



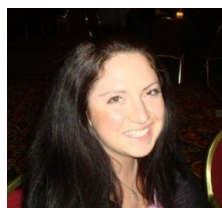
FELLOWS & YOUNG INVESTIGATORS NEWSLETTER

Volume 13 Issue 2 June 2013



From the Editor's Desk

Welcome to the Summer edition of the Fellows and Young Investigators Newsletter. So far, this year has been packed with events, including the 13th Annual FYI Colloquium held in March, reflected in this issue, as well as the Spring Research Festival. We highlight the events that took place at the 2013 Annual Colloquium, including a spotlight on the International Workshop. As in the past issues, we continue to bring you Conference Highlights from around the country and the world that our fellows have attended and graciously highlighted for your reading interest. Additionally, in this issue you will find a reflection on the "VFC Science Voices from Home" event about the Wellcome Trust/DBT India alliance funding opportunities. For those who are interested in postdoctoral life elsewhere, you will find an article about the postdoctoral life of Dr. Shruti Sharma in École Polytechnique Fédérale de Lausanne (EPFL), in Switzerland. Finally, we bring you a CCR Research Highlight on the work of Dr. Kuppusamy Balamurugan from Dr. Sterneck's group, recently published in Nature Communications. Please contact us if you are interested in contributing to the CCR-FYI Newsletter and enjoy reading what we have prepared for you in this issue!



Majda Haznadar, PhD

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IF YOU HAVE ANY COMMENTS, SUGGESTIONS OR WOULD LIKE TO CONTRIBUTE TO FUTURE NEWSLETTERS, PLEASE EMAIL US AT nciccrfyi@mail.nih.gov, or majda.haznadar@nih.gov

CCR-FYI News

CCR-Fellows and Young Investigators (CCR-FYI) Annual Colloquium Highlights

CCR-Fellows and Young Investigators (CCR-FYI) Colloquium is a meeting that has something to offer to everyone including investigators, postdoctoral fellows, post baccalaureate and graduate students. It is designed to meet the scientific training needs of fellows and gives an opportunity for close networking with successful intramural and extramural scientists. This year's colloquium was held on March 25th-26th, 2013 at the Advanced Technology Research Facility (ATRF) in Frederick, MD and was attended by more than 200 researchers.

Like in previous years, the Colloquium planning did an excellent job in organizing the event. However, unlike previous years, the first day kicked off by a snowstorm early in the morning. There was a two-hour delayed opening of the venue that triggered a last minute adjustment(s) to the day's schedule by the committee.

Co-chairs of the colloquium subcommittee, Dr. Vijay Walia and Dr. Barbara Rath opened the stage by welcoming the attendees and inviting Dr. Jonathan Wiest, Director for Training and Education, Center for Cancer Research at the NCI for the opening remarks. An overview of the FYI activities was provided by the Co-Chairs, Dr. Majda Haznadar and Mr. John Simmons. This was followed by valuable words by Dr. Robert Wiltrout, who encouraged all post-doctoral fellows to form a mentoring committee and to devise a plan early on in their career.

The highlights of the first day included a talk by the invited keynote speaker, Dr. Saraswati Sukumar, co-director of the Sidney Kimmel Comprehensive Cancer center at Johns Hopkins University. Dr. Sukumar talked about the pivotal role of the transcription factor, HOXB1, in breast cancer. The next events included concurrent oral

presentations by selected postdocs and postbacs and concurrent workshops. The workshop entitled, "Transition to Academia" was the most attended workshop on the first day. The cancer survivorship presentation by Ms. Noreen Fraser touched the audience's hearts and left everyone with tears in their eyes. Her story of struggle with stage IV metastatic breast cancer is an inspiration to continue the fight against cancer. Dr. Michael Gottesman delivered the second keynote

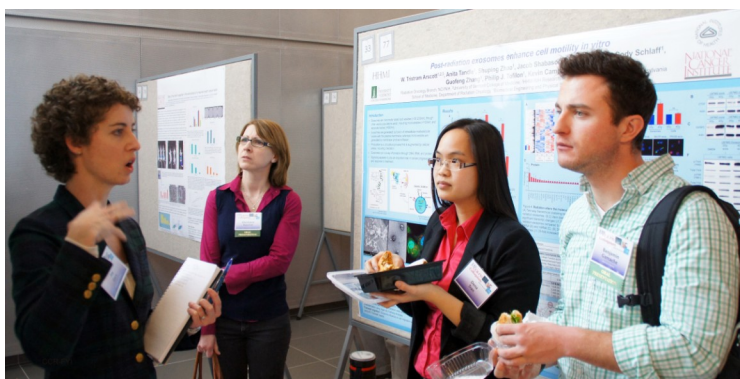
address, entitled "New Approaches to Drug Resistance in Cancer". The first day concluded with a social hour at Brewer's Alley restaurant. This was a wonderful opportunity to interact with workshop panelists and speakers, learn from them and get detailed insight into their work lives. Overall,

the day went smoothly with something interesting for all present, and it was well attended.

