FYI

CCR Fellows & Young Investigators Newsletter

Center for Cancer Research

Volume 23, Issue 1 **Winter 2024**

Winter Newsletter

Happy Winter, CCR-FYI. Although this winter has only occasionally felt like an actual winter, with snow and cold, I hope you have made it through the cold, short days and are looking forward to the green and warmth of spring. This issue is broad, and the topics covered range from applying to medical school, applying for career transition grants, books for cancer researchers, and the experiences of being a clinical fellow in Bethesda.

Our next issue will be dedicated to the CCR-FYI colloquium; however, for issues at the end of the year, we are interested in your input about what topics and themes we might cover. If you've got ideas for themes for future issues, if you want to write an article, or if you want to help in some way, please email me at: riley.metcalfe@nih.gov.

Please also remember to register for the CCR-FYI colloquium in April! There are details in an advertisement at the end of the newsletter. Our next edition of the newsletter will be dedicated to the colloquium, so if you are attending, please consider writing an article! The CCR-FYI steering committee is also seeking new members, with several open positions, so please consider joining.

Thank you for reading the newsletter and I hope you have had a good start to 2024!

Riley Metcalfe, Editor-in-Chief

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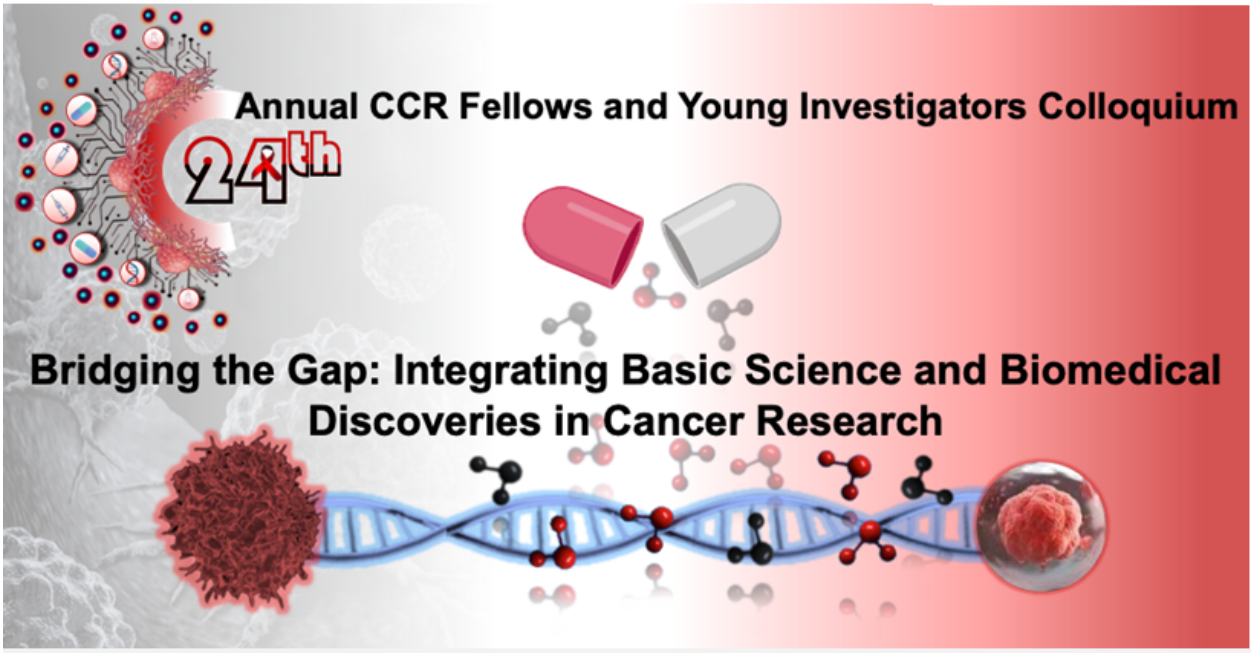


