THE DOSSIER

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

December 2017 Issue 30

From the Editor

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

This issue contains information from Tom Misteli, Ph.D., Director, CCR, and David Goldstein, Ph.D., Associate Director and Chief, Office of Science and Technology Resources, and an overview of the Annual SSSC Professional Development Day by the Head of our Professional Development Committee, Swati Choksi, Ph.D., along with Bethesda SSSC Vice-Co-Chair, Lakshmi Balagopalan, Ph.D. In our PI Corner, Munira A. Basrai, Ph.D., discusses the Staff Scientist role, and in our Core Corner, William C. Reinhold, B.S., describes the Genomics and Bioinformatics Group's CellMiner application. We also highlight the published work of Izumi Horikawa, M.D., Ph.D., in our Author's Corner, and in our Clinical Corner, we obtain the viewpoints of Mark J. Roschewski, M.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)
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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.

Facilitating CCR Science through Advanced Technologies and Scientific Resources

CCR scientists have access to a vast array of scientific and technical resources that help CCR achieve its mission and enable our labs to accomplish their goals. The goal of the Office of Science and Technology Resources (OSTR) is to ensure CCR scientists have access to emerging technologies and advanced methodologies either through centralized core labs or biotechnology companies. These scientific resources, available through over 70 NCI Cores and Facilities or partnerships with companies, contribute to making the CCR one of the richest environments in the world to conduct basic, translational, and clinical research.

A variety of advanced technologies, tools, and research services available to the CCR community can be found at the OSTR website (https://ostr.cancer.gov/). Partnerships with many biotechnology companies have been established to provide CCR researchers access to a broad range of bioinformatics software and biotechnology products, and services in the areas of proteomics, genomics, metabolomics, and imaging. The cost of many of these resources are subsidized through the Supplemental Technology Award Review System (STARS) established at the beginning of last fiscal year (https://ostr.cancer.gov/STARS).

In most areas of clinical and translational science, access to core resources has evolved from being useful to essential. One of OSTR's primary goals is to ensure NCI Cores offer the most advanced instrumentation managed by highly skilled staff. Many of these Cores are headed by Staff Scientists, who are technology leaders committed to helping with experimental design and applying the latest methods to solve complex research problems. CCR Cores and Facilities fall into nine basic disciplines ranging from genomics and proteomics, to bioinformatics and clinical research support. Several years ago, OSTR was involved in the establishment of CCR-dedicated Cores as part of the Cancer Research Technology Program (CRTP) in Frederick. These diverse laboratories provide an extensive number of valuable services, including mass spectrometry-based protein characterization, protein expression and purification, genomic characterization, and electron and optical microscopy. These Cores allow you to apply innovative, integrated, and customized solutions to complex research challenges. They are heavily subsidized by CCR OD and OSTR and are available to help all CCR investigators through services and collaborations. Information about these and all NCI and NIH Cores is available through a platform developed by the OSTR, called the NIH Collaborative Research Exchange (CREx).

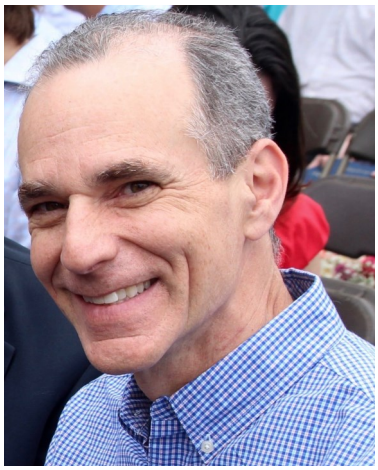
The field of single-cell genomics is generating many new insights into complex biological systems, including the genomics of human cancer. Single-cell (SC) sequencing studies have now begun to dissect intratumor genetic heterogeneity at single-cell resolution. To ensure CCR scientists have access to the latest single-cell methodologies, the OSTR will soon be establishing a new Single Cell Analysis Facility (SCAF). The SCAF will provide CCR investigators an opportunity to confidently explore the nature and role of cellular heterogeneity in the context of cancer development. It will implement state-of-the-art single-cell technologies and provide high-throughput isolation of rare and single cells for downstream library preparation and sequencing of RNA and DNA. The SCAF will also serve as a central hub for SC technology assessment, data analysis, and focal point for collaboration and idea exchange with CCR Laboratories and Centers of Excellence, NCI Cores and Facilities, as well as other research groups at NIH focused on cutting-edge SC research. The mechanisms for how to initiate a project with this new facility will be announced soon.

