

Office of Education
Division of Intramural Research

Fellows Newsletter

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Office of Education, DIR, NHLBI

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From the Director of the Office of Education

Thanksgiving is past us, and now we begin the Holiday Season. To celebrate, the NHLBI Office of Education is sponsoring a Holiday Cookie Bakeoff on December 16th. More information is provided on the last page of this newsletter, but the entry fee is either a plate of home-made cookies or a donation of \$1. Any proceeds will go to the Children's Inn, so please come and contribute.

Along with the Holidays, this season is also the beginning of the Stadtman Tenure Track interviews. As noted in the article below, the candidates invited to campus all have outstanding records, and so this provides an opportunity for Fellows to see what a real job talk is like.

Finally, we should all seek to help those in need in this Holiday Season by donating to the Combined Federal Campaign.

FEATURED ARTICLE

The Stadtman Searches and You

By: Herbert M. Geller, Ph.D.

Are you planning to apply for a faculty position? If so, you should take advantage of the Stadtman search process now underway which will bring over 80 candidates for Tenure Track positions to campus for interviews in December.

The Stadtman process, the major

way in which NIH recruits Tenure Track Investigators, involves a single call for applications each year. All applications are then reviewed by a group of field-specific committees which identify the top candidates who are invited for an on-campus interview. These committees are charged with identifying the most promising researchers, as well as those whose research is especially suited to NIH. The final

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Meet the New Fellows



Vicent Butera is a Post-Baccalaureate Fellow in the Hematology Branch under Dr. Adrian Wiestner. Vicent earned his BS

in Biology at Jackson State University. His initial project at NIH is studying drug resistance in lymphoma and developing immunotherapy for leukemia.



Dr. Teegan Dellibovi-Ragheb is an IRTA Fellow in the Cell Biology and Physiology Center under Dr. Nihal Altan-Bonnet.

Teegan earned her Ph.D. at Johns Hopkins University. Her initial project at NIH is comparing cell lines from different host species, including monkey, dog, bat and insect, to understand the differences and similarities in their response to infection with vesicular stomatitis virus.



Ezigbobiara Umejiego is a Post-Baccalaureate Fellow in the Systems Biology center under Dr. Mark Knepper. Ezigbobiara earned his BS in Biology at Kennesaw State University. His initial project at NIH is evaluating the effect of Roflumilast, an FDA-approved phosphodiesterase 4 inhibitor, in increasing water permeability within collecting duct cells in the kidney disease model of X-Linked Nephrogenic Diabetes Insipidus.



Sam Znati is a Post-Baccalaureate Fellow in the Biochemistry and Biophysics Center under Dr. Han Wen. Sam earned his BS in Chemistry at Northwestern University. His initial project at NIH is focused on the fabrication of silicon gratings for an X-Ray Phase Contrast imaging system.

THE SCIENCE BEAT by Robert Gahl

Vire B, Skarzynski M, Thomas JD, Nelson CG, David A, Aue G, Burke TR Jr., Rader C, Wiestner A "Harnessing the FcγR Receptor for Potent and Selective Cytotoxic Therapy of Chronic Lymphocytic Leukemia" Cancer Res. 2014 Oct 24. pii: canres.2030.2014

Chronic lymphocytic leukemia (CLL) is a common form of leukemia that causes an over-accumulation of mature monoclonal B cells in the blood, bone marrow, spleen, and lymph nodes. While there are treatments that show effective initial responses, most patients are susceptible to relapse. One factor that largely contributes to relapse is that current treatments target both healthy and malignant B cells. As a result, patients are more susceptible to infection and other complications. Dr. Adrian Wiestner and co-workers in the Hematology Branch here at NHLBI have demonstrated an effective delivery method for cytotoxic treatments for CLL that target only malignant B cells.

The key to incorporating specificity into their method was to take advantage of the fact that the FcγR receptor is over-expressed in CLL B cells compared to normal B cells. Therefore, their strategy was to design a scaffold for cytotoxic drugs to that can mimic the FcγR receptor so it will only target and subsequently destroy malignant cells. The architecture of the delivery system was modeled after the scaffold of the IgM receptor. The FcγR encoding sequence followed after repeats of C-terminal constant domains, C_μ, of human IgM. Capping the protein was a His6 repeat used for recombinant purification as well as a SECIS sequence that allowed for selective attachment of the cytotoxic payload. For this study, the selective cytotoxicity of the tubulin polymerization inhibitor monomethylauristatin F (MMAF) was determined. Both a conjugated form and freely-diffusing form of MMAF, MMAF-tBu, were examined.