Thursday and Friday, April 18th and 19th, 2024

NCI Shady Grove Campus, Rockville, MD

For Registration Site, Scan QR Code:

REGISTRATION DEADLINE: March 22nd, 2024

https://events.cancer.gov/cct/fyi-colloquium

Speakers: Douglas R. Lowy, M.D.; W. Kimryn Rathmell, M.D., Ph.D. M.M.H.C.; Curtis Harris, M.D.; Kris C. Wood, Ph.D.; Glenn Merlino, Ph.D.; James Gulley, M.D.; Christine Heske, M.D.; Ashani Weeraratna, Ph.D.; Naomi Bartley, M.S.; and Tom Misteli, Ph.D.

Workshops:

- Communicating with Confidence and Clarity
- Empowering your Training Journey: Navigating NCI Resources
- Grant Writing Decoded

Panels:

- Exploring Careers at the Bench: Academia and Beyond
- Navigating Career Transitions into Science Writing, Policy, and More
- Cultivating Inclusion: A Roadmap for Scientists in Training

Supported by CCT Office of Training and Education and CCR Office of the Director

Inside Cancer Careers: a podcast that brings insights and perspectives on researchers' journeys from early trainees to established professionals.

By: Alida Palmisano

Do you want to hear directly from researchers shaping the present and future of cancer research? Are you curious about their journey into science, the lessons learned and advice you can apply to your career today? Then, don't miss an episode of ***Inside Cancer Careers***, a podcast from the National Cancer Institute (NCI), hosted by Dr. Oliver Bogler (Director of the Center for Cancer Training [CCT]).

Inside Cancer Careers is available where you get your podcasts, including on Apple Podcasts and Spotify. You can also register for email alerts.

Dr. Bogler engages in insightful conversations with scientists from all fields of cancer research highlighting highs and lows, U-turns and side-hikes, successes, and challenges in their career journeys.

The podcast covers a wide variety of topics relevant to all researchers such as science policy, health disparities, small businesses, finances, AI and much more. Practical actionable tips are shared every week, so if ***you*** want to grow your cancer research career, tune in every first and third Thursday of the month. All episodes are available on the CCT website or wherever you listen to podcasts.

Here are some pearls of wisdom from four episodes that I found interesting. I recommend listening to the full conversations.

In Episode 9, **Dr. Vasty Osei Amponsa** and **Dr. Marja Brolinson** talk about networking resources, and leadership opportunities at the NIH. If you are a current post-doc,

Inside Cancer Careers podcast cover art featuring a woman holding a magnifying glass to her face.

postbaccalaureate (post-bac) or early career researcher at NIH, you should listen to this conversation to make the most out of your time at NIH.

Dr. Brolinson is a clinical fellow at the NIH Clinical Center and FelCom Co-Chair, and Dr. Amponsa is a post-doctoral fellow in the Center for Structural Biology at NCI, FelCom Co-Chair and member of our own CCR-FYI! FelCom is an NIH-wide committee that fosters communication among fellows and enhances the intramural training program by sponsoring events designed specifically for fellows. CCR-FYI is the CCR Fellows & Young Investigators Association organized by non-tenured and non-tenure-track M.D.s, Ph.D.s or equivalent, graduate students, and post-bac intramural

scientists to foster the professional advancement of scientists at CCR (it also disseminates the newsletter you are reading!).

Dr. Amponsa and Dr. Brolinson describe the value that fellow led groups have in bringing the vastly different concerns of fellows together. These groups are a forum to get answers, to access helpful resources, and to disseminate information to other fellows that have similar questions. Connecting with colleagues outside one's individual lab is challenging due to the variety of cultural and educational backgrounds of fellows in an institution the size of the NIH. Joining committees, like FelCom and CCR-FYI, and attending skill-building workshops are great ways to make friends, socialize with people outside your lab, and start building a network of scientists that can support you throughout your career.

The episode also includes the perspectives of **Dr. Eugene Manley Jr.**, who shares his path from bench science to roles in non-profit organizations. To hear more about the leadership opportunities in fellow-led committees at NIH, and about transitioning from bench science to non-bench careers, listen to the full episode!

