

Office of Education
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Fellows Newsletter

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The Fellows Newsletter is published monthly by the Office of Education, Division of Intramural Research, National Heart, Lung, and Blood Institute and distributed to NHLBI DIR members to promote the interest of DIR Fellows.

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From the Director of the Office of Education

We hope you all had a great summer. The weather was nearly perfect, with very few of the hazy, hot and humid days that make the summer in DC less than enjoyable. We had a great crop of summer interns, most of whom presented their research at poster day. And we can now look forward to fall, which can be the nicest season of all in this area.

The Office of Education is planning a full set of activities for the coming year. If you would like to be part of this planning process, please join the Fellows Advisory Committee which meets monthly. We need all the input we can get!

See the box announcing the latest recipients of the Lenfant Fellowships. This is a prestigious award given to new NHLBI Fellows, with deadlines of April and October of each year. If you are an NHLBI fellow with less than two years experience, you are eligible to apply. See the announcement for more information about how to apply.



NHLBI 2014 Summer Students with Dr. Geller and Marie Cha

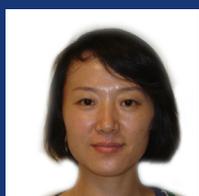
Meet the New Fellows



Dr. John Eicher is a new IRTA Fellow in the Cardiovascular Epidemiology and Human Genomics Branch under Dr. Andrew Johnson. Dr. Eicher earned his Ph.D. at Yale University. One of his initial projects at NIH is gene expression analysis of platelet cells derived from two different subtypes of myocardial infarction in order to determine whether there are differences.



Dr. Helena Mora-Jensen is a new IRTA Fellow in the Hematology Branch under Dr. Adrian Wiestner. Dr. Mora-Jensen earned her PhD at Copenhagen University. Her initial project at NIH is testing the effects of three drugs in the treatment of chronic lymphocytic leukemia, both as single agents and in combination with each other.



Dr. Xin Zhao is a new Visiting Fellow in the Hematology Branch under Dr. Neal Young. Dr. Zhao earned her M.D. at Peking Union Medical College. Her initial project at NIH is researching the mechanism of bone marrow failure.

THE SCIENCE BEAT by Zhiyun Ge, Ph.D.

Warner, K. D., Chen, M. C., Song, W., Strack, R. L., Thorn, A., Jaffrey, S. R., & Ferre-D'Amare, A. R. (2014). Structural basis for activity of highly efficient RNA mimics of green fluorescent protein. *Nat. Struct. Mol. Biol.* 21, 658-663.

The green fluorescent protein (GFP) was first isolated from the jellyfish *Aequorea victoria* and exhibits bright green fluorescence when exposed to light in the blue to ultraviolet range. GFP emits light at 509 nm, which is in the lower green portion of the visible spectrum. In cell and molecular biology, GFP is widely used for reporting gene expression and protein localization by fusing its gene to other protein encoding genes. Recently, a RNA aptamer was generated via in vitro-evolution and was described to bind fluorophores that resemble the fluorophore in GFP. The RNA-fluorophore complexes emit light that spans the entire visible spectrum. Among them is Spinach, a 97-nt RNA aptamer. When bound to DFHBI ((Z)-4-(3,5-difluoro-4-hydroxybenzylidene)-1,2-dimethyl-1H-imidazol-5(4H)-one), a small-molecule mimic of the GFP fluorophore but is not fluorescent in isolation, Spinach emits a green fluorescence comparable in brightness to GFP. These RNA mimics of GFP, when genetically encoded as fusions, enables us to perform live-cell, real-time imaging of biological RNAs directly. In this paper, Warner et al. aimed at revealing the mechanism of fluorescence activation of Spinach by deciphering the structural basis of Spinach's activity.

