From the Director of the Office of Education

What are my career goals and how do I get there? These questions are frequently asked by NHLBI fellows. The Fellows Progress Report is focused on addressing these questions, but only provides a skeleton which must be fleshed out. A new tool from the AAAS, myIDP, is designed to help you do this. In short, this web-based tool provides you with the tools to create a personal Individual Development Plan, including suggestions of career choices based on an initial assessment of your interests, and then helps you design a roadmap to help you acquire the skills to get there. While I've suggested that you use the printable IDP provided on our web page, this new tool provides significant advantages. I encourage you all to read the article below by Dr. Jue Chen, who took myIDP for a "test drive", and then visit the myIDP web site to start your own personal IDP.

The Fellows Advisory Committee is planning activities for FY2013: we begin with a Halloween Social event on the 30th (see page 5 for more details) and a one-day DIR Retreat in the Spring at the Ronald Reagan Building on the mall. I invite you all to join the committee and suggest additional activities to build our NHLBI DIR community.

myIDP- Your Career Development Helper

By Jue Chen, Ph.D.

The web-based career-planning tool myIDP (http://myIDP.sciencecareers.org) was recently launched by AAAS to help graduate students and postdocs in the sciences to define and pursue their career goals. I found it is useful for the following reasons: 1) it helped me to narrow down and identify my career goals; 2) it forced me to make a plan to achieve my goals; and 3) it encouraged me to have a productive conversation with my mentor about career development and to have his support.

This is how myIDP works. You do need to set up an account, which should take no more than 5 minutes. After log in, you will see four sections on the left panel: 1) Assessment, 2) Career exploration, 3) Set goals, and 4) Implement plans.

The first thing you do is to assess your skills, interests, and values, which will help you to find career paths that alignment best with your unique sets of skills and interest, and that meet your values. Even if you have already identified your career goal, it'll still be helpful to find hidden career options that might be a good fit for you. All the skills, interests and values are rated on a 1-5 scale and it's better to have them spread widely in that range. It's hard to rate some skills because I have no idea what are considered
new NHlbi Fellows

Christopher Alexander, Ph.D., is a Visiting Fellow in the Laboratory of Cell Biology under Dr. John Hammer. Dr. Alexander earned his Ph.D. in Biochemistry from the University of Kent, Canterbury. Before coming to the NIH he was a Research Associate at the University of Kent where he was awarded the 2012 International Honor Fellows travel award to attend 56th Annual Biophysical Society Meeting. Dr. Alexander’s research project it to investigate the role of myosin Va and ER localisation within Purkinje neurones.

Zhang Li, Ph.D., is a Visiting Fellow in the Translational Research Section under Dr. Joel Moss. Dr. Li earned her Ph.D. in Biology from the University of Zurich, Switzerland. She previously worked in the Pharmacology and Toxicology Institute at the University of Zurich. Dr. Zhang will be initially researching Lymphangioleiomyomatosis disease.

Wenjing Yang Ph.D., is a Research Fellow in the DNA Sequencing & Computational Biology Core under Dr. Jun Zhu. Dr. Yang earned her Ph.D. in Physics from The George Washington University, DC. She was the recipient of the 2011 Fischer Family Fund Endowment Fellowship Award in Physics from The George Washington University. Dr. Yang’s research project is studying alternative polyadenylation in resting and activated human T cells, through computational analysis on high-throughput sequencing data.

Kevin Ramkissoon, Ph.D., is a Visiting Fellow in the Laboratory of Kidney and Electrolyte Metabolism under Dr. Maurice Burg. Dr. Ramkissoon earned his Ph.D. in Microbiology and Immunology from the University of North Carolina at Chapel Hill, North Carolina. He was awarded the 2010 SRI International Spot Award for performance above and beyond expectations. Dr. Ramkissoon will be researching characterization of the C-terminal domain of the NFAT5 transcription factor using mass spectrometry-based proteomics.

highly proficient. In addition, I had to redo my values rating several times to achieve an even distribution of ratings. All the values are important and it’s hard for me to pick just a few as the most important ones. But it’s the hard question I need to ask myself when I face a career decision. There is no perfect career that will satisfy all the values. It comes down to what you can and cannot sacrifice and I’d rather think through this earlier. The rating of values is not used to match your career path, which you will see in the second section, because it is very subjective and dependent on individual employer. That’s something you need to do on your own to figure out by talking to people.