A second inspiring episode delves into the life of an accomplished trailblazer cancer researcher who dedicated her life to science and gender-inequality issues plaguing the field. **Dr. Nancy Hopkins**, Amgen Professor of Biology Emerita at Massachusetts Institute of Technology (MIT), shares the exciting early days of the molecular biology revolution she was part of, discusses the obstacles she encountered in her career, and gives advice on selecting a path in science. Dr. Hopkins also describes the movement she led to achieve gender equality at MIT and beyond, discussed in depth in a book by journalist Kate Zernike titled "The Exceptions: Nancy Hopkins, MIT, and the Fight for Women in Science". Dr. Hopkins became an assistant professor at MIT's Center for Cancer Research in 1973. She used genetics to map the genes of mouse RNA tumor viruses, identify genes that determine viral host range, and characterize cancers that mouse retroviruses cause. Dr. Hopkins switched research areas in the middle of her career to identify genes required for early vertebrate development using the zebrafish model. Towards the end of her career, Dr. Hopkins became an advocate for cancer prevention and early detection research.

Dr. Hopkins' scientific journey is inspiring! It was riveting to hear from the person narrating her own breakthrough in science at a time when genetics discoveries were just starting. But, to me, the most thought-provoking aspects of the conversation were around broader questions such as "what does it take to be a great scientist?" She highlights how science is intense and often so exciting that she didn't want to go home. But she recognizes that not every scientist has to think this way: while a deep passion for discoveries is common among scientists, the way it is implemented can vary while still being "great scientists." In her generation women felt they couldn't be parents or have interests outside the lab and *also* be a great scientist. Today, many junior faculty have families and can succeed in multiple aspects of life.

It was also interesting to hear that she didn't understand how gender discrimination affected her own career until she read the (part biography) book. While living through the challenges, she saw the differences in treatment she received, but she didn't link them to the systemic source that cumulatively was discrimination.

After 20 years of watching how other women were treated in science research, she understood that the differences were due to systemic inequality. While living through challenges, one can always think, "Maybe I'm not good enough," but when you observe the treatment of others, it is much easier to see objectively when discriminatory treatments happen. To hear Dr. Hopkins talking more about the MIT report and her exceptional scientific career listen to the full episode!

In Episode 16, we hear from **Dr. Brian Rivers**, Director of Cancer Health Equity Institute at Morehouse School of Medicine in Atlanta. Dr. Rivers shares the importance of cancer health disparities research and his journey into the field.

Dr. Rivers explains that health disparities research is poised to help better understand why cancer disproportionately impacts certain populations. Dr. Rivers delves deep into all the multidisciplinary aspects of his research program, his experience with PACHE (Partnerships in Advanced Cancer Health Equity, a program from NCI Center to Reduce Cancer Health Disparities), and his leadership roles in the American Association for Cancer Research (AACR) community.

Asked what advice he might give to people beginning in health disparities research, Dr. Rivers highlights some programs within the NIH and NCI. Examples include the CCT, the Center to Reduce Cancer Health Disparities and the iCURE program, which offer opportunities to explore various careers in cancer research from bench to bedside, in the community, or in policy. Dr. Rivers encourages fellows to get involved, network at conferences, meet program officers, and identify mentors. He emphasized building a team of mentors to help you develop different facets of your scientific career.

To hear more about cancer health disparities, diversity training, and workforce diversity with the perspectives of **Dr. Tiffany Wallace**, Program Director at NCI Center to Reduce Cancer Health Disparities (CRCHD) and lead for the Disparities and Equity Program (DEP), listen to the full episode!

In another episode, we hear from **Dr. Otis Brawley**, Bloomberg Distinguished Professor and Professor of Oncology at Sidney Kimmel Comprehensive Cancer Center. Dr. Brawley leads a broad interdisciplinary research program of cancer health disparities at the School of Public Health and the Kimmel Cancer Center at John Hopkins University. Dr. Brawley is a globally recognized expert in cancer prevention and control. He revolutionized patient treatment by working to reduce over-screening of medical conditions, increasing quality of life, and reducing health disparities.