The second day began with the second poster session followed by a keynote presentation by Dr. Pamela Ohashi. Dr. Ohashi talked about the regulation of CD8 immunity. She is a professor at the Department of Immunology at the University of Toronto. Dr. Ohashi's talk was concluded with an announcement of two vacancies for academic investigators at her institution. In addition, the career fair organized by the colloquium planning committee provided an opportunity for additional networking and investigating current job opportunities. Numerous companies, including MedImmune, participated in this event and drew many attendees.

The keynote speaker for the afternoon session was Dr. Deborah Morrison, Chief of the Laboratory of Cell and Developmental Signaling at the NCI. She talked about Raf kinase signaling in normal and disease states, a topic emphasized

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CCR-FYI Colloquium attendees discuss research at the poster session held the first day of the event.

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Drs. Wiltrout and Wiest in the audience on the first day of the Colloquium.

in cancer biology. This was followed by concurrent workshops with the “Science Culture in Industry” workshop being the most attended. Dr. Brid Ryan, recipient of the Outstanding Post-Doctoral Fellow award gave the final keynote talk on “An Integrative and Translational Approach to Lung Cancer Research”. The winners for travel awards were announced and presented with certificates by Dr. Jonathan Wiest in the concluding session. The winners for the outstanding oral presentations were Jason Horton of the Radiation Oncology Branch, Christiane Kuschal of the Dermatology Branch, Bruce Huang of the Laboratory of Tumor Immunology and Biology and Christopher Switzer of the Radiation Biology Branch. The outstanding poster presentation winners were Minggian Feng of the Laboratory of Molecular Biology, Yeong Sang Kim of the Chemical Biology Laboratory, Ina O’Carroll and Steven Smith of the

HIV drug Resistance Program. The Outstanding Post-Graduate Trainee award was presented to Adrienne Long of the Pediatric Oncology Branch.

Overall, the CCR-FYI Colloquium provides an excellent opportunity for CCR trainees to present their research, gain experience in judging science, and an overall learning and networking opportunity with peers and outstanding keynote lecturers. Keep an eye on our next announcement at the end of this year for the 2014 Colloquium. An old saying in *Sanskrit* that scientific learning increases exponentially by sharing your discoveries and thoughts with others held true at this year’s FYI Colloquium.



The 2013 Colloquium Planning Subcommittee (from left): Kimberly Boelte, Leigh Great-house, Ravikiran Yedidi, Smita Kakar, Vijay Walia, Ravindra Veeranna, Barbara Rath, Jacqueline Salotti, Ishminder Mann, Julie Heinecke, Jessie Kiu, Fanching Lin.

Submitted by:
Smita Kakar, PhD
Biomolecular Structure Section
Macromolecular Crystallography Laboratory

The “International Opportunities” Workshop at the 2013 CCR-FYI Annual Colloquium

The “International Opportunities” workshop led by Ravi Yedidi and Cristina Rangel was designed to highlight the opportunities for postdoctoral fellows during their career transition in the US and abroad. The workshop consisted of three panelists: Mr. Candelario Zapata, Director of the Division of International Services (DIS) at the NIH, Mr. Kevin Bialy of Fogarty International Center, NIH, and Dr. Shawn Mullen, Deputy Director for post-doctoral services, Office of Intramural Training and Education (OITE), NIH.

The workshop began with a discussion regarding visa issues for foreign nationals working

green card.

Following the discussion on visa issues, the workshop focused on funding opportunities in the US as well as abroad. Mr. Bialy discussed Fogarty funding mechanisms to foreign institutions or funding opportunities for U.S. institutions with a foreign collaboration(s). He mentioned that the low and middle-income countries (based on the World Bank classification) are targeted through a collaborative mechanism such as the Global Infectious Disease (GID) Research Training Program. While answering a question about the discontinuation of the Global Research Initiative Program



From left: Mr. Zapata, Mr. Bialy and Dr. Mullen speak about issues facing foreign nationals and strategies for career transitions in the country and abroad.