After the assessment process, it will compare your interests and skills to 60 different career paths within 20 career categories in the database and then rank the career paths that fit you best. The list gives you the % of match in both skills and interest for each career path. If you click the % sign, it will expand and show a table of your rating and experts’ rating for each skill and interest. This will allow you to know skills to be improved to be more competitive for that career and where your interest intersects with that career. The list is not going to define your best future career but it is a good starting point of career exploration. One thing I found really helpful is the “read more” option right by each career path that will lead you to resources such as online reviews, blogs and book chapters to learn more about those careers. The career exploration section also offers tips on how to reach out and learn more about career opportunities by attending events and informational interviews. You can keep an electronic log of career workshops and informational interviews you’ve attended or plan to attend to help you keep on track. If you prefer keeping electronic record, you’ll like this better than the paper-based IDP. Right now, the attend events and talk to people tabs under the career exploration section only serve as a log and don’t have links to external resources. If there are links to events and workshops under each career path, that will be more helpful.

Once you have explored all the options and narrow down your choices, it’s time to develop your career plans using the next section set goals, SMART goals. SMART stands for specific, measurable, action-oriented, realistic, and time-bound. I think another important factor of setting goals is to make sure you can be held accountable. You’ll be asked the question of “How will you be accounta-
Recent Publications by NHLBI Fellows


Have you heard a good speaker lately?

Please nominate them for our 2013 Retreat,
email us at direducation@nhlbi.nih.gov
Cell migration is a highly integrated multistep process involved in all aspects of cell biology. It is a central process in the development and maintenance of multicellular organisms and is an essential process during developmental morphogenesis, tumor metastasis, and immune responses. The migrating cell is highly polarized and relies on complex regulatory pathways involving the orchestrated interplay between microtubule (MT) and actin cytoskeletal systems. It is well established that directed cell migration requires polymerization of actin (specifically F-actin) in order to drive the lamellipodia protrusions in the cell leading edge (direction of migration) while contraction of actomyosin bundles in the cell are responsible for the retractions of the trailing cell rear. However, the role of MTs in this directed cell migration is less understood but MTs are thought to establish this polarization in the cell thereby allowing the cell to spatially regulate the protrusion forces at the leading edge and contractile forces at the cell tail. This dynamic instability by MTs allows for control of opposing forces, alternating between persistent growths and shortening of MTs and thereby polarizing the migrating cell. Specifically, MTs in the lamellipodia grow more slowly, persistently and parallel to the cells leading edge and these leading edge MTs, also known as “pioneer MTs” are thought to guide migration by localizing signals that promote actin dynamics in the lamellipodia and/or facilitate turnover of leading edge local adhesions. Rac1, a Rho family small GTPase, has been identified as a key regulator locally controlling cytoskeleton dynamics through multiple effectors. In migrating cells, activated Rac1 accumulates in the lamellipodia and facilitates local actin polymerization, which drives leading edge protrusion. The study by Nishimura et al. identified regulators of leading edge MTs downstream of Rac1 in migrating cells by combining both high-resolution, quantitative live cell imaging and RNAi screening. Their image-based RNA screen identified microtubule-affinity-regulating kinase 2 (MARK2) as a major target that suppresses Rac1-induced MT assembly in the leading edge of migrating cells.

To monitor the effects of Rac1 activity on MTs dynamics in migrating cells, Nishimura et al. used live-cell imaging techniques to track the motions of the fluorescently-labeled EB3 protein, a MT plus-end binding protein. Utilizing plusTipTracker, an automated image analysis program, they first measured MT growth dynamics in cells expressing a constitutively active form of Rac1 (CA-Rac1). Using this automated tracking procedure, they were able to measure three important components of pioneer MT dynamics: (1) growth speed; (2) growth persistence lifetime; and (3) spatial distribution or orientation. As previous reports have shown, CA-Rac1 expression has a major effect on MT organization, inducing a bundle of MTs parallel to the cell edge in lamellipodia, suggesting that Rac1 activity promotes formation of “oriented” lamellipodial MTs (or pioneer MTs) in various cell types. These growth dynamics of MT assembly was classified as “slow” or “fast” for growth speed and “short-lived” or “long-lived” for growth lifetime based on the mean measurements from the image analysis program. Expression of CA-Rac1 increased the proportion of slow, short-lived MT growth in cells. More importantly, this increase in slow, short-lived MT assembly is localized to cell periphery near the cell edge. Given that pioneer MTs grow parallel to the cell edge, the authors further classified the orientation of MT growthtracks and found that expression of CA-Rac1 promoted slow MT growth in the cell periphery parallel to the cell edge while promoting long-lived MT growth in the cell center. This observation that CA-Rac1 mediates pioneer MTs growth parallel to the leading edge by promoting slow, short-lived MT growth excursions in lamellipodia is the foundation of the RNAi screen the authors used to identify protein regulators that modulate MT dynamics downstream of Rac1.