Selective toxicity of MMAF was observed in a variety of assays. To determine the cytotoxicity of free and conjugated MMAF in vitro, the IC50 was measured for FcγR-positive and FcγR-negative MCL cell lines. When compared to the potency of MMAF-tBu, conjugated MMAF was 1000 times more potent towards FcγR-positive cells. Peripheral blood mononuclear cells (PMBC) were isolated from 30 patients and analyzed ex vivo. Conjugated and free MMAF was toxic to CLL B cells but normal T cells were only killed by free MMAF. In in vivo experiments, a 74% and 65% reduction in tumor burden in blood and spleen cells, respectively, was observed after conjugated MMAF treatment in a NDL/CLL xenograft model. The viability of normal T cells in this model was unaffected.

A functional scaffold and the right conjugation chemistry contributed to the successful selectivity of MMAF toxicity. By using site-specific labeling of MMAF, side-reactions of the drug to other catalytic sites on the scaffold are eliminated, thus preserving the recognition of the FcγR sequence. In fact, the circulatory half-life of the scaffold was similar to the half-life of human IgM, ~1 day. Also, by having a non-cleavable linker to conjugate MMAF, cytotoxicity only occurs after the anti-body degradation in the lysosome. The potency of the drug is not decreased by premature cleavage from the scaffold before it reaches its destination.

In conclusion, Wiestner et al. have demonstrated a delivery system to increase the specificity and potency of a cytotoxic drug. This is another successful application of antibody-drug conjugates (ADC). ADCs have only been utilized only for a couple of years and show tremendous promise in cancer therapeutics. This work lays the foundation for the development of future drug candidates and opportunities for treatments in translational medicine.

STADMAN SEARCHES

level of selection then takes place by the IC that has an open slot.

Each step of the process has its own requirements. The first is based upon the written record – C.V., statements of long term goals and a research plan, and letters of recommendation. Candidates invited for an interview are those with novel research areas and who have a high level of productivity. Because many fields are broad, and not every application is read by every committee member, successful applications are easy to read – career goals and research statements are clearly written and are not highly technical or full of jargon. While not all have publications in “high-impact” journals, there is a surprisingly high correlation between that and the ability to propose a captivating project. In addition, most have letters of reference from well-known scientists, not all of whom were their advisors.

Applicants selected by the committees are invited for an on-campus interview in December, at which time they present a research seminar. The formats of these seminars vary – some committees arrange for candidates to participate in a “Symposium” where they each get a 1 hour time slot, while others invite individual candidates one per day. The rest of their day is spent talking to PIs on campus. The seminar is perhaps the most critical part of the interview process. For NHLBI Fellows, attending these seminars can provide incredibly useful insights into both how to and, even more importantly, how not to present research. Many candidates make the canonical mistake of assuming that everyone in the audience is conversant with their field. Others try to oversimplify and thus do

not get across why their research is cutting edge. And some get it right. It is also useful to observe what kinds of questions get asked, and how they are answered. For example, sometimes I wish a candidate simply answered “That’s a good question, but I don’t know the answer”, rather than trying to work around the issue. A complete list of Stadtman seminars is here: <https://ccrod.cancer.gov/confluence/display/NIHStadt/Stadtman+Presentation+Schedule+2014+-+2015>

The day concludes with a dinner with some or all of the committee members and other interested PIs, and this provides insights into how you might find the person as a colleague, and also a chance for committee members to probe their breadth of knowledge. After all the interviews, the committee then rates each of the candidates as to whether they should be recommended to an IC for consideration or not. Candidates who are then identified by specific ICs for consideration are invited back to campus for a second interview, which invariably includes a “chalk talk” – a more informal session that explores future research and career goals. And then final decisions are made as to whether to make an offer of a position.

While the overall process is similar to that in academia – the criteria might be slightly different with less emphasis on grant-getting ability and more on breakthrough science – fellows would be wise to attend seminars to learn both about what kinds of science are considered “hot” and to see how job candidates are treated. Because it’s better to see this for the first time from the audience’s perspective than from the podium.