at the NIH. Mr. Zapata discussed fellows’ legal obligations, such as maintaining lawful status, planning things ahead of time to avoid any break in the legal status in the US, and other issues that the international fellows may face. During the discussion regarding green cards (permanent residency), Mr. Zapata talked about the employment-based immigration procedures, such as the Permanent Labor Certification Program (PERM) and the non-employment-based immigration procedures, such as the outstanding-researcher, as options for obtaining a permanent residency in the US. While addressing a question about the number of peer-reviewed publications required for one to qualify for a green card application based on the extraordinary/outstanding-researcher, Mr. Zapata stated that a higher number of publications with fewer citations might be equivalent to fewer publications with a higher number of citations. He also clarified that the number of publications is just one of the several criteria that the U.S. Citizenship and Immigration Services (USCIS) utilizes to assess the overall qualifications of the applicant for a

(GRIP), Mr. Bialy said that the Fogarty is currently looking into a new program for fellows. He described in detail the NIH-Brazil collaboration designed to train Brazilian postdocs with potential seed-funding upon their return to Brazil. Mr. Bialy concluded his discussion by highlighting a few recent achievements such as the NIH-Colombia Grant Writing and Scientific Peer Review Workshop, loaning NIH surplus equipment to Chilean universities affected by a tsunami and loaning portable ultrasound machines to aid cholera diagnosis in Haiti.

The workshop concluded with a short discussion by Dr. Mullen on how to prepare for a career transition. He particularly insisted on the importance of networking in the context of a job search, whether looking for jobs in the U.S. or abroad. He stressed that while planning for jobs abroad, one should also consider potential visa issues, which might be time consuming. Followed by his presentation, Dr. Mullen showed a video of four former NIH fellows that made successful tran-

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sitions in the U.S. and abroad (Singapore, India and Canada), that highlighted the key points important for a successful transition based on their own experiences. The video depicted the real scenario that one has to go through during a career transition. Overall, the workshop was well attended and received.

Submitted by:
Ravikiran S. Yedidi, PhD
Experimental Retrovirology Section
HIV and AIDS Malignancy Branch



NCI Center for Cancer Research
Fellows & Young Investigators



What is the CCR-FYI?

The NCI CCR Fellows and Young Investigators (CCR-FYI) Association was organized to foster the professional advancement of young scientists at the CCR and is supported by the NCI CCR Office of Training and Education (OTE).

Who can participate?

All young investigators including postdocs, postbacs, graduate students, research fellows, clinical fellows, technicians, and staff scientists.

Articles

2013 Spring Research Festival

The 17th Annual Spring Research Festival, which showcases the scientific research carried out on the Fort Detrick campus, was held on May 8th-9th. This was the first year that the Festival was sponsored by The National Interagency Confederation for Biological Research (NICBR). The main location for festival events took place in large tents along Porter Street, behind the Odom Fitness Center.

Festival week kicked off with the annual postdoctoral/post-baccalaureate symposium. The theme of this year's talks was "Host Response to Disease". The talks given by 17 fellows from various agencies on the Fort Detrick campus were of very high quality. Six individuals were selected for awards. Best speakers among the postbacs were Katie Stagliano and Shakir Saud, both from NCI. Best speakers among the postdocs were Mandy Kendrick, USDA; Mairi McLean, NCI; Janani Varadarajan, NCI; and John Trefry, USAMRIID.

Poster presentations given by scientific staff of all levels from organizations such as NCI, FDA, and USDA were featured on both days. The festival also included the Commercial Science and Technology Expo, which provided an opportunity for hands-on demonstrations of the latest in equipment, services, and technology presented by major national and regional vendors from biomedical/biotech industries. The Health Education and Community Services Exhibition had a number of booths from a wide range of national and local health-related organizations as well as safety and scientific exhibits. Information on relevant health issues such as cancer, AIDS, mental health issues, fitness, and aging were available at these booths.

Each year, the theme of the Spring Research Festival is chosen from a natural product that is being used in research. This year the selected theme was the fungus-growing ant, an extraordinary insect with potentially beneficial health implications. The fungus-growing ant is a species that engages in mutualistic interactions with naturally occurring fungi. In some species, the ants and fungi are dependent on one another for survival. The molecular make-up of the antibiotics that are created through these mutualistic associations is shared with a well-researched group of antitumor agents. In addition to antitumor agents, research in biochemistry and metagenomics on the ant microbiome has also started to discover new antifungal agents. Researchers at NCI and Frederick National Laboratory for Cancer Research are investigating the molecular pathways to identify new leads for antitumor drugs to be used in cancer treatment.



