the progress that has been achieved in unraveling the structure of proteins and in understanding their interactions in controlling signal transduction. These advances have been made possible by new experimental approaches developed by highly trained scientists and postdoctoral fellows who are able to spend the time on method development and application. For example, Lisa Jenkins, Ph.D., one of my former post-doctoral fellows, learned mass spectrometry in my group and now, as a staff scientist, manages the Mass Spectrometry Unit of the Collaborative Protein Technology Resource, which provides mass spectrometry support for CCR investigators. As technology continues to advance, I look forward to seeing how much better we can understand signaling and regulation in the cell.

Ettore Appela, M.D.
Senior Investigator and Head,
Chemical Immunology Section
Laboratory of Cell Biology

The SSSC Corner

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



I joined the group of Giovanna Tosato, M.D., in the Molecular and Cell Biology Section of the Laboratory of Cellular Oncology at CCR in 2010 as a Supplemental Visiting Fellow of NIH and a Fellow of Young Researcher Overseas Training Program of Japan Society for the Promotion of Science. The training program lasted for three years and I had planned to leave NIH after that time. However, this has been a fascinating place to work and I decided to extend my time here.

During my post-doctoral work, I worked in the field of tumor angiogenesis. Our work revealed molecular mechanisms of how blood vessels are formed and pruned. In those projects, I used various molecular biology assays including the proximity ligation assay and proximity extension assay. These techniques are amazingly sensitive and helped me to prove protein-protein interactions, which were virtually impossible to detect and quantify by conventional immunoprecipitation-Western blotting in physiological and pathological conditions. Those experiences gave me an idea of a new experimental method for acquiring locational information of different types of proteins and the modifications on the genome at the single-cell level. I was encouraged to proceed with the project by Dr. Tosato and received the NCI Director's Innovation Award. In 2017, Dr. Tosato hired me as a Staff Scientist to give me time to complete the project and expand the possibilities of the new method in the field of cancer biology. As you know, a post-doc position is a time-limited position and it is not easy to take a high risk. I would not have started the project without their support. The project is now in the closing stage. The new method has versatility in scientific experiments. Soon, I would like to introduce the new method to CCR researchers and contribute to their research.

Hidetaka is pictured with his son, Kenta and daughter, Mana

Outside of work, I am a father of my young son and daughter. I play with and am learning a lot from my kids. They are teaching me the beauty of life. Sometimes, I talk to my son about science and my research, which is fun. When I was a first-year elementary school student, I wrote a letter to myself. Fourteen years later, the letter was delivered to me through a postal service called "time capsule." In the letter, my first-year elementary student self-described my dream to become a scientist and discuss science with great scientists who love what they do. Dr. Tosato and my colleagues of NIH love science and I am enjoying working with such great scientists.

Hidetaka Ohnuki, Ph.D. (SS)
Laboratory of Cellular Oncology

Phase I Trial of M7824 (MSB0011359C), a Bifunctional Fusion Protein Targeting PD-L1 and TGFβ, in Advanced Solid Tumors

Strauss J, Heery CR, Schlom J, Madan RA, Cao L, Kang Z, Lamping E, Marté JL, Donahue RN, Grenga I, Cordes L, Christensen O, Mahnke L, Helwig C, Gulley JL. Clin Cancer Res. 2018 Mar 15;24(6):1287-1295.

In recent years multiple agents targeting the programmed death 1 (PD-1)/programmed death ligand 1 (PD-L1) pathway have received regulatory approval, demonstrating impressive durations of response for several tumor types. Unfortunately, not all cancer types seem to respond to these agents, and, even among susceptible cancer types, the percentage of responding patients is usually less than 20%. To increase the rate of response to these therapies, many ongoing trials are evaluating anti-PD-1/PD-L1 agents in combination with other immunotherapies. One potential promising combination strategy are agents which dually block the PD-1/PD-L1 and transforming growth factor β (TGF-β) pathways. TGF-β is a pleiotropic cytokine. In the premalignant state, it has tumor-suppressive effects and suppresses tumorigenic inflammation. However, in patients with cancer, TGF-β is associated with malignant progression, evasion of immune surveillance, invasion, and metastasis (1-2).

M7824 is a novel bifunctional fusion protein which targets PD-L1 and TGF-β. It is composed of a fully human IgG1 monoclonal antibody against human PD-L1 fused, via a flexible glycine-serine linker, to the soluble extracellular domain of human TGF-β receptor II (TGF-βRII), which functions as a TGF-β "trap." The anti-PD-L1 moiety of M7824 is based on avelumab, which is currently in Phase III clinical trials in multiple tumor types and was recently FDA approved for metastatic Merkel Cell Carcinoma and urothelial carcinoma. Preclinical work in murine models showed that M7824 had improved antitumor activity compared with either an anti–PD-L1 antibody or TGFβ trap alone, extended survival and conferred long-term protective antitumor activity in cured mice upon tumor rechallenge, and substantially increased $CD8^+$ T-cell and natural killer (NK) cell infiltration while decreasing myeloid-derived suppressor cell (MDSC) infiltration within the tumor compared with an anti–PD-L1 antibody (3).