Next Nishimura et al. performed RNAi to knock-down several MT-regulatory proteins and used the image-based analysis to observe if depletion suppresses this slow, short-lived MT growth parallel to the leading edge that was induced by CA-Rac1. To this end, they once again analyzed the speed, lifetime, and orientation of MT growth excursions in cells treated with either siRNA or shRNAs, targeting one of 23 total MT regulatory proteins with and without the additional expression of CA-Rac1. As expected, in the absence of activated Rac1 signaling, depletion of MT regulatory proteins did alter MT growth dynamics compared to non-RNAi targeting controls. However, out of the 23 MT regulatory proteins tested, only RNAi-mediated depletion of one of these proteins, the microtubule-affinity-regulating kinase 2 (MARK2) suppresses both the slow-short lived MT growth and the parallel orientation of MTs at the leading edge of migrating cells.
edge induced by Rac1 overexpression. Analysis of MT dynamics showed that MARK2 depletion in cells expressing CA-Rac1 increases the population of fast, long-lived MT growth excursions while decreasing the slow, short-lived growth, thereby increasing the mean growth speed and lifetime compared to the cells expressing CA-Rac1 alone. In addition, RNAi knockdown of MARK2 in a cell expressing CA-Rac1 reduces the population of parallel pioneer MT at the leading edge. This result suggests that MARK2 may be a key regulator of Rac1 signaling by promoting leading edge pioneer MTs, which coordinate both MT growth speed and growth lifetime, as well as growth orientation at the cell periphery. To further validate their results from the image-based RNAi screen, the authors rescues the effect for MARK2 depletion by using a GFP-MARK2 construct, showing that the transition from slow, short-lived to fast, long-lived MT dynamics is specifically mediated by MARK2. This rescue construct reestablished the formation of the elongation pioneer MTs in the lamellipodia parallel to the cell edge. Taken together, these results clearly show that MARK2 promotes pioneer MT formation in lamellipodia downstream of Rac1 by inducing short-lived MT growth excursions parallel to the cell edge.

To further characterize the exact function of MARK2, Nishimura et al. compared the role of MT dynamics and organization in non-polarized and polarized cells. These set of experiments were critically important to determine if the observed MARK2 function on MT was dependent on Rac1-induced signaling. It is well established that Rac1 is localized at the leading edge in polarized cells (unlike non-polarized cells) and that this Rac1-induced signaling pathway controls MT growth and lamellipodial protrusions, which in turn control directed cell migration. MT image analysis in non-polarized cells (lacking Rac1-induced signaling) show that MARK2 depletion only alters two of the three parameters tested (MT growth speed and growth lifetime), while having no effect on MT orientation at the cell periphery. This contrasts with the result in activated Rac1 (CA-Rac1) cells that revealed an effect on all three parameters tested (MT growth speed, growth lifetime, and growth orientation). This result suggests that in the absence of Rac1 signaling, MARK2 promotes short-lived MT growth excursions and has little effect on MT organization or growth orientation. To resolve these differing results, they monitored MT dynamics and orientation in polarized cells undergoing directed migration in a scratch wound assay, where Rac1 activity has been shown to be polarized to the leading edge. As was observed with expressing CA-Rac1, depletion of MARK2 in polarized wound-edge cells exhibit the characteristic loss of slow, short-lived MT growth excursion that were more often parallel to the cell edge. Using the image analysis program, changes in all three MT parameters (MT growth speed, lifetime and orientation) at the leading edge were indistinguishable from the rest of the whole cells suggesting that MARK2 localizes to the leading edge of directionally migrating cells in a Rac1-induced manner and possibly regulates MT organization in these regions. Overall, the authors were able to convincingly show that MARK2 is required for polarizing MT growth dynamics to form pioneer MTs that exhibit slow, short-lived growth parallel to the leading lamellipodia in polarized, directionally migrating cells.

In conclusion, this study utilized automated image analysis to screen for regulators of MT assembly dynamics induced downstream of Rac1 activation. This is the first published paper using image-based analysis to monitor the parameters of MT growth dynamics and orientation coupled with phenotypic screening and should prove to be a useful automated screening technique for live cell imaging to observe other protein dynamics in the near future.

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**HALLOWEEN DESSERT POTLUCK**

*Please bring a dessert to share*

*All are invited!*

**Sponsored by the OE and Fellows Advisory Committee**

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Halloween Dessert Potluck

Tuesday, October 30th

1 PM- 2:30 PM

Building 10/CRC, 1 SE Patio

*Please bring a dessert to share*

All are invited!

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