Advanced high-throughput 'omic technologies, such as Next Generation Sequencing (NGS), proteomics, and metabolomics, allow us to collect vast amounts of information on the molecular workings of biological systems. However, this abundance of information also presents many hurdles. In order to address these significant challenges, the OSTR has established two bioinformatics resources: The first is the CCR Collaborative Bioinformatics Resource (CCBR), which has a broad range of expertise and provides a

The Office of the Director: Guest Editorial Con't

comprehensive solution for designing, analyzing and interpreting high-throughput biological experiments on a collaborative basis. In addition, the OSTR has established The Bioinformatics Training and Education Program (BTEP: https://ostr.cancer.gov/bioinformatics) to increase the awareness and understanding of bioinformatics techniques and processes. The goal of this program is to empower CCR scientists to perform a basic, informed set of analyses on their own behalf. During last fiscal year, BTEP has hosted a variety of training sessions and lectures in the areas of NGS analysis (RNA-Seq and ChIP-Seq), methylation analysis, and pathway analysis.

A goal of CCR is the discovery and translation of scientific advances into interventions that help our patients. The CCR OD, through the OSTR, strives to make resources available to assist you in accelerating the process of moving scientific breakthroughs from the bench to the clinic. Thank you for the hard work that all of you do each day whether it be supporting the research agenda of a Principal Investigator or managing a Core or program that assists the broader CCR community.



David Goldstein, Ph.D.
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Tom Misteli, Ph.D.
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The PI Corner

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

Munira A. Basrai, Ph.D., is pictured in the laboratory with Staff Scientist, Prashant K. Mishra, Ph.D.

As a Senior Investigator and the Head of the Yeast Genome Stability Section, I have had the privilege of working with Prashant K. Mishra, Ph.D., a Staff Scientist in my research group within the Genetics Branch of the Center for Cancer Research, NCI. Research in my laboratory is focused on the role of kinetochore proteins in the assembly of centromeric chromatin. The centromere is critical for faithful chromosome segregation due to its essential role in kinetochore function, spindle microtubule attachment and checkpoint activation. Errors in chromosome segregation lead to chromosomal instability (CIN) and this contributes to aneuploidy, which has been observed in many cancers. Hence, the identification and functional characterization of kinetochore genes is critical for the advancement of cancer biology.

The PI Corner Con't

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

The Staff Scientist program brings manifold and enormous benefits to the diverse research activities ongoing at the NIH. Dr. Mishra has brought novel ideas, exceptional intellect, unique technical expertise and critical insights for our research projects. Dr. Mishra has presented his research findings at numerous conferences and has published highly significant papers from my laboratory. His pioneering studies have provided novel insights into the role of kinetochore proteins in the assembly of centromeric chromatin. Using budding yeast as a model system, he has defined the molecular roles for evolutionarily conserved kinetochore proteins such as Cse4 (CENP-A in humans), Scm3 (HJURP) and its interacting partners Pat1 (PATL1), Sgo1 (SGOL1) and Cdc5 (PLK1). Overexpression of human homologs of these yeast genes has been observed in many cancers, however, the physiological consequences of these observations remained unexplored. Dr. Mishra showed that overexpression of Scm3 and Cse4 contribute to CIN phenotypes in yeast and human cells[1]. These results indicate that balanced stoichiometry of kinetochore proteins is critical for faithful chromosome segregation[1]. In another study, Dr. Mishra described a novel role for Pat1 at the kinetochore[2], and in collaboration with Dr. Kerry Bloom (Univ. of North Carolina, Chapel Hill) we defined the number of Cse4 molecules at the budding yeast kinetochore[3]. Our results showed that Pat1 is required for maintaining centromeric Cse4 levels for high fidelity chromosome segregation[4]. Dr. Mishra also established that centromeric association of polo like kinase, Cdc5 is required for removal of centromeric cohesin during the metaphase to anaphase transition in mitosis[5]. His recent studies provided the first evidence for a role of Cse4 in the centromeric association of Sgo1, a key regulator for cohesins on chromosomes[6]. Overall, Dr. Mishra's research has significantly contributed to our understanding on the assembly of centromeric chromatin and how errors in chromosome segregation may contribute to CIN and aneuploidy in human cancers.