First, Warner et al. obtained the crystal structural of a Spinach-DFHBI complex at 2.8 Å by single-wavelength anomalous dispersion (SAD). In the crystal structure, Spinach folds into a single coaxial helical stack composed of three canonical A-form duplexes separated by two irregular junctions (J1-2 and J2-3). Further Small-angle X-ray scattering (SAXS) analyses on both free and DFHBI bound Spinach revealed that Spinach is largely prefolded in the absence of chromophore. The structure also revealed unambiguously that DFHBI binds the core of J2-3 described above, which is a three-tetrad quadruplex, composed of two G-quartets stacked above a mixed-sequence tetrad and is stabilized by two K⁺ ions. The Spinach chromophore is sandwiched between G25 and G65 of the top G-quartet and the Hoogsteen-paired U61 and A64 of the base triple of J2-3. The imidazolone and phenyl rings of the chromophore are aligned on the same plane and form highly intricate interaction networks with the Spinach RNA.

An unexpected observation the authors made from the crystal structure of the Spinach-DFHBI complex is that, despite the lack of any canonical G-quadruplex sequence motifs, Spinach possesses a G-quadruplex formed by G residues distant in sequence and is of an unprecedented non-parallel folding topology. Half of the Gs in the quadruplex is non-consecutive, resulting in five connecting loops of at least 1 nt each and the longest being 34 nt. In the 5' half of Spinach, two pairs of Gs are parallel and adopt the conventional anti conformation. On the other hand, three the four Gs on the 3' side of the G-quadruplex adopt syn conformation and one adopts an anti conformation, and each lies above or below a G of opposite strand polarity. The mixed tetrad of Spinach serves as an adaptor to connect the four-strander, mixed-polarity G-quadruplex in J2-3 to the canonical antiparallel P2 duplex. In addition, Spinach uses additional noncanonical base pairs to gradually transition from quadruplex to P2 duplex. Furthermore, the G-quadruplex of Spinach is linked to antiparallel A-form duplexes on both sides. The transition from the upper side of the quadruplex to the duplex P3 is facilitated by the base triple above DFHBI. The discovery of a G-quadruplex in Spinach is

Next the authors compared the Spinach chromophore to that of GFP and found major differences in the molecular interaction between the chromophore and the RNA/protein molecule. In summary, the chromophore of GFP is buried in the pocket and interacts with also buried, ionizable amino acids through van der Waals contacts, while the chromophore of Spinach is accessible to bulk solvent and interacts mainly with neutral moieties and sometimes cations in Spinach. Despite the difference, the fluorescence intensity and spectra of Spinach-DFHBI and GFP are comparable.

Lastly, the authors performed mutational analysis that further confirmed that the G-quadruplex and the interaction between DFHBI and Spinach are essential for Spinach fluorescence. Mutations in the base triple atop DFHBI led to a significant reduction of fluorescence, as well as a 45-nm blueshift of the excitation maximum, leading to the prediction that the DFHBI fluorescence is intimately linked to the electronic properties of the nucleobases sandwiching it and can possibly be fine-tuned. More interestingly, based on the structural observation that the interactions between Spinach and DFHBI are restricted to J2-3, the authors generated a miniaturized Baby Spinach consisting only of J2-3 flanked by A-form duplexes. The Baby Spinach retained 95% of Spinach fluorescence intensity when in complex with DFHBI, providing a more versatile tool for studying cellular RNAs due to its smaller size.

One Mentor is Not Enough!

By: Herbert M. Geller, Ph.D.

The original Mentor was a character in Homer's "The Odyssey". When Odysseus, King of Ithaca went off to the Trojan War, he entrusted the care of his kingdom to Mentor. Mentor served as the teacher and overseer of Odysseus' son, Telemachus. Mentor's role has now evolved to become a generic term (mentor), with the dictionary definition being "an experienced and trusted adviser". My own experience is that a mentor should also be someone who is invested in your future, but is also honest in giving advice, even if the advice is not what their mentee wants to hear.

For NIH Fellows, the likely response to "Who is your mentor?" is to

identify the Principal Investigator of their lab. But scientific prowess is only one area needed for success in a career. Moreover, mentoring needs change with time and situation, suggesting that rather than depending upon one mentor, a better approach would be to have a group of mentors, each of whom provides a unique set of skills perspective. This echoes graduate education, where students normally have a thesis committee, or even in industry, where companies will have a Board of Directors, each with their own perspective and skill set.