Throughout his career, Dr. Brawley combined medicine and science. He reflects on the fact that still seeing patients today keeps him grounded and informs his research with a real understanding of obstacles that patients and their caring doctors face in their everyday lives.

When asked if he thinks we are making progress in diversifying the cancer research workforce, Dr. Brawley candidly stated he is grateful that so many people in cancer medicine and cancer research acknowledge that we need to do better. While the recognition that we need a more diverse workforce is critical to advance equity and inclusion, one aspect not receiving too much attention is the science taught in grade schools, especially inner-city grade schools where minority kids go to school. Dr. Brawley passionately advocates for the need to stress STEM in high school and create opportunities for early teens to go into labs and experience science first-hand.

To hear Dr. Brawley share more about his career journey, his thoughts on the future of cancer research, and the need to care for the whole person with wisdom and focus, listen to the full episode.

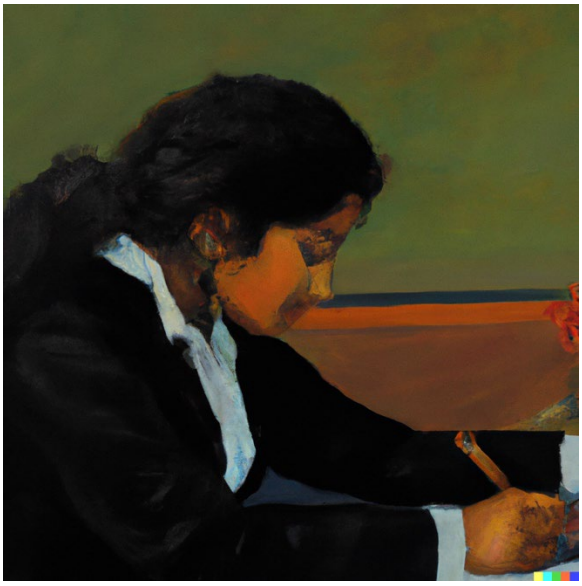
I hope these extracts gave you a taste of the exceptionally interesting content shared in the "Inside Cancer Career" podcast. I encourage you to listen to episodes you may have missed and tune in for more, wherever you listen to podcasts!

Applying for a K99/R00 Transition to Independence Award

By: Riley Metcalfe

This year, I wrote a K99/R00 'Transition to Independence' application. Like most postdocs in the intramural program, this was the first full-length grant that I've ever written. It is a beast to write – mine was 85 pages long (although 'only' 30-40 pages of technical writing), and very different from the manuscript writing which I'd mostly done previously. I'm not the first NCI fellow to apply for a K99, and I won't be the last, so a week or two after submitting the award, I decided that it would be a good exercise to write down for this newsletter my experience in applying to the grant, both for the benefit of future applicants and for my own sake (plus, after writing the ~10,000 words for the K99, what's another few thousand words?). It's worth stressing that this is my own individual experience. – I don't have any special insight into the K99/R00 application process, beyond being an applicant.

As the name implies, the K99/R00 is a 'transition' or 'career development' award. It's *not* a traditional fellowship or training award (like the NRSA/F grants which you may have applied for as a graduate student) or a purely research award (like an R01 or R22 award). It's a kind of hybrid award, intended to facilitate the last few critical years of postdoctoral training, the transition to an independent position, and to provide you with a baseline level of support during the first years as an assistant professor. This is something you need to keep in mind when writing the award, your research proposal is obviously important (maybe the most important part) but you need to keep the training goals of the award in mind when writing it –a common mistake is to focus on how awesome you are, without justifying the need for the extra years of postdoctoral training (after all, if you're so awesome already, why not just apply for a faculty job now?).



DALL-E 2 output for 'an oil painting image of a postdoctoral fellow writing a grant.'