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The Author's Corner

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

Δ133p53 Represses p53-Inducible Senescence Genes and Enhances the Generation of Human Induced Pluripotent Stem Cells

Izumi Horikawa, Kye-yoon Park, Kazunobu Isogaya, Yukiharu Hiyoshi, Han Li, Katsuhiro Anami, Ana I. Robles, Abdul M. Mondal, Kaori Fujita, Manuel Serrano, Curtis C. Harris. *Cell Death and Differentiation. 2017 Jun;24 (6):1017-28*.

Human pluripotent stem cells, in particular, induced pluripotent stem cells (iPSC), are a valuable source in regenerative medicine towards treatment of aging-associated or injury-induced degenerative disorders. Genome stability and the non-tumorigenic nature of iPSC, which are critical to their clinical application, have long been in hot debate[1] since iPSC generation by Yamanaka factors (i.e., Oct4, Sox2, Klf4 and c-Myc) was first reported in 2006. The tumor suppressor protein p53 plays essential roles in genome stability and tumor suppression through the regulation of cell differentiation, cell cycle progression and senescence, apoptosis and DNA damage repair. The undifferentiated status and self-renewing cell divisions of iPSC are not compatible with the ability of p53 to induce cell differentiation, cell cycle arrest and cellular senescence. On the other hand, p53-mediated DNA repair and apoptotic elimination of severely damaged cells are required for iPSC to maintain genome stability. As predicted from these apparently conflicting activities of p53, while inhibition of p53 (e.g., p53 knockdown or knockout) accelerates iPSC reprogramming, genome instability and oncogenic transformation could be a serious concern in the resulting iPSC[2]. A recent study published in *Cell Death and Differentiation*, led by Curtis C. Harris, M.D., Chief of the Laboratory of Human Carcinogenesis (LHC), and Izumi Horikawa, M.D., Ph.D., Staff Scientist in LHC, provides evidence that a natural p53 protein isoform coordinates the balanced regulation of self-renewing capacity, DNA damage repair and apoptosis in human pluripotent stem cells.

The human *TP53* gene encodes not only full-length p53 protein (FLp53) but also multiple p53 protein isoforms due to alternative mRNA splicing, transcriptional initiation from alternative promoters, and alternative initiation of protein translation (Figure 1A). Δ133p53, an amino-terminally truncated isoform lacking the first 132 amino acid residues, physiologically originates from a transcriptional initiation from the alternative promoter within intron 4 (Figure 1A). Unlike proteasome-mediated degradation of FLp53, Δ133p53 is degraded via chaperone-assisted selective autophagy[3]. The authors have first found that all human pluripotent stem cells examined, including iPSC and embryonic stem cells (ESC), consistently express abundant levels of endogenous Δ133p53 protein (at least 10-fold higher than human fibroblasts and attributed to both increased mRNA levels and reduced autophagic degradation), while FLp53 protein levels in iPSC and ESC widely vary from 0.3- to 2.3-fold of the levels in human fibroblasts. These human iPSC and ESC express reduced levels of p53-inducible genes that primarily mediate cellular senescence (such as $p21^{WAF1}$ and microRNA-34a), but maintained or increased levels of those involved in apoptosis and DNA damage repair (such as BAX, PUMA and p53R2). Overexpression of exogenous Δ133p53 in human fibroblasts, while not repressing BAX, PUMA and p53R2, significantly represses $p21^{WAF1}$ and microRNA-34a by dominant-negatively displacing FLp53 from the promoter regions of these genes, reproducing the p53-inducible gene expression profile in iPSC and ESC with endogenously up-regulated Δ133p53 (Figure 1B). This functional analysis suggests that Δ133p53 contributes to the differential regulation of different subsets of p53-inducible genes in iPSC and ESC, which is consistent with their self-renewing capacity (incompatible with p53-induced senescent proliferation arrest) and genome