Miranda Hanson, PhD

*Submitted by:
Miranda Hanson, PhD
Laboratory of Molecular Immunoregulation
Cancer and Inflammation Program*



Conference Highlights of Winter/Spring 2013

2013 Annual AACR Meeting

More than 18,000 researchers from around the world attended the American Association for Cancer Research (AACR) Annual Meeting 2013 which was held from April 6th-10th at the Walter E. Washington Convention Center in Washington, DC. AACR announced Charles L. Sawyers, M.D., as the president of the organization for 2013-2014. The meeting once again highlighted the latest and most exciting discoveries in the field of cancer. Over 6000 posters and many oral presentations covered all aspects of cancer research. The theme for this year's meeting was "Personalizing Cancer Care through Discovery Science". Plenary sessions, concurrent symposia, forums, educational sessions, methods workshops, poster presentations, conversations with experts and a career fair, promised the attendees a wealth of new information, inspiration and focus in their work. A wide array of companies displayed their latest products and services for laboratory and clinical research at the Exhibit Show. Being at the AACR



Khyati Kapoor, PhD

Annual Meeting for the first time was truly overwhelming but indeed a great pleasure. My focus was particularly the sessions discussing drug resistance in cancer. An excellent plenary session on "Cancer Evolution and Resistance" highlighted the fact that the heterogeneity in resistant clones within individual patients may pose additional challenges to overcome drug resistance. The mobile app for the meeting made it very convenient to browse and search sessions and presenters. Another highlight of this meeting was "Rally for Medical Research" on April 8, which united cancer researchers from all parts of the world to make life-saving medical research funding a national priority. Overall, this meeting is very significant for any cancer researcher and provides great network opportunities.

*Submitted by:
Khyati Kapoor, PhD
Laboratory of Cell Biology
Transport Biochemistry Section*

Keystone Symposia: Metabolic Control of Inflammation and Immunity

From January 21st-26th, I attended a Keystone Symposia Conference titled Metabolic Control of Inflammation and Immunity in Breckenridge, CO. World-renowned immunologists, biologists, and biochemists such as Richard Flavell, Charles Dinarello, and Michael Karin gave excellent presentations on their current research interests. This year, there was a heavy emphasis on how the inflammasome shapes immunity and inflammation in various pathologies including diabetes mellitus, cancer, and inflammatory bowel disease. One aspect of the conference I really enjoyed was that there were no concurrent presentations. Thus, I was able to see every presentation and didn't have to worry about missing



Walt Baseler and his PI Daniel McVicar at the Keystone Symposia in Breckenridge, CO.

a specific talk due to overlapping schedules that occur at larger conferences. Poster presentations were in the same area as dinner, so registrants could eat and then easily make their way to the 40 or so posters being presented that night. Keystone conferences are also interesting because they give you a break in the middle of the day before resuming in the evening, instead of running straight through from morning to afternoon. In Breckenridge, registrants were able to participate in many outdoor activities during their free time. Overall, I thoroughly enjoyed my time at the Keystone conference and would recommend it if there is a symposium topic close to your research interests.

*Submitted by:
Walt Baseler, PhD
Laboratory of Experimental Immunology
Cancer and Inflammation Program*

2013 American Society for Biochemistry and Molecular Biology Annual Meeting

This was the first time I attended the American Society for Biochemistry and Molecular Biology (ASBMB) annual meeting held at the Boston Convention and Exhibition Center in Boston, MA, from April 20th-24th, and was awed by the magnitude of this meeting. This is by far the biggest meeting I have attended! The ASBMB meeting was held as part of the 2013 Experimental Biology meeting, which brings together annual meetings of six different scientific societies, including ASBMB, whose focus area includes pathology, anatomy, nutrition, physiology, and experimental therapeutics. There were tens of thousands of registered participants who comprised of post-docs, graduate students, and undergraduates. Having won a travel award to present my work at the meeting, I was required to attend the pre-meeting special program for the travel awardees, and also present my poster to the other travel awardees.

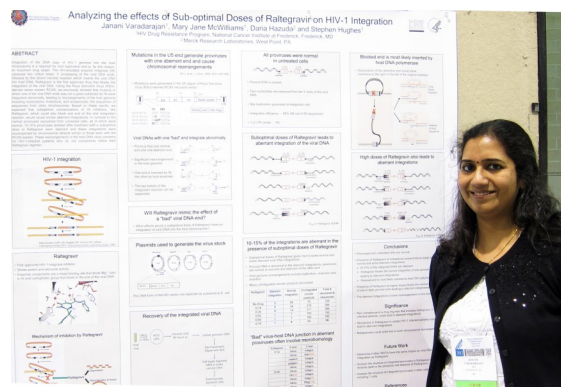
The highlight of this special program was the Graduate/Postdoctoral Professional Development program where an entire day was devoted to helping the graduate student/postdoctoral travel award winners take advantage of the informative career development workshops and networking luncheon with the speakers from different workshops.