Meet the New Fellows



Dr. Robert Trachman is a IRTA Fellow in the Biochemistry and Biophysics Center under Dr. Adrian Ferre-D’Amare. Dr. Trachman earned his Ph.D. at Johns Hopkins University. His initial project at NIH is characterizing biologically important RNA molecules.



Dr. Randi Parks is a Visiting Fellow in the Systems Biology Center under Dr. Tish Murphy. Dr. Parks earned her Ph.D. at Dalhousie University. Her initial project at NIH is following up on studies using the mitochondrial calcium uniporter knockout mice, to determine how mitochondrial and cytosolic calcium handling are altered when the uniporter is removed.



Patricia Theard is a Post-Baccalaureate Fellow in the Cardio-Vascular Pulmonary Branch under Dr. Stewart Levine. Patricia earned her BS in Biology at Florida International University. Her initial project at NIH is identifying alternative biochemical pathways of respiratory inflammation and asthma.



Milad Emamian is a Post-Baccalaureate Fellow in the Systems Biology center under Dr. Mark Knepper. Milad earned his BS in Bioengineering, BA in Government and Politics and BA in Economics at the University of Maryland, College Park. His initial project at NIH is an investigation of the effects of vasopressin on ribosome levels in collecting duct cells of the kidney.

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QUESTION & ANSWER WITH AN INVESTIGATOR

Postdoc Kevin Ramkissoon interviews Dr. Rosa Puertollano, Senior Investigator, Protein Trafficking and Organelle Biology.



Dr. Rosa Puertollano is a Senior Investigator in the Cell Biology and Physiology Center. Dr. Puertollano's primary research interests are protein trafficking and organelle biology. Dr. Puertollano earned her Ph.D. in molecular biology and biochemistry from Consejo Superior de Investigaciones Cientificas and did her postdoctoral training from 1999 to 2004 in the Cell Biology and Metabolism Branch of the National Institute of Child Health and Human Development at the NIH. From 2001 to 2004 she was an NIH visiting fellow and subsequently became a tenure-track Investigator at the NHLBI.

When did you decide that you wanted to become a scientist?

My decision came relatively early – during my first year of high school. I was really fascinated by the study of Mendelian genetics, cell biology and the like. Initially I wanted to pursue an MD and conduct research, but after discussing my interests

with my mentors, I decided to pursue my PhD in molecular biology and biochemistry.

You first came to the NIH as a visiting fellow. Can you briefly describe your experience as a NIH fellow?

It was great. I came to the US from Madrid in 1999 and joined the Bonifacio lab in NICHD. I was amazed by the quality and work ethic of the postdocs, as well as the very high caliber of the research being done in Juan's lab; and the NIH by extension. I really enjoyed my time as a fellow and thrived in the dynamic environment that surrounded me.

What were the most challenging and/or rewarding aspects of doing a postdoc in a foreign country?

For me, doing a postdoc in the US didn't pose any "culture shock" so to speak, but language and communication did pose challenges. As a non-native speaker of any language, even if you understand 90% of a seminar, or a conversation in the lab, the 10% that you don't understand does create some anxiety. It took time and some effort to overcome this, but seeking out opportunities to present my research, in addition to everyday conversation with friends and colleagues, helped tremendously.

What do you enjoy most about the research environment here?

Interesting and unexpected results and questions arise all the time during research. I really enjoy the flexibility and freedom that I have as an NIH investigator to pursue new paths of investigation; which is made easier by having access a diverse array of scientific experts, cutting-edge equipment and techniques here at the NIH. I also appreciate that I am able to devote a lot of time to my research; in part thanks to the great core facilities we have access to but also because I am not constantly writing grants (or preparing for the next grant cycle).

What was/were the challenge(s) you encountered during your transition from postdoc to an independent investigator?

You have to learn to be patient and keep your eye on the long-term future. An individual project may succeed or fail but you have to keep focused on the bigger picture and ultimate goals of your research. As a postdoc, you design experiments and sometimes manage projects, but the time scale is different. Instead of thinking in 1 – 3 year increments, you now think on the order of 5 – 10 years. In addition, managing a group of

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QUESTION & ANSWER WITH A POST-DOC

Postdoc Agila Somasundaram interviews Dr. Kevin Ramkissoon, Postdoctoral Fellow in the NHLBI Systems Biology Center



What factors influenced your decision to come to the NIH?