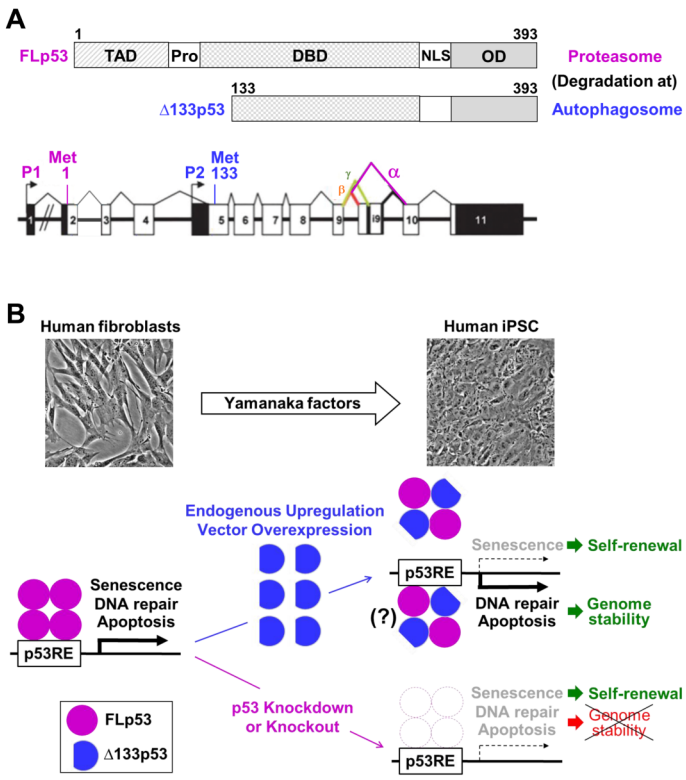

Figure 1. Δ133p53: a p53 isoform enriched in human pluripotent stem cells. (**A**) The human *TP53* gene encodes multiple p53 protein isoforms due to alternative mRNA splicing (a, b and g) and transcription from alternative promoters (P1 and P2). The P1 promoter and a splicing generate full-length p53 (FLp53) protein. The alternative transcription from the P2 promoter, along with a splicing, generates Δ133p53, an amino-terminally truncated p53 isoform translated from the codon 133 methionine. In contrast to proteasome-mediated degradation of FLp53, Δ133p53 is degraded via selective autophagy[3]. TAD, transactivation domain; Pro, proline-rich region; DBD, DNA-binding domain; NLS, nuclear localization signal; and OD, oligomerization domain. (**B**) Δ133p53, whether endogenously upregulated or exogenously overexpressed, enables iPSC reprogramming with genome stability in human cells. While human fibroblasts are committed to expressing p53-inducible genes involved in cellular senescence, apoptosis and DNA damage repair, human pluripotent stem cells are characterized by the preferential repression of those involved in cellular senescence (allowing self-renewal), which is attributed to the activity of upregulated Δ133p53. Δ133p53 physically interacts with FLp53 and dominant-negatively inhibits its binding to the p53 response element (p53RE) likely in a promoter context-dependent manner, although the exact stoichiometry of the Δ133p53-FLp53 interaction is still unknown (a heterotetramer consisting of two each is shown in this scheme). The molecular mechanisms by which Δ133p53 differentially regulates different subsets of p53-inducible genes are under investigation (indicated by a question mark). Total inhibition of p53 activities such as p53 knockdown or knockout, although previously reported to enhance iPSC reprogramming[2], could lead to genome instability due to impaired DNA repair and failure of apoptotic elimination of severely damaged cells.

stability (through p53-mediated repair of DNA damage and apoptosis of damaged cells) (Figure 1B). When induced to reprogram to iPSC by Yamanaka factors, Δ133p53-overexpressing human fibroblasts show 2- to 3-fold increased efficiency of iPSC generation compared with vector-transduced control fibroblasts, suggesting that increased levels of Δ133p53 plays a causative role in reprogramming human cells to pluripotent state.

The iPSC clones established from Δ133p53-overexpressing fibroblasts in this report, when injected into immuno-deficient mice, form well-differentiated teratomas with differentiation into all three germ layer-derived tissues and without malignant pathology. These iPSC clones also have normal karyotype without gross chromosomal abnormalities and have stable microsatellite repeats and mitochondrial DNA. Strikingly, the number of somatic mutations (single nucleotide substitutions and small insertions/deletions) in these iPSC clones (0.2-1.2 mutations per megabase) is similar to that in control iPSC clones (0.1-1.8 mutations per megabase) and much fewer than in iPSC generated from p53-knocked-down fibroblasts (5.1 mutations per megabase). These data indicate that, in contrast to general inhibition of p53 activities leading to genome instability, Δ133p53 is not oncogenic or mutagenic at least by itself during reprogramming processes. Overall, these findings support that p53 activities in human pluripotent stem cells are not simply inhibited, but rather are coordinately regulated by Δ133p53 to enable the establishment and maintenance of self-renewing capacity with secured genome stability (Figure 1B).