Your eligibility for a K99/R00 ends four years after you finish your PhD (with allowance for career disruptions), so part of the reason for the award is to provide a mechanism for postdocs to transition to an independent position without having to have a long postdoc. It's worth emphasizing that four years post-PhD is a very tight timeline. Ideally, you want to submit a K99/R00 application approximately eight months before your eligibility expires (to have a window for resubmission if not awarded the first time), so you want to start thinking about what a suitable project might be in the second year of your postdoc. This will come up quick – so if you are a first- or second-year postdoc, and you're thinking about going for a tenure-track position after your postdoc, keep these deadlines in mind! If you have any doubt,

contact the program officer (PO) for the Institute/Center (IC) that you are planning to apply to for clarification on when your eligibility ends – different ICs do have marginally different eligibility rules.

How does the K99 facilitate this 'transition to independence'? The simple reason is that this award gives you a fair bit of money and a good launching off point for an independent career. At an extramural institution, the K99 gives you two years of mentored postdoctoral training and provides salary and (modest) research support for this period (although you do not get the postdoctoral research support portion of the award if you remain in the intramural program). During the K99 period, you are expected to apply for, and be offered, a tenure-track assistant professor (or equivalent) position at an US research institution and submit a transition plan to the NIH IC that gave you the award. This activates the 'R00' phase of the award, which gives you three years of support at the new institution. Due to the guaranteed few years of funding for the first few years of their lab, and proven success in writing NIH grants, K99/R00 awardees tend to do well in the job market. Approximately 90% of K99 awardees go on to activate the R00 phase [1], indicating that they obtain an appropriate extramural faculty position. It's also worth noting that if you accept a tenure-track position in the NIH intramural program (such as a Stadtman or Lasker investigator) you won't receive the R00 transition award.

Two things are of special note for fellows in the NIH intramural program. First, most extramural fellowships do not accept applications from intramural fellows but the K99/R00 does, so it's arguably the best way to get grant writing experience while in the intramural program. Second, the K99/R00 has no citizenship/residency requirements. Visiting fellows on a non-immigrant visa (such as a J-1 or H-1B visa) are eligible for the award. It's worth mentioning that there is a second K award that US citizen and permanent resident NIH fellows can apply for, the K22 'Transition Career Development' award. The K22 award has a much longer eligibility window (from 2-8 years post-PhD). It has no transition period – after you receive the notice of award for the K22, you have a year to go onto the job market, and then three years of support. In this article I'll focus on the K99/R00 award as it is the one that I applied for; however, the K22 is worth keeping in mind if you are past the K99/R00 eligibility period and are a US citizen/resident. It's also worth noting that NCI (uniquely) offers an 'early' K99/R00 award, which has a shorter eligibility window (2 years post-PhD), which is intended for postdocs in fields where long postdocs are not common (the four fields which the NCI supports using this mechanism are 'data science', 'cancer control science', 'molecular/precision cancer prevention', and 'other science').

A final (and somewhat delicate) question which often comes up is how 'good' your CV needs to be prior to applying for the award. Clearly, a successful publication track record through both your graduate and postgraduate training is helpful – but this doesn't necessarily mean publications in high-impact journals (although that won't hurt). It can be worth looking at the Google Scholar of recently funded applicants to get a feeling about how a profile of a successful candidate looks like. Likewise, views differ on the importance of publications during your postdoctoral period – these *strictly speaking* aren't required, but it is common way that otherwise-fundable applications miss out, so *ideally* you want to wait until you have a first-author publication from your postdoc training prior to apply for the K99/R00 award. Yes, getting all your graduate papers published,

getting a publication from your postdoc through the publication process *and* getting preliminary data on a new project for a K99 *and* writing a K99 is tight timeline! Personally, I'm of the opinion that it's worth applying if you are aiming for a faculty position after your postdoc, if you've got a well-developed research plan, even if your CV is not where you want it to be, as the experience of writing a K99, and having it reviewed, is itself worthwhile.