My decision to come to the NIH was influenced by a combination of personal and professional factors. NIH is con-

sidered to be a great place to be a postdoc and do cutting-edge science, and had been on my radar since graduate school; but I didn't fully appreciate all the benefits until I got here. A hard-to-say-no-to industry position delayed my coming here a couple of years, but joining NIH was one of the best professional decisions I've made.

Could you briefly describe your current research?

I work in the laboratory of Dr. Maurice Burg in the NHLBI Systems Biology Center. Our lab is interested in studying os-

moregulation and the cellular response to osmotic stress. I employ molecular biology and quantitative proteomic techniques to elucidate the mechanisms underlying gene-regulation by the transcription factor nuclear factor of activated T-cells 5 (NFAT5), which plays a key role in regulating cellular response and adaptation to osmotic stress.

What are your short and long-term career goals?

My short-term career goal is to transition to a career in science and *Cont'd on page 5*

Q&A WITH AN INVESTIGATOR

people with different personalities so that they are at their most productive can be challenging for some, as can be mentoring and guiding the careers of fellows. It can be very rewarding but it's a huge responsibility.

You were recently awarded tenure (congratulations!). What advice would you give to fellows pursuing tenured positions at research-intensive institutions?

My advice is to be dedicated and diligent in your research, do your best to publish well, and network. It's important to develop a plan now for your future research career. Think about what you want to do; not just what your PI wants you to do. Start gathering the skills and building the collaborative networks you will need. It's not an easy path; it's important to stay motivated. Enjoying what you do will help to balance any stress. Things won't always go according to plan, but having a good one can make all the difference!

As an NHLBI investigator, one of your roles is mentoring the next generation of scientists. How would you describe your approach to mentoring fellows?

I've found that mentoring styles can be highly varied and depend

a lot on the personality of the PI, as well as the fellow. Generally speaking, I feel it's important that postdocs become independent. I try to be open and available but don't babysit my fellows or their experimental design. I believe this fosters the critical and analytical thinking skills they need to succeed as independent investigators, and helps build self-confidence in their scientific abilities.

Had you not chosen a path as a research scientist, what do you think would be your career today?

Realistically speaking, if I hadn't chosen to pursue a PhD research career, I would likely have stayed on the path to becoming a medical doctor; though I do think I would still have incorporated research into my job. My dream job however would have been one that allowed me to combine my love of photography and travel... maybe I'd be working for National Geographic.

What hobbies or activities do you enjoy away from the lab?

As mentioned before, I enjoy photography and traveling, but between my research and my family (I have a 5 year old at home) it's difficult to find the time for an active hobby. Luckily, I also enjoy reading and listening to music.

Q&A WITH A POST-DOC

technology policy where I can leverage my scientific training to shape the policies that guide scientific research and development, drive innovation, and help improve lives. I have strong interests in science communication and outreach, global health, and science diplomacy and envision that my long-term path will entail working with/for institutions that have impact in one or more of these areas.

What steps have you taken as a postdoc at the NIH towards achieving those goals?

A few months before I started at the NIH, I attended the annual NIH Career Symposium organized by OITE. This was such a good experience that I helped organize the following year's symposium. A few weeks after coming to the NIH, I was accepted into the NIH Science Policy Discussion Group (SPDG). A year later I was leading the group and networked extensively with science policy professionals at NIH and in the DC area. I also contributed to the NHLBI Fellows Newsletter, Visiting Fellows Newsletter, and NIH Catalyst, and participated in career and professional development seminars organized by the NHLBI Office of Education (OE) and OITE. Engagement with Dr. Geller in the OE early in my postdoc was an important step and ultimately led to a rotation in one of NIH's policy offices, where I am currently gaining practical experience in policy analysis and development.

Do you have any advice/suggestions for new and current fellows at the NHLBI?

NIH has a lot of resources for scientific and professional growth. The key is to identify and leverage the ones that fit your personal career goals and time. It's important to have a plan. Find mentors in your chosen field, meet with OE and OITE staff, explore the various Scientific Interest Groups on campus and in the MD/DC area, arrange informational interviews, and network. If a career in research is in your future, be diligent at the bench and publish well; but also attend seminars, present your research outside the NIH, build collaborative networks, and leverage grant writing opportunities here. If you're looking beyond the bench to science writing/editing, teaching, consulting, entrepreneurship, policy, etc., there are numerous resources at the NIH you can and should be using.