While mentors are normally chosen for their experience, mentors do not need to be very senior to be valuable. We have all experienced what is now called "peer mentoring" – advice from students or postdocs in our lab or program. This type of mentoring can be very help-

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Meet the New Fellows



Dr. Luca Melli is a new Visiting Fellow in the Cell Biology and Physiology Center under

Dr. James Sellers. Dr. Melli earned his Ph.D. at the University of Florence. His initial project at NIH is mechanics of nonmuscle myosin II filaments.



Dr. Jianhua Xiong is a new Visiting Fellow in the Center for Molecular Medicine under

Dr. Toren Finkel. Dr. Xiong earned his Ph.D. at Peking University. His initial project at NIH is metabolic regulation in heart and lung disease.



Dr. Ilker Tunc is a new Visiting Fellow in the Systems Biology Center under Dr. Xujing Wang.

Dr. Tunc earned his Ph.D. at the College of William and Mary. His initial project at NIH is the physiological function of oscillation and synchronization of the mitochondria network and the possible relationships with the diseases

RECENT PUBLICATIONS BY NHLBI FELLOWS

Abraham, T. M., Massaro, J. M., Hoffmann, U., Yanovski, J. A., & Fox, C. S. (2014). Metabolic characterization of adults with binge eating in the general population: The framingham heart study. *Obesity*. (Silver. Spring). 10.

Fertrin, K. Y., van Beers, E. J., Samse, L., Mendelsohn, L. G., **Saiyed, R.,** Nichols, J. S., Hepp, D. A., Brantner, C. A., Daniels, M. P., McCoy, J. P., & Kato, G. J. (2014). Imaging flow cytometry documents incomplete resistance of human sickle F-cells to ex vivo hypoxia-induced sickling. *Blood*. 124, 658-660.

Galletta, B. J., Guillen, R. X., Fagerstrom, C. J., Brownlee, C. W., **Lerit, D. A.,** Megraw, T. L., Rogers, G. C., & Rusan, N. M. (2014). Drosophila Pericentrin requires interaction with Calmodulin for its function at centrosomes and neuronal basal bodies, but not at sperm basal bodies. *Mol. Biol. Cell*. mbc-0617.

Hatch, J. & Mukouyama, Y. S. (2014). Spatiotemporal Mapping of Vascularization and Innervation in the Fe-

tal Murine Intestine. *Dev. Dyn.* 10.

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Meet the New Fellows



Dr. Kalindi Parikh is a new Clinical Fellow in the Cardiovascular-Pulmonary Branch under Dr. Andrew Arai. Dr. Parikh earned her M.D. at Chicago Medical School. Her initial project at NIH is with cardiac MRI, assessing if there are detectable wall motion abnormalities on cardiac MRI with Regadenoson stress testing.



Craig Pearson is a new Pre-Doctoral Fellow in the Cell Biology and Physiology Center under Dr. Herbert Geller. Craig earned his B.S. from Michigan State University. His initial project at NIH is looking at guidance cues in the optic chiasm and investigating how glial cells and extracellular matrix proteins influence the growth and pathfinding of regenerating retinal ganglion cell axons in the optic nerve.



Idalia Yabe is a new Pre-Doctoral Fellow in the Hematology Branch under Dr. Cynthia Dunbar. Idalia earned her M.S. at Georgetown University. Her initial project at NIH is testing the genotoxicity of various lentiviral vectors that potentially can be used for gene therapy.

FEATURED ARTICLE CONT.

ful to gain a perspective on a particular situation in the lab. When looking for a new position, your best mentor might be someone who recently went through the process and can provide you with insights into particular aspects of the recruitment process. If you are planning on writing a grant, the best mentor would be someone who is experienced at both writing and reviewing grants, but also someone who you trust to give you realistic feedback. And sometimes the relationship changes – the person who was my postdoctoral advisor is someone who now comes to me for advice.