This study may open up a new strategy for improving the quality of pluripotent stem cells as a therapeutic source for regenerative medicine. It is of great interest to examine the roles of Δ133p53 in adult tissue stem cells and cancer stem cells. The non-oncogenic and non-mutagenic nature of Δ133p53 also encourages efforts to explore this natural p53 isoform as a therapeutic target in a wider range of human diseases. The examples include Δ133p53-mediated functional restoration of tumor-associated exhausted $CD8^+$ T lymphocytes for efficient anti-cancer immunotherapy[4] and Δ133p53-mediated conversion from neurotoxic to neuroprotective astrocytes towards a new treatment of Alzheimer's and other neurodegenerative diseases[5]. Mechanistically, the molecular details of the Δ133p53

regulation of different subsets of p53-inducible genes are currently under investigation (Figure 1B). Finally, since Δ133p53 is a human/primate-specific p53 isoform[5], Δ133p53-humanized mouse models for further *in vivo* studies are under development.

Izumi Horikawa, M.D., Ph.D. (SS)
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Izumi, a Staff Scientist at LHC, works closely with Dr. Curtis Harris, Chief of LHC, to lead basic research projects on cancer and aging-associated diseases. His research focuses on p53-regulated biological processes, including cellular senescence, apoptosis and DNA damage response. He mentors many LHC fellows and students in a highly enthusiastic and dedicated manner. Izumi has also made outstanding contributions to LHC intellectual property.

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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 decided to interview an accomplished, well known and respected clinician, who has been a role model for many of us that became Staff Clinicians.

An Interview with Mark J. Roschewski , M.D.

What is your general role as staff clinician?

I have officially been a Staff Clinician in the Lymphoid Malignancies Branch since 2013. I did also spend about five years prior to that working with both Wyndham Wilson, M.D., Ph.D., Kieron Dunleavy, M.D., Ola Landgren M.D., Ph.D., and Adrian Wiestner, M.D., Ph.D., on a variety of clinical research protocols and projects. As a Staff Clinician under Dr. Wilson, my main role has been to development clinical protocols, manage patients on our research protocols, present data at a variety of meetings, and publish manuscripts. I have always felt that Dr. Wilson has provided a good deal of autonomy with respect to choosing projects that I find of interest. Our group has spent many years developing dose-adjusted EPOCH-R as a platform for the treatment of aggressive lymphomas, but we have also had a number of other research topics including exploring the use of circulating tumor DNA as a biomarker for disease recurrence. I have taken the lead on some of those projects. Another important role as a Staff Clinician within a research team includes mentoring trainees and assisting in the day-to-day management of the entire team of nurses, extended providers, and patient care coordinators.

Could you point out steps and difficulties to implement a clinical trial?

The biggest challenge, in my view, is to development a clinical trial that holds enough novelty to be of interest for the CCR and also maintain relevance with the academic community at large. It is important that we do innovative trials here at CCR that cannot be done easily elsewhere, but it is also critical that our studies have generalizability in order to make an impact on the field. Since our environment is different than the extra-mural world, we have unique challenges. In the world of lymphoid malignancies, many novel agents are highly effective and a number of outside centers have many more patients than we do. That enables them to accrue to clinical trials more quickly than we can. Hence, our group has focused on rarer lymphoma sub-types founded on translational science that cannot be easily done elsewhere. Our model, however, requires that we have strong relationships with outside oncologists that are willing and able to refer patients to our trials. It is highly disheartening to spend a few years developing a trial only to watch that project suffer from poor patient accrual.

What was your contact with the Staff Scientists? Any report of cooperation bench to bedside?

Well, our main contact with Staff Scientists has been indirectly through our collaboration with Lou Staudt, M.D., Ph.D., and his lab. Our group is set up where we meet regularly with Dr. Staudt, but have less direct interaction with Staff Scientists. I think those interactions can be highly valuable, but not always practical with our busy workflow.

How do you see patient care at NIH? Can you give examples of benefits and limitations?

The patient care at NIH is extremely comprehensive and compassionate. All patients seem to value their experiences here. An obvious limitation is that not all patients are eligible for clinical trials. Our group tries to write entry criteria as broadly as possible, but it is impossible to have an open protocol for every patient in every situation. I personally have a very difficult time with scenarios in which I have to transition a patient of mine on trial (i.e. “my patient”) to the outside when that decision is driven by a lack of an open trial here at NIH. Oncology is an ownership specialty and those situations are counterintuitive to my instincts. I understand why those limitations exist, but I do not like them.