Julius Strauss, M.D., Staff Clinician and Co-Director of the Clinical Trials Group in the Laboratory of Tumor Immunology and Biology (LTIB), and his colleagues conducted a first-in-human Phase I clinical trial of M7824 in patients with advanced solid tumors. They found that this agent efficiently bound to and saturated PD-L1, as well as sequestered TGFβ1, -β2, and -β3. They also found this therapy to be generally well tolerated with a similar toxicity profile to other PD-1 or PD-L1 inhibitors with one additional toxicity being the development of keratoacanthomas, a low grade squamous cell carcinoma of the skin, in about 10% of treated patients. These skin lesions which have been described with other novel TGFβ depleting therapies were easily managed with local therapy and did not require drug discontinuation. The drug was also found to be clinically active producing durable responses in a number of different solid tumor types (4). Based upon this early safety and efficacy signal, disease specific expansion cohorts have been opened to further evaluate this drug.

One group of solid tumors which may benefit from this therapy are HPV associated malignancies. Genome wide association studies have shown the TGFβR1 pathway to be frequently dysregulated and significantly associated with HPV carcinomas (5). On the Phase I trial, a confirmed objective response rate (ORR) of 35% in 17 patients with HPV associated malignancies (cervical, anal, head and neck squamous cell carcinoma) and a confirmed ORR of 42% in 12 patients with known HPV positive malignancies (6) were observed. These response rates compare favorably to the historical response rates to anti PD-1/PD-L1 therapy of 15-20% for these diseases. Based upon this promising response rate Dr. Strauss is currently accruing to an ongoing phase II trial evaluating M7824 in patients with HPV associated malignancies (NCT03427411).

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

Dr. Strauss serves as a Staff Clinician in the LTIB and is part of a larger combined effort between the LTIB, under the leadership of Jeffrey Schlom, Ph.D., and the Genitourinary Malignancies Branch (GMB), under the leadership of James Gulley, M.D., Ph.D., to evaluate novel combination immunotherapies in patients with advanced solid tumors.

Julius Strauss, M.D. (SC)
Co-Director, Clinical Trials Group
Laboratory of Tumor Immunology and Biology

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The Core Corner

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

The Confocal Microscopy and Digital Imaging Facility at the Experimental Immunology Branch

The Confocal Microscopy and Digital Imaging Facility at the Experimental Immunology Branch (EIB) supports the experimental needs of researchers studying lymphocyte differentiation and maturation, cell biology of immune response, cell signaling and other aspects of basic immunology. The main instruments within our core have the following capabilities.

The Zeiss AxioObserver widefield imaging microscope is used mainly for imaging large sections of tumor and normal tissues for histological analysis as well as sections immunostained with multiplexed fluorescent antibodies. Its ZEN software allows for assembly of very large mosaics (hundreds of tiles) as well as imaging of multiwell plates (to analyze response of cells to drugs, for example). Moreover, this microscope setup can be easily adapted to other imaging scenarios, including long-term time-lapse imaging of live cells and tissues to observe their responses to treatment in real time or to characterize cell-to-cell interactions and cell migration.

The Yokogawa spinning disk confocal setup, attached to the Nikon Eclipse Ti2 microscope, contains four lasers covering commonly used excitation bands of 405, 488, 561 and 635nm as well as a LED light engine for widefield imaging. Altogether, this allows for detailed imaging of cells and tissues immunolabelled or fluorescently tagged with a variety of fluorophores. It is also used to acquire mosaic images of

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

tissue samples and cells, but with the added advantage of out-of-focus background rejection. Moreover, the use of extra-long working distance objective enables imaging of live tissues mounted on thick substrates.

The Zeiss LSM880-NLO microscope allows for state-of-the-art imaging experiments. This setup is equipped with a Coherent Chameleon femtosecond laser tunable from 680nm to 1080nm. It can be used to excite fluorophores deep within the sample, allowing high resolution, two-photon imaging of any marker – from short-wavelength dyes such as Indo or Fura, through fluorescent proteins like GFP or YFP, to red shifted probes such as RCaMP. High peak power enables optimum native fluorescence excitation or SHG imaging. Currently, in addition to imaging, it is also used to generate double and single-strand DNA breaks to study DNA repair in individual cells. An additional argon laser (458, 488 and 514nm lines), as well as UV (355 and 405nm) and visible lasers (561, 594 and 635nm) enable single-photon confocal laser scanning as well, and the instrument can perform real-time analysis of photobleaching and FCS.