An essential prerequisite for finding effective mentoring is identifying your goals and needs – which will likely change as you move through your career. Thus, if you move to a position in academia, you will need mentors who can shepherd you through starting up your laboratory, obtaining research funding and preparing yourself for tenure. In an industrial position, you'll want mentors who are familiar with that career path and guide you to obtain the skills required for advancement. In a future column, I'll address how you can go about finding people who will be effective mentors.

Congratulations!

To our recent Lenfant award winners:



Adrienne Campbell under Dr. Robert Lederman with *Development of magnetic resonance imaging methods for effective and safe visualization of passive devices during MRI-guided cardiovascular interventions.*



Michel de Messieres under Dr. Jennifer Lee with *Dependence of Apolipoprotein C-III membrane binding properties on membrane curvature and lipid composition.*



Scott Gordon under Dr. Alan Remaley with *Development of bi-functional peptides for the treatment of hyperlipidemias.*



Christopher Jones under Dr. Adrian Ferre-D'Amare with *Characterization of the cyclic-di-AMP riboswitch toward the development of novel antibiotics.*

The next Lenfant deadline is October 15th, 2014. For more information on applying for the Lenfant awards visit our intranet site, available at <https://intranet.nhlbi.nih.gov/general/the-lenfant-fellowships>.

ABOUT TOWN

End of Summer: September Festivals

By: Liz Cox, Program Coordinator

As Labor Day weekend came and went, so did summer itself. September brings an end to days that last longer than nights, the pool closing, and the start of school. Fingers crossed it will also (eventually) bring an end to DC's notorious summer heat. As the temperatures begin dropping, September becomes the perfect time to take advantage of some outdoor festivals in the DC area. With the weather not-too-hot but not-too-cold, street festivals, food tastings, and cultural events abound, ready for you to enjoy. There is a wide array of festivals and themes to choose from throughout September.

Festivals range from centering on heritage to food and wine, music, and art. Some of the heritage festivals include the Greek Festival, the Cambodian Community Day Festival, the Latino festival, and the Turkish festival. For food and wine, don't miss Taste of Georgetown and the Virginia Wine festival, in addition to the Oktoberfests that start towards the end of the month. Looking for some music to go with your 71-degree day? Rosslyn and Silver Spring have a jazz festival and Takoma Park hosts a Folk Festival, in addition to the live music at most street festivals. There is no shortage of other forms of art on display either, from film to performance art to open galleries. The crowd favorite DC Shorts Film Festival will return this September, along with the Alexandria King Street Art Festival, Arlington Festival of the Arts, and the Hyattsville Arts Festival.



There are numerous other festivals as well, including street festivals and sports days. Street festivals are great neighborhood celebrations that some describe as a bigger block party. Two popular ones include the H Street Festival and Adams Morgan Day. Both feature music, dance performances, children's activities, international foods and more. As far as sports goes, both spectators and those looking to participate have options. The Nation's Football Classic and the Redskins Opening Game are held in September, alongside the Nation's Triathlon and WalkingTown / BikingTown DC.

In addition to festivals, many counties in the area hold their county fair in September. Counties including Anne Arundel, Charles County, Frederick and Calvert County will be among those hosting a fair. You can find more information on all the festivals and more [here](#).

So pack a sweater (for when the temperature goes down at night) and enjoy some summer-finale festivals!

Meet the New Fellows



Rachel Kaspari is a new Post-Baccalaureate Fellow in the Systems Biology Center under Dr.

Susan Harbison. Rachel earned her BS in Biology at Macalester College. Her initial project at NIH is examining the sleep phenotypes and counting the number of ovarioles in mutated *Drosophila melanogaster* to look for a connection between sleep and reproductive fitness.



Milton Williams is a new Post-Baccalaureate Fellow in the Genetics and Development

Biology Center under Dr. Robert Adelstein. Milton earned his BS in Plant Science at Fort Valley State University. His initial project at NIH is the study of the structure, function, and cause of stress granules in mammalian cells.



Andrew Cangelosi is a new Post-Baccalaureate Fellow in the Center for Molecular

Medicine under Dr. Haiming Cao. Andrew earned his BS in Biology at Duke University. His initial project at NIH is studying a long non-coding RNA that has been demonstrated to influence glucose metabolism.