The meeting opened to the general participants with two keynote lectures focusing on the contribution of chaperones in protein folding, which was then followed by a networking reception that encouraged networking with fellow participants.

The five day meeting was filled with numerous daily events, including plenary and special award lectures, concurrent symposiums, and career development workshops designed specifically to help attendees meet the experts in various scientific career paths, and explore the different career options available to them. Not surprisingly, there were also many hundreds of posters on display daily in the huge exhibit hall of the Convention Center, which further gave me the opportunity to learn about the interesting work of some of the fellow participants. I also got to present my poster for the second time, this time to all the participants. My work was well-appreciated and I received very good feedback both times I presented my poster during the meeting. Additionally, there were hundreds of exhibitors from various biotech

companies, medical institutes, scientific societies, and universities show casing their products and latest technologies. There were also a few universities and other non-profit medical institutes that were advertising for available positions in their institute.

Finally, the organizers surely did not forget about the lighter and fun side of such conferences – the social events! The day-long informative sessions and workshops were followed by social and networking receptions in the evenings like the Welcome Networking Mixer hosted by the ASBMB Minority Affairs Committee, ASBMB Women Scientists Networking event and the Young Scientists Dance Party! Overall, I found the meeting to be useful as well as enjoyable! I am happy to have been able to make new connections and expand my network through this meeting. Though I was overwhelmed by the number of activities that were occurring simultaneously, the best part about this meeting is that I could attend any workshop or special event hosted by any of the six societies participating in this meeting! I would highly recommend this meeting for all the trainees at the NCI.



Jan Varadarajan at the American Society for Biochemistry and Molecular Biology Annual Meeting in Boston, MA, presenting her poster.

Submitted by:
Janani Varadarajan
Retroviral Replication Laboratory
HIV DRP Host-Virus Interaction Branch

The Cell Symposia – Microbiome and Host Health, Lisbon, Portugal

Microbiome and Host Health Symposium was held from May 12th-14th. The conference brought together leaders in the field of microbiome research, which has exploded since the U.S. NIH funded Human Microbiome Project and the European Commission funded MetaHIT project, which first began more than five years ago. One major reason for this rise in microbiome research has been the significantly reduced cost of sequencing of microbes along with the development of relatively user friendly alignment tools such as mothur, qiime and clovr, which has opened access for almost any lab.

One of the foremost leaders in microbiome research, Dr. Rob Knight, who pioneered the development of such tools as UniFrac, which measures bacterial diversity between groups, as well as qiime, kicked off the meeting. He presented a menagerie of his current work ranging from a crowd source funded American Gut project, which anyone with \$50 can have their gut microbes sequenced, to the novel concept of "PATRIC" pathogens - in which a pathogen leaves one person debilitated yet another person unharmed. While most of the work of Dr. Knight's lab uses 16S rRNA sequencing to identify the taxonomic profile of each sample, another type of sequencing is on the rise - shotgun metagenomics.

Leading the way in this field is Peer Bork (EMBL, Germany), who leads a formidable team of bioinformaticians that have created multiple tools for analysis. However, this tsunami of data comes at a steep price of about \$800/sample, as compared to \$26/sample for 16S (MiSeq), though you get not only taxonomy but also the bacterial genomes, as long as you have the computational expertise to extract the information. His lab has also designed a similar user interface called "my microbes", which was designed to give the individual providing the sample disease prediction (~6 diseases) and risk of antibiotic resistance. Among his many interests include the colon cancer microbiome. Applying his metagenomic sequencing talents to 124 samples, including samples along the complete continuum of colon cancer, he has been able to demonstrate a specificity/sensitivity of 83% when using the microbiome as input.

Other highlights included a talk from Eihanan Borenstein (U of Wash), who introduced the idea of "super-metabolism" in which he describes how microbe A secretes metabolite X

which microbe B uses to grow. In addition, famous virologist, Skip Virgin, described how chronic viral infection changes gene expression in an organ-specific manner, such that virus + gene(mut) --> phenome and Crohn's disease, where as gene (mut) alone --> colitis. Also, a short talk from Philippe Cabriero (Univ College London) described the highlights of his recent Nature paper, in which he demonstrated the life extending mechanisms of metformin in *C.elegans*. Metformin alters folate metabolism and restricts methionine in bacteria of the *C.elegans*, conferring increased longevity.

The two major concepts the audience was left with for future microbiome studies were 1) the importance of genotype in controlling the host microbiome community response and structure, and 2) the importance of combining 'omics' with microbiome (blood, stool, tissue) to build better prediction tools for the clinic and functional discovery.