In addition to use within the branch, there is a range of collaborative activities involving other scientists at CCR. Thus, the three main instruments of the facility are well utilized. However, we are always interested in advancing research across CCR, so please do not hesitate to contact me to discuss any potential studies.

Jan Wisniewski, Ph.D.
Manager, Confocal Microscopy and
Digital Imaging Facility
Experimental Immunology Branch

The Professional Development Corner

The 2018 Annual NCI SS/SC Professional Development Day

The SSSC Professional Development Committee is proud to announce the 2018 Annual NCI SSSC Professional Development Day which will be held in Bldg.50, NIH Bethesda Campus on Friday November 16, 2018.

This event is uniquely developed to serve the Staff Scientist/ Staff Clinician community. We are delighted to have Hannah Valentine, Ph.D., as our first speaker of the day for this event. Dr. Valentine joined NHLBI in 2014 to continue her research while also serving as the first NIH Chief Officer of Scientific Workforce Diversity. Next, we will have an introduction to the new SSSC Enrichment program. We have invited the coordinators of this program to answer all of your questions. Do you want to convey your science in an impactful way? Later in the day, Scott Morgan will sharpen our skills through an interactive workshop on how to make the best elevator pitch. As always, there will be a session on the what, when and how to have the best Quad Review.

This year we will end with an open and interactive discussion. Pizza lunch will be provided! Join us for this unique professional development opportunity. Your continued enthusiastic support is what makes this event a success. Registration for this event will open on October 15, 2018. Details will be sent via email.

Swati Choksi, Ph.D. (SS)
Head, Professional Development Committee
Laboratory of Immune Cell Biology

The Personal Development Corner

Section Editor: Brunilde Gril, Ph.D., M.P.S. (*SS*)

An Enrichment Program for Staff Scientists

Behold Staff Scientists! Here is what you have been waiting for all those years: the opportunity to flourish in your position and materialize your vision. Ofelia Olivero, Ph.D., Chief of the Intramural Diversity Workforce Branch (IDWB), in the Center for Cancer Training (CCT), in collaboration with Cynthia Masison, Ph.D., Associate Scientist in the Office of the Director, Center for Cancer Research (CCR) and the Office of Workforce Planning and Development (OWPD), is launching the first enrichment program for Staff Scientists. The program combines a judicious choice of lectures, workshops, learning assignments, networking and mentoring opportunities, all embedded in a positive and empowering framework highlighting each participant's strengths and talents. The application process will start November 16 and close on December 15, 2018. The program is free. It will last four months with activities once or twice a month. The enrichment program is a ticket to work fulfillment.

We are all well-trained scientists, often experts in our fields, with extensive scientific knowledge. However, taken the whirlwind of our workload and responsibilities, we rarely take time to pause and reflect on what we really want in life, nor have we been given the tools to investigate our personal needs and vision of work fulfillment and success. Many of us have felt discouraged by the lack of opportunities for career advancement in our position. With the proper guidance, we can break many apparent obstacles and reinvent our current position and ourselves. Participating in the enrichment program will give you the tools to take control of your career.

As part of the program, you will have the opportunity to develop a formal mentoring partnership with the person of your choice. A mentor has an invaluable role and can have a profound impact on your career development (Olivero, 2013; Reh, 2018). A mentor supports your growth and offers advice, information and guidance to help you in achieving your professional goals. While your supervisor is a key player in helping you navigate your career, experts in the field of coaching and mentoring caution people about having a supervisor as a unique mentor (Luecke, & Ibarra, 2004; Olivero, 2013), as it implies inevitable conflicts of interest. A mentor outside of your chain of command has the sole agenda and genuine desire to guide and empower you. The program offers you an official framework to choose your mentor in any field/institute NIH wide and explore new avenues. If you dream about expanding your scientific knowledge to a new disease (e.g., explore another type of cancer or collaborate with another institute) or a new technique (e.g., single-cell sequencing, *in vivo* two-photon imaging) to bring new perspectives to your work or if you long for career advice and inspiration, the mentor is your path to creativity and fulfillment. Pick your mentor wisely in a field that excites you, challenges you and opens new opportunities. Think about the characteristics you are looking for in a mentor: do you put emphasis on empathy, honesty, scientific knowledge, patience, empowerment, accessibility…? You will be guided to know how to choose a mentor that fits your needs, your goals and your philosophy. Mentoring is a mutual relationship; both mentee and mentor gain professional expertise. I cannot emphasize enough the importance of having a mentor and it could be the primary reason you decide to enroll in this program.