The Clinical Corner Con't

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

What is the career path of a Staff Clinician? Where do they go from here?

I think it is a mistake to think that there is a singular path of a Staff Clinician. I think there are a number of models and it depends on the individual's goals, their field of study, and their desire for growth. Everyone desires growth over time, but it comes in many ways. For instance, some people really value an increasing amount of responsibility within the NIH structure. Others value growth within their own academic field. Those are important distinctions. Both of these are obtainable as a Staff Clinician, but take motivation, diligence, and perseverance. I have seen Staff Clinicians make significant impact within their academic field. I don't find the title very descriptive, but titles are also not very important to me.

Any final advice for new Staff Clinicians or about collaboration between Staff Clinicians & Staff Scientists?

I don't think that one can overstate the importance of face-to-face and iterative discussions. I would extend it beyond Staff Clinicians and Staff Scientists and say that the most successful people that I have worked with here at NIH have spent much time with continuous discussions with a variety of people in order to learn about opportunities. Self-starters can flourish at NIH. I would say that it is important to not be afraid of taking a few risks here and there and trying new avenues. We all sometimes get stuck in our ways and that can be quite limiting – particularly as technologies and strategies evolve. It is a bit cliché to say this, but I personally do not let the word "No (you can't)" be a reason why I stop pursuing something that I believe to be of value.

Mark J. Roschewski, M.D. (SC)
Lymphoid Malignancies Branch

The Core Corner

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

The Genomics and Bioinformatics Group: CellMiner and its Application

The primary function of the Genomics and Bioinformatics Group (GBG) is to make available to the scientific community cell-based systems pharmacogenomic data and tools that allow users to query that data without the necessity of having a bioinformatics or computer scientist team. Our main tool to fulfill this purpose is CellMiner (https://discover.nci.nih.gov/cellminer/), an internationally used application with users from ~67 countries each month. The overview of types of information included under the multiple tabs of the site are described in Figure 1. During the development of CellMiner, we have i) made to date 21 NCI-60 cancerous cell line databases (detailed under the "Data Set Metadata" tab from Figure 1), ii) developed, maintained, and expanded web-applications that facilitate the exploration of that data (including our "NCI-60 Analysis Tools"), and iii) provided both introduction to and interpretation of that data in first author and collaborative publications. Currently we are in the process of expanding our functionality with CellMiner Cross Database (CDB) (https://discover.nci.nih.gov/cellminercdb/), which increases the information we make available to that from the Genomics of Drug Sensitivity in Cancer (GDSC, http://www.cancerrxgene.org), Cancer Cell Line Encyclopedia (CCLE, http://www.broadinstitute.org/software/cprg/?q=node/11), and Cancer Therapeutics Response Portal (CTRP,

https://portals.broadinstitute.org/ctrp/). This effort expands the number of cell lines for which we have data, and facilitates cross-database analyses.

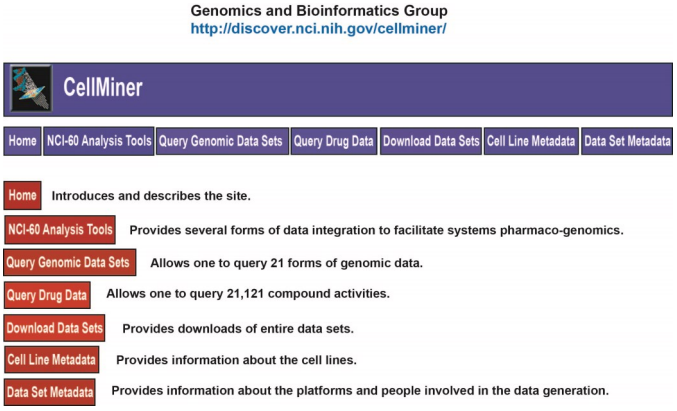

Figure 1. The Genomics and Bioinformatics Group's url, and CellMiner Website Tabs