Leigh Greathouse, PhD

Submitted by:
K. Leigh Greathouse, PhD
Laboratory of Human Carcinogenesis

The Fifth International Meeting on the Role of Nitrite and Nitrate in Physiology, Pathophysiology, and Therapeutics Highlights

The Fifth International Meeting on the Role of Nitrite and Nitrate in Physiology, Pathophysiology, and Therapeutics was held on May 4th-5th in Pittsburgh, PA and was attended by over 150 scientists. This meeting highlighted the diverse roles of nitrogen oxides, which have been established to be major regulators of multiple biological processes. Nitrate has long been thought of as a carcinogen. However, recent work, by many scientists at this meeting, shows that increasing dietary nitrate consumption has beneficial effects. Nitrate is present in high concentrations in beets and leafy vegetables and once ingested, it is reduced by bacteria in the mouth and the gut to generate nitrite. Nitrite is then reduced in the body to nitric oxide, and it is these two small molecules that are associated with the bioactivity of nitrogen oxides. This meeting was interesting for me because I am currently a postdoc in David Wink's lab where we are trying to understand the signaling pathways of nitric oxide in cancer.

Amrita Ahluwalia, Nicholas Khoo, Eddie Weitzberg, and Naomi Cermak showed that the nitrate in beetroot juice was responsible for decreased hypertension and increased exercise performance in humans. It was found to regulate gastric mucus formation and help with metabolic syndrome related to obesity. There were also multiple talks on endogenous and therapeutic doses of nitrite, as it too has many beneficial effects. Exciting work by Shruti Shiva and Michael Frenneaux demonstrated that nitrite could decrease myocardial infarct size, in response to ischemia reperfusion injury, and has the potential to be used in transplants and heart attacks. Hunter Champion showed that inhaled nitrite could decrease pulmonary arterial hypertension in a clinical trial and Alan Schechter, who is a PI in NIDDK, gave a great presentation on the use of nitrite in platelet aggregation.



Julie Heinecke, PhD

I also really enjoyed the chemistry talks, which is not surprising as I was trained as a chemist. Marcus Knipp, Peter Ford (my former Ph.D. advisor), and Doug Thomas all gave great presentations on some possible mechanisms for biological nitrite activation. There were over 75 posters at the conference, and their diversity really showed how the fields encompassing nitrite/nitrate/nitric oxide have grown. It is clear to me that this area is proving to be very important for understanding normal biological regulation as well as advancing therapeutics, and I look forward to hearing about the future work surrounding these important bioactive small molecules.

*Submitted by:
Julie Heinecke, PhD
Radiation Biology Branch*

To all CCR trainees

Did you know that the CCR Office of Training & Education:

- Assists trainees and mentors with mentoring issues
- Assists in submitting applications for various funding mechanisms
- Provides opportunities for expanding collaborative interactions
 - Assists trainees in the transition to different career paths
 - Provides numerous courses
 - And much more!

CCR Office of Training & Education

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VFC Science Voices From Home: Wellcome Trust/ Department of Biotechnology India Alliance

The Visiting Fellows Committee (VFC), a sub-committee of FelCom, in collaboration with Fogarty International Center (FIC), Office of Intramural Training and Education (OITE) and NIH-INDIA (Association of Indian fellows at NIH) organized Science Voices from Home (SVH) on May 13th. This event focused on funding opportunities in India, with a guest speaker Dr. Shahid Jameel, the newly appointed C.E.O. of Wellcome trust/Department of Biotechnology (DBT) India Alliance. Dr. Jameel is a senior scientist and leader of a Virology group at the International Centre for Genetic Engineering and Biotechnology (ICGEB) in India. This event was well attended by more than 60 NIH fellows and investigators.

Dr. Jameel started his talk by highlighting the four types of funding mechanisms through this alliance: early career, intermediate, senior and margadarshi fellowships. He had noted the Wellcome/DBT India Alliance has £80 million allocated for the aforementioned fellowships in the next five years. He then elaborated on each individual funding mechanism. The early career fellowship is for applicants with 0-4 years of postdoc experience that requires a mentor in a host institute in India. This fellowship pays \$15,000 towards salary and ample research funds for 4 years with up to 2 years of training abroad in an international collaboration. The intermediate-level fellowship is for applicants with 4-7 years of postdoc experience, with a \$20,000 salary. The senior-level fellowship is targeted for applicants with 7-12 years of postdoc experience, with a \$30,000 salary. The margadarshi fellowship is for applicants with 10-years experience as an independent principal investigator. The intermediate, senior and margadarshi fellowships include ample research funds for 5 years. Dr. Jameel continued on to discuss that the same scheme applies to public health and clinical research for applicants with an MD degree.