"Know thyself" is a precept originating from Greek antiquity that has been used and re-used over the millennia. Despite the utter importance of self-knowledge and self-awareness, it is not innate and not a widespread human characteristic. Worry not! An important goal of the program is to improve your self-awareness to empower you and help you make conscious and appropriate choices. Self-reflection assignments, journaling and assessments will guide you to identify your talents and define your short and long-term career objectives. During one of the first sessions, you will be offered a self-report assessment called the DiSC® (John Wiley & Sons, Inc., 1997-2010). The DiSC® will highlight your preferred working styles. Understanding your preferred styles will enable you to understand why you behave a certain way. It will provide you with the tools to adapt your behaviors to situations and to build stronger professional relationships.

Other activities include optional shadowing or creating a new project through rotation in different labs, following career skill advising workshops and participating in team activities with peers. Should you feel the need to explore entirely new horizons in other positions, a workshop on job searching skills will enlighten your journey.

Work fulfillment is a choice; it is our responsibility to work toward this goal. Our institute is giving us the tools to achieve this through wisely and carefully

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Section Editor: Brunilde Gril, Ph.D., M.P.S. (*SS*)

designed enrichment tools. This new initiative is not only for your personal benefit. Happiness is contagious and through finding your calling, you will contribute to the work fulfillment of your colleagues and supervisors. Enjoy!

Brunilde Gril, Ph.D., M.P.S. (SS)
Women's Malignancies Branch

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The Clinical Corner

Section Editor: Alexandra Zimmer, M.D. (*SC*)

Getting to Know our Staff Clinicians

The main goal of this section is to increase the participation of Staff Clinicians, and make their work better known at NIH. In this issue, we interview our Staff Clinician, Geraldine O'Sullivan Coyne, M.D., Ph.D., to hear perspectives about her work and collaborations at NIH.

An Interview with Geraldine O'Sullivan Coyne, M.D., Ph.D

What is your general role as Staff Clinician?
I have been a Staff Clinician since 2016, under the mentorship of Alice P. Chen, M.D., and James H. Doroshow, M.D. My main role is to design and conduct early-phase clinical trials concentrating on oncology drug development. These types of trials have changed a lot in the last decade: more scientifically driven, focused on safety but also informing proof of mechanism early in the development of promising agents while de-prioritizing ones that don't achieve the required efficacy. However, my most important role is to provide clinical leadership and the highest level of clinical care to the patients who enroll on a trial with our team.

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Section Editor: Alexandra Zimmer, M.D. (*SC*)

Could you point out steps and difficulties to implement a clinical trial?
Performing innovative early phase trials starts with a strong pre-clinical rationale, a suitable trial design and the appropriate correlative parameters to best answer the scientific question. The aim is to inform decisions regarding the fitness of novel agents to move forward (ie 'fail fast') and is crucial to expediting drug development timelines. Once a trial is open, the complexity shifts to monitoring, safety reporting, as well as getting the scientific endpoint answered- this entire effort is collaborative and needs a team.

What is your contact with Staff Scientists? Any report of cooperation from bench to bedside?
Our group focuses on the incorporation of pharmacodynamic assays for rational drug selection, so we work closely with PADIS and MoCha laboratories at NCI Frederick to carry out target validation and biomarker identification. We also contribute to the development of the national Patient Derived Models Repository, a clinically-annotated national database of PDXs, to support drug discovery.

How do you see patient care at NIH? Can you give examples of benefits and limitations?
It is a true research hospital, with a unique and highly specialized environment. The capacity to carry out mechanistically complex and meaningful trials, within a strong patient-centered safety and care framework, is remarkable. Clinical trials provide a lifeline for patients in need of treatment and without options in the community.

What is the career path of a Staff Clinician? Where do they go from here?
There is a rich diversity of interests and expertise in this group. The NIH has a lot of possibilities in the translational and clinical settings, with access to world class expertise and ample opportunities for career development.

Any final advice for new Staff Clinicians or about collaboration between Staff Clinicians and Staff Scientists?
I think the most important thing is to define your interest and area of expertise. Collaboration is key, maximize every opportunity through networking.

Have you identified any differences or challenges in being a woman scientist? Any specific advice to other young women starting in that path?
I have been deeply fortunate, as I look back on my training, to have come through various environments with very capable women in leadership positions. The medical workforce demographic is changing, and we can all work towards reducing disparity in career choices. My best advice is to find a mentor that wants to work with you and to stay focused on shaping your career.

Geraldine O'Sullivan Coyne, M.D., Ph.D. (SC)
Developmental Therapeutics Clinic

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 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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