McMahon, G. M., Preis, S. R., Hwang, S. J., & Fox, C. S. (2014). Mid-Adulthood Risk Factor Profiles for CKD. *J. Am. Soc. Nephrol. ASN.*

Mehta, N. N., Dagur, P. K., Rose, S. M., Naik, H. B., Stan-sky, E., Doveikis, J., Biancotto, A., Playford, M. P., & Mc-Coy, J. P., Jr. (2014). IL-17A Production in Human Psoriatic Blood and Lesions by CD146+ T Cells. *J. Invest Dermatol.* 10.

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Plotnikov, S. V., Sabass, B., Schwarz, U. S., & Waterman, C. M. (2014). High-resolution traction force microscopy. *Methods Cell Biol.* 123:367-94. doi: 10.1016/B978-0-12-420138-5.00020-3, 367-394.

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per, M. A. (2014). A Knowledge Base of Vasopressin Ac-tions in Kidney. *Am. J. Physiol Renal Physiol.* ajprenal.

Subramanian, S., Liu, C., Aviv, A., Ho, J. E., Courchesne, P., Muntendam, P., Larson, M. G., Cheng, S., Wang, T. J., Mehta, N. N., & Levy, D. (2014). Stromal cell-de-rived factor 1 as a biomarker of heart failure and mortal-ity risk. *Arterioscler. Thromb. Vasc. Biol.* 34, 2100-2105.

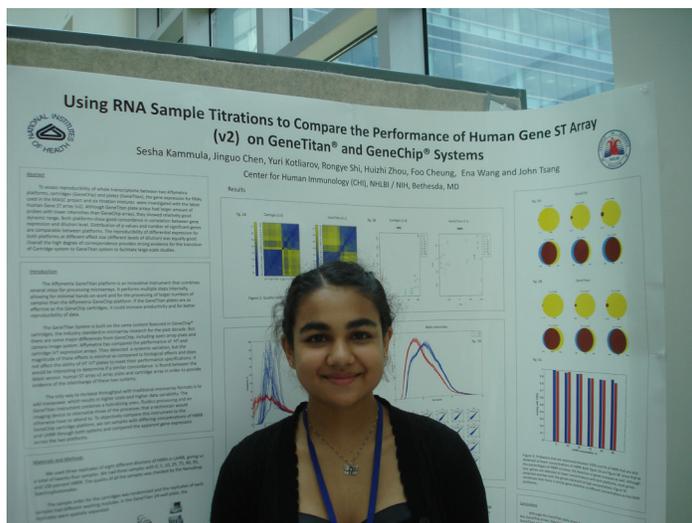
Sun, Y., Desierto, M. J., Ueda, Y., Kajigaya, S., Chen, J., & Young, N. S. (2014). *Peromyscus leucopus* mice: a potential animal model for haematological studies. *Int. J. Exp. Pathol.* 10.

Toepfer, C. & Sellers, J. R. (2014). Use of fluorescent tech-niques to study the in vitro movement of myosins. *EXS.* 105:193-210. doi: 10.1007/978-3-0348-0856-9_9., 193-210.

Uchida, N., Hsieh, M. M., Platner, C., Saunthararajah, Y., & Tisdale, J. F. (2014). Decitabine Suspends Hu-man CD34+ Cell Differentiation and Proliferation dur-ing Lentiviral Transduction. *PLoS. One.* 9, e104022.

Wang, R., Ferraris, J. D., Izumi, Y., Dmitrieva, N., Ram-kissoon, K., Wang, G., Gucek, M., & Burg, M. B. (2014). Global discovery of high NaCl-induced changes of pro-tein phosphorylation. *Am. J. Physiol Cell Physiol.* ajpcell.

Warner, K. D., Chen, M. C., Song, W., Strack, R. L., Thorn, A., Jaffrey, S. R., & Ferre-D'Amare, A. R. (2014). Struc-tural basis for activity of highly efficient RNA mimics of green fluorescent protein. *Nat. Struct. Mol. Biol.* 21, 658-663.



Snapshots of NHLBI summer students at Summer Student Poster Day