A recent collaboration with Anish Thomas, M.D., an oncologist currently in the Developmental Therapeutics Program (DTP), provides examples of the translationally relevant and omic nature of our results [1]. The scientific question that was presented in this study on precision medicine trials, was why the DNA-damaging drugs, that remain the workhorse drugs in every oncology center in the world, were being left out of the patient selection and directed treatment designs in those trials. The GBG facility provided the intellectual and data inputs that lead to the question being raised, clarified the extent of the problem, and suggested a strong candidate solution. On the intellectual side, by assessing the recent and current clinical trials in a systematic fashion, and considering the types of drugs being employed in toto, we made clear that there was a systematic omission of the DNA-damaging drugs. On the data side, the organization of our drug data, that provided easy access to mechanism of action categories for those drugs, prevented us from having to dig out specific information on each of the included-in-trial drugs individually from the literature. A putative solution for this problem came from our prior work on a candidate DNA-damaging drug biomarker with potentially wide applicability, SLFN11 expression. Figure 2 illustrates the strong association between the gene expression and drug activities, an association that has been shown to be causal. Our involvement in the development of this exciting candidate biomarker is detailed in several publications [1] [2] [3] [4] [5].

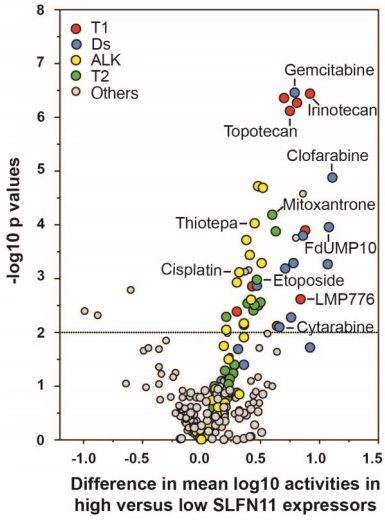

Figure 2. Volcano plot of the effect of SLFN11 expression on the 108 FDA-approved and 70 clinical trial drug activities in the NCI-60. The x-axis is the difference in mean log10 growth inhibition 50% activities, based on SLFN11 transcript levels z scores at higher (>-0.3) or lower (<-0.3) levels. The y-axis is the -log10 p value as calculated by t test. The dashed horizontal line is at the p<0.01 level of significance.

This single study provides a clear illustration of some of the potential uses of the CellMiner website, with its provision of large repositories of both drug and molecular data, all clearly organized and presented. It's high usage and value result from its facilitation of systems pharmacological studies of translational nature, based on the questions, domain expertise and insight of the users.

The GBG is currently undergoing a name change to the Genomics and Pharmacology Facility (GPF). Administratively, it falls under the umbrella of the Developmental Therapeutics Branch (DTB)/ Center for Cancer Research (CCR)/ National Cancer Institute (NCI). We have additional tools, located at https://discover.nci.nih.gov, but these fall outside of the scope of the current article.

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The Professional Development Corner

The Annual NCI SSSC Professional Development Day 2017

The SSSC Professional Development Committee held the Annual NCI SSSC Professional Development Day on October 13th, 2017. It was a widely attended event with over 70 people registered. As always, Professional Development Day addresses topics that are important for the advancement of the SSSC community. The opening remarks from CCR Director, Tom Misteli, Ph.D., were inspiring and his words gave confidence to the Staff Scientists and Staff Clinicians about their career choice. Dr. Misteli reminded us that, though we are an extremely heterogeneous group, our talents are vital to the success of the NCI mission. Then Rena Rodriguez, Deputy Director, Office of Management, NCI and Cynthia Masison, Ph.D., Program Specialist, Office of Scientific Programs, Office of the Director, NCI started the first session, *Quadrennial Review - How you can be outstanding in your next Quad Review.* They did an excellent job in covering the details of the Quadrennial Review Process from start to finish. Of note, Dr. Masison informed us of the addition of a yearly quadrennial review informational session targeted to PIs. Both Ms. Rodriguez and Dr. Masison stressed the importance of a well-written PI letter that covers all the points in the quad review checklist. In this session, for the first time, we included the perspective of someone who is on the quad review panel, David Roberts, Ph.D., Senior Investigator, Laboratory of Pathology, Head, Biochemical Pathology Section. Dr. Roberts has served on this panel for many years and is the Chair of the Promotion Review Panel. He gave us an interesting perspective of the process and emphasized that a well put together Quad Review package helps the reviewers determine the contributions of the Staff Scientist to their Lab's/Branch's research program, the NCI and the larger scientific community. The session ended with a Q&A panel with the speakers, as well as Dr. Misteli. When asked, Dr. Misteli said that SSSC need to take responsibility for their quad review process and get involved early in the process. An interesting point was brought up from the audience regarding the lack of an appeal process of the quad review outcome. Drs. Misteli and Masison both stated that an appeal process that resulted in a

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Pictured from left to right are the panel on *Quadrennial Review*: Rena Rodriguez, Cynthia Masison, Ph.D., David Roberts, Ph.D., and Tom Misteli, Ph.D.