What hobbies or activities do you enjoy away from the lab?

I haven't had much time for hobbies recently, especially since I started pulling double duty in the office and lab, but the career building activities I have been focused on have proved both fun and fulfilling. That said, I am working on ramping up my hobbies again, particularly photography and travel. I also hope to get back into Latin/ballroom dance and learning Spanish.

RECENT PUBLICATIONS BY NHLBI FELLOWS

Amar, M. J., **Sakurai, T.**, Sakurai-Ikuta, A., Sviridov, D., Freeman, L., Ahsan, L., & Remaley, A. T. (2014). A Novel ApoC-II Mimetic Peptide that Activates LPL and Decreases Serum Triglycerides in ApoE-KO Mice. *J. Pharmacol. Exp. Ther.*

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Du, N., Kwon, H., Li, P., **West, E. E.**, Oh, J., Liao, W., Yu, Z., **Ren, M.**, & Leonard, W. J. (2014). EGR2 is critical for peripheral naive T-cell differentiation and the T-cell response to influenza. *Proc. Natl. Acad. Sci. U. S. A.* 111, 16484-16489.

Dumitriu, B., Feng, X., Townsley, D. M., **Ueda, Y.**, Yoshizato, T., Calado, R. T., Yang, Y., Wakabayashi, Y., Kajigaya, S., Ogawa, S., Zhu, J., & Young, N. S. (2014). Telomere attrition and candidate gene mutations preceding monosomy 7 in aplastic anemia. *Blood.*

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Jain, N. A., Ito, S., Tian, X., Kurlander, R., Battiwalla, M., Lu, K., **Savani, B. N.**, Malkovska, V., Rezvani, K., Le, R. Q., Shenoy, A., Hourigan, C. S., Keyvanfar,

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Stevens, L. A., Barbieri, J. T., Piszczek, G., **Otuonye, A. N.**, Levine, R. L., Zheng, G., & Moss, J. (2014). Nonenzymatic Conversion of ADP-Ribosylated Arginines to Ornithine Alters the Biological Activities of Human Neutrophil Peptide-1. *J. Immunol.* 1303068.

Vire, B., **Skarzynski, M.**, Thomas, J. D., Nelson, C. G., David, A., Aue, G., Burke, T. R., Jr., Rader, C., & Wiestner, A. (2014). Harnessing the Fc micro Receptor for Potent and Selective Cytotoxic Therapy of Chronic Lymphocytic Leukemia. *Cancer Res. canres.*

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Zadrozny, L. Z., Neufeld, E. B., **Lucotte, B. M.**, Connelly, P. S., Yu, Z. X., Dao, L., Hsu, L. Y., & Balaban, R. S. (2014). Study of the Development of the Mouse Thoracic Aorta Three-Dimensional Macromolecular Structure using Two-Photon Microscopy. *J. Histochem. Cytochem.* 0022155414559590

Meet the New Fellows



Hilary Koech is a Post-Baccalaureate Fellow in the Cell Biology and Physiology Center under Dr. Edward Korn. Hilary earned his BS in Biochemistry from the University of Maryland, College Park.



Devin Jackson is a Post-Baccalaureate Fellow in the Cell Biology and Physiology Center under Dr. John Hammer. Devin earned his BS in Human Biology at the University of Texas at Austin. His initial project at NIH is helping to understand the true role of Myosin 19.



Corinne Pittman is a Post-Baccalaureate Fellow in the Hematology Branch under Dr. Courtney Fitzhugh. Corinne earned her BA in Evolutionary Anthropology at Duke University. Her initial project at NIH is hydroxyurea dosing in patients who are homozygous for sick cell disease to monitor fetal Hb response.



Jessica Choi is a Post-Baccalaureate Fellow in the Genetics and Developmental Biology Center under Dr. Yosuke

Mukoyama.

NHLBI Holiday Cookie Bake-Off Party!

Tues., Dec. 16th from 3pm – 4pm, Bldg 10, FAES Terrace

Participate by bringing home made cookies OR \$1.

All participants can vote for the winner, who will receive a cash prize! Any excess contributions go to the Childrens Inn.