Dr. Jameel, while discussing the details of the application process, mentioned that the committee makes the selections based on the applicant's track record and recommendation letters, host institute infrastructure and collaborators, and contents of the proposal (research question, hypothesis, novelty, feasibility, strengths and weaknesses, requested resources, etc.). He also said that the entire process takes between 6 to 8 months starting from the preliminary application to the final award. He mentioned that the applica-

tions are peer reviewed by scientists from across the globe and once granted, the award must be activated within one year of the approval date. Dr. Jameel re-emphasized that these fellowships are available for both citizens and non-citizens of India as long as the host institute is in India and is a non-profit organization.

Dr. Jameel concluded his discussion by showing some statistics related to the number of awardees from 2009 to date. He said that out of 93 total fellowships awarded to date, 80 were activated by the applicants, among which 28 were early career, 47 intermediate-level, and 17 senior-level and 1 Margadarshi fellowship. He said that the progress of awardees is assessed annually at the fellows meeting. For more details please contact: info@wellcomedbt.org or visit www.wellcomedbt.org. This event was followed by a traditional Indian lunch buffet sponsored by the IUSSTF (Indo-US Science and Technology Forum).



Dr. Shahid Jameel, C.E.O. of Wellcome Trust/
DBT India Alliance.

*Submitted by:
Ravikiran S. Yedidi, PhD
Experimental Retrovirology Section
HIV and AIDS Malignancy Branch*

Postdoctoral Life in Switzerland: Dr. Shruti Sharma

The NIH-INDIA group organized an informal talk on May 17th as a part of the 2013 NIH-INDIA seminar series. The speaker was Dr. Shruti Sharma, a peer-postdoctoral researcher from École Polytechnique Fédérale de Lausanne (EPFL), Switzerland. Dr. Sharma initially focused on her research projects and then gave an overview of research life in Switzerland from her own experiences.

With a Masters degree in Pharmaceutical Biotechnology from India, Dr. Sharma began her journey abroad for her doctoral studies in Switzerland. Chosen among the eight finalists, Dr. Sharma successfully started her doctoral studies in Dr. Andreas Mayer's lab at the University of Lausanne, Switzerland. "Lausanne is a beautiful place to live," Dr. Sharma said. She pointed out that initially the language barrier was challenging due to four official regional languages – German, French, Italian and Roman. She said that the predominant spoken language was regional but not English. Dr. Sharma said "My first year in Lausanne, being closer to the French border, I took French classes to navigate the city. Fortunately, at the University and now at EPFL, English is the main spoken language." She mentioned that everybody in the lab spoke basic English so it was easy for her to communicate with her colleagues. On the other hand, she also mentioned that once she learned basic French, she was able to connect with the city life.



Shruti Sharma, PhD

"As far as research goes, Switzerland is a rich country and science is well-funded," said Dr. Sharma while talking about the funding. She described that all doctoral students are fully funded by their advisors. She further explained that once a doctoral student becomes a post-doctoral researcher they are expected to write their own

grants. However, these grants are easily funded. She went on to say that a typical postdoctoral research fellowship is only for four years; approval from the principal investigator is required for further extension. She said, "Of course the extensions are based on the progress and performance in the first four years." Discussing collaborations within the institute or across the country, she said that it was easy to collaborate and complete interdisciplinary research in a timely manner. Given the size of the country, traveling across the country was not a problem for scientific collaborations.

While talking about a typical day, she said that everybody follows a similar, typical 9-5 schedule. She emphasized that the evenings and weekends are often spent with families/friends or personal life rather than long hours in the lab. Dr. Sharma highlights that, "One could always work long hours to get things done faster, but people try to maintain the work-life balance without getting stressed-out." Dr. Sharma concluded her talk by saying that she is interested more in teaching with a research component as her future career plan, whether it is in her home country, India, or abroad. She highly recommends Switzerland whether to work or to visit.

Please note that an extension of this article will appear in a future issue of the VFC Newsletter.

Submitted by:
Amie D. Moody, PhD
Systems Biology Group,
Laboratory of Pathology
&
Ravikiran S. Yedidi, PhD
Experimental Retrovirology Section
HIV and AIDS Malignancy Branch

CCR Research Highlight: CCR Research Highlight: FBXW7 protein acts as tumor suppressor and inflammatory pathway inhibitor

Toll-like receptors (TLRs) are largely responsible for inducing innate immune responses to infection. TLR4 binds lipopolysaccharide (LPS) from Gram-negative bacteria and begins a signaling cascade to activate inflammatory responses. TLR4 has been implicated in diseases such as sepsis and chronic inflammatory disorders. In tumor cells, TLR4 is involved in weakening immune surveillance, and increasing proliferation, inflammatory cytokine production, and invasive migration. Determining how TLR4 expression and signaling is regulated may enable these adverse conditions to be better managed.