Pictured from left to right are the panel on *Detailing*: Karyl Swartz, Ph.D., Ofelia Olivero, Ph.D., Michael Difilippantonio, Ph.D., and Chris Corey.

change of the quad review score would prove difficult due to the heterogeneity of the SSSC population and the inability to recapture the reviewer discussions in the context of the entire review. However, SSSCs were assured that appeals are taken into consideration for Staff Scientist renewals and the quad review-associated salary increase. The resounding take-home message from all panelists in this session was "get involved" – give input early and through the process to your PI about the memo that needs to be written, get involved in the package that is prepared for your review and get involved in the scientific community, whether it be in SSSC or other committees – step forward and make a contribution!

The next session tackled, *Detailing: Broaden your expertise and boost your CV.* This session started with Mr. Chris Corey, Director, CCR Administrative Resource Center, defining detailing as it pertains to SSSC. He explained to us the CCR placement process for SSSC from labs that have closed (for a variety of reasons). It was very encouraging to hear the individual attention that SSSC receive in being placed in a new lab that is a good fit for both the SSSC and the PI. Karyl Swartz, Ph.D., Associate Director for Diversity and Workforce Development, introduced us to another form of detailing involving a Training Program at the Center for Scientific Review. This program is open to SSSC with permission from their PI that may lead to a new career path. Links to details of this program can be found on the SSSC website. We then had a personal account of transitioning through a detail by Michael Difilippantonio, Ph.D., Program Manager for Therapeutic and Diagnostic Initiatives. He gave some keen insights on how to make a transition from being a Staff Scientist at the bench to a new position away from the bench, by successfully pursuing a detail. The big take away was that you are ready for change when you begin thinking about thinking about thinking of making a change! Thank you, Michael! At last year's session, some of you may remember, Ofelia Olivero, Ph.D., Chief, Intramural Diversity Workforce Branch, Center for Cancer Training, NCI, had left us with a cliffhanger of new career development program for the SSSC saying that there was more to come in the coming months. Well Dr. Olivero delivered. She laid out details of a new *NCI-SSSC Career Enrichment Program* that will be shortly available to us. The program promises to be helpful for those seeking to improve their experiential qualifications as well as those who are on looking for alternative career paths. Sign me up!

After a much-needed break for lunch, the afternoon session, *Science and Innovation,* looked at innovation in industry, here at NIH – in the lab and at the bedside. Herren Wu, Ph.D., SVP, Chief Technology Officer, Global Head of Antibody Discovery and Protein Engineering, MedImmune/AstraZeneca, gave us a detailed look at the innovative approach that Medimmune takes to drug development. We next heard from Christopher P. Austin, M.D., Director of the National Center for the Advancement of Translational Sciences (NCATS). It was very exciting to learn how NCATS is driving the fast pace of translational innovation here at the NIH. Next, we heard from Jennifer Kanakry, M.D., Clinical Head of Transplant, Experimental and Transplantation and Immunology Branch (ETIB), and her experience of how innovation is driven by continuous recognition of patterns, learn-

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-ing from failures in the clinic and feedback from the lab.

We ended the day with a workshop on *Managing Innovation,* by Mahesh Joshi, Ph.D., George Mason University, Associate Professor, Global Strategy and Entrepreneurship, Director of Research & Practice, Center for Innovation & Entrepreneurship. To say that this session was stimulating is an understatement. Dr. Joshi made us laugh, made us uncomfortable, but most of all he made us think. We are all capable of small innovations, but game-changing innovations take more than just a brilliant idea.

This Training Day provided information relevant to the career development of the Staff Scientist and Staff Clinician. Slides from the various presentations have been made available on the website: https://ccrod.cancer.gov/confluence/display/CCRSSSCArchive/Home

Thank you for attending this meeting and with your continued support we will bring you programs that promote professional development.

Pictured from left to right are the panel on *Science and Innovation:* Christopher P. Austin, M.D., Herren Wu, Ph.D., and Jennifer Kanakry, M.D.

Swati Choksi, Ph.D. (SS)
Head, Professional Development Committee

Lakshmi Balagopalan, Ph.D. (SS)
Bethesda SS Vice Co-Chair

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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.

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