Previous studies have shown that the transcription factor CCAAT/enhancer binding protein delta (C/EBP δ) increases LPS signaling and is needed for LPS-induced gene expression and the clearance of Gram-negative bacterial infection. Data from experiments performed in mice lacking C/EBP δ suggest that the gene may have a role in systemic inflammatory diseases such as sepsis and multiple sclerosis. Esta Sterneck, Ph.D., in CCR's Laboratory of Cell and Development Signaling, Kuppusamy Balamurugan, Ph.D., a Postdoctoral Fellow in her lab, and colleagues previously reported that C/EBP δ directly inhibits expression of the F-box and WD repeat domain containing protein 7 alpha (FBXW7 α) in mammary tumor cells. FBXW7 α is a tumor suppressor in solid cancers and targets several mammalian oncoproteins for degradation. The lab has also shown that hypoxia-induced C/EBP δ inhibits FBXW7 α , leading to an increase in mTOR, and the hypoxia-inducible factor 1 alpha (HIF-1 α).

Because C/EBP δ and HIF-1 were both known to be important for inflammatory signaling the researchers set out to test whether the C/EBP δ -FBXW7 α -HIF-1 pathway is involved in macrophage activation. Their data indicate that

macrophages express FBXW7 α and that this expression is downregulated by C/EBP δ and LPS. When FBXW7 α was removed, C/EBP δ and HIF-1 α expression increased, demonstrating that FBXW7 α suppresses C/EBP δ expression. In mouse macrophages lacking C/EBP δ , HIF-1 α accumulation was rescued by knockdown of the elevated FBXW7 α . These findings show that C/EBP δ promotes HIF-1 α expression in activated macrophages by inhibiting FBXW7 α expression.

The next step was to investigate FBXW7 α 's regulation of C/EBP δ expression. They found that FBXW7 α is required for ubiquitination and degradation of C/EBP δ , and that C/EBP δ binding to its own promoter increases when FBXW7 α is silenced. These results demonstrate a negative feedback loop from FBXW7 α to C/EBP δ . Further, the kinase GSK-3 β , which is responsible for the phosphorylation of most FBXW7 α substrates, was found to directly phosphorylate C/EBP δ , which led to a decrease in C/EBP δ levels in untreated macrophages. In activated macrophages, LPS was able to activate C/EBP δ expression partly by inhibition of the GSK-3 β /FBXW7 α pathway.

The researchers hypothesized that FBXW7 α may have an inhibitory role in pro-inflammatory signaling. They found that FBXW7 α suppressed all tested responses of macrophages to LPS, such as iNOS, C/EBP δ , and COX-2 levels. Suppression of LPS responses by FBXW7 α suggested that upstream factors in the LPS signaling pathway are downregulated by FBXW7 α . When FBXW7 α was silenced in macrophages, C/EBP δ depletion prevented TLR4 upregulation, indicating that FBXW7 α downregulates TLR4 through inhibition of C/EBP δ expression.

After finding that C/EBP δ acts upstream



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of LPS signaling by directly activating TLR4 gene expression, the researchers investigated whether C/EBP δ modifies TLR4 expression in tumor cells. Depleting C/EBP δ in a mouse mammary tumor cell line or in human breast tumor cells led to reduced TLR4 protein expression and increased FBXW7 α levels. In addition, many inflammatory markers were decreased in mammary tumors from C/EBP δ -deficient mice.

This paper identifies the tumor suppressor FBXW7 α as an important attenuator of inflammatory signaling and may provide a new mechanistic link between inflammation and tumor progression. Interestingly, the GSK-3 β enzyme, typically regarded as a pro-inflammatory agent, is implicated as an inhibitor of the inflammatory response. Drugs that inhibit GSK-3 β 's activity are being developed for diseases such as Alzheimer's, cancer, and diabetes. The anti-inflammatory role that is demonstrated in this work may complicate clinical application of such GSK-3 β inhibitors or could be exploited by manipulation of FBXW7 α expression.

Balamurugan K, Sharan S, Klarmann KD, Zhang Y, Coppola V, Summers GH, Roger T, Morrison DK, Keller JR, Sterneck E. FBXW7 α attenuates inflammatory signalling by downregulating C/EBP δ and its target gene Tlr4. *Nat Commun.* 2013 Apr 9.

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