In the interests of space, I won't provide a complete guide to writing a K99/R00 here, but I have included links to resources I found useful at the end of the article. One thing I'd like to stress is that you need to give yourself a lot of time to write the award, and ideally have a complete application 6-8 weeks before the deadline. As this is likely your first experience in writing such an application you will want as many people to read it as possible before the deadline (such as your mentor, other people in your branch or people in your lab). Personally, I spent about six weeks writing a 'first draft', which was ready about two months before the deadline. I then forgot about it for a month while others were reading it, and then spent 2-3 weeks editing it after receiving feedback. Second, keep in mind the career training/development aims of the grant when writing it. When the proposals are assessed, the career development aspects are given equal weight to the research aspects, so you need to take it seriously. You need to show that you have a solid plan in the K (postdoc) period of the award to set you up for a successful transition to an independent faculty position in the R phase. This means having a research proposal that is sufficiently distinct from your primary mentor so there is limited overlap, while developing the necessary transferrable 'soft skills' and showing that you have the support in your current lab and branch in the faculty search and transition. This is particularly relevant if your primary mentor is a tenure-track investigator, as you'll need to convince the reviewers that you are not going to compete or overlap in the R (faculty) period of the award.

At NCI, you should take advantage of the support available for you from the Center for Cancer Training. Terry Moody (moodyt@bprb.nci.nih.gov) runs a yearly 'K Class' and (in-person) 'K grant tutorials' which are well worth attending. Olivia Moore (olivia.moore@nih.gov) is (at the time of writing, January 2024) the CCT staff member in charge of K99 applications and will be the person submitting the application for CCR postdocs, so it is worth contacting her well in advance of your application to register your intention to apply. As stressed above, contact the program officer of the IC that you are intending that you are planning to apply to, to establish your eligibility and to ensure that your specific aims are fundable by that IC. For the NCI, these can be found here. Finally, ask around your lab and branch, as it is likely that previous or current postdocs have written K99s, and will be willing to share advice and complete applications.

Finally, and most importantly, if there's one thing to take from this article, it's that you need to start thinking about your K99 application early – much earlier than you think!

Useful resources:

Here is a list of resources I found useful when preparing my own K99/R00 application:

The K99/R00 'Notice of Funding Opportunity (NOFO)'. This provides the instructions and review criteria for the award. Keep in mind that this changes periodically, so make sure you are using the latest version. Pay close attention to how it is reviewed.

The 150-page 'Career Development Instructions for NIH and other PHS agencies' is the 'rules' for how you should format your grant and what you should include. If you have questions about how to format your grant or what should be included, this is what you check.

The National Institute on Aging (NIA) has provided two sample K99/R00 applications with review comments.

Informative personal essays from previous K99 applicants. Keep in mind that these are the experiences of one person – although informative, always keep that in mind.

Jordan Ward's 'How to Write a Successful K99 - One Canuck's Perspective'

Anita Devineni wrote an excellent (although note, a little dated) post on applying for a K99.

It steps through the various components of the application very well.

Graham Erwin's 'Advice on how to apply for the NIH K99/R00 Pathway to Independence Award'.

Samir Amin wrote a similarly comprehensive guide to applying for a K99/R00 award.

The most useful resource is previous applications – so ask around, but keep in mind that requirements change year-to-year.

Reference:

1. Woitowich NC, Hengel SR, Vilgalys TP, Babdor J, Tyrrell DJ. Analysis of NIH K99/R00 Awards and the Career Progression of Awardees. bioRxiv. 2023:2023.01.26.525751.

Book Recommendations for Cancer Researchers

By: Giana Vitale

As lab-based cancer researchers, our days are spent poring over and writing papers, prepping chemicals and reagents, running experiments, caring for cells and animals, processing reams of data, and performing other tasks which are highly focused on unlocking some special bit of information about cancer. While our passion for diving into the nitty-gritty of the mechanisms and processes that cause cancer is necessary for expanding our knowledge of the disease, we can easily get caught up in the complexities of our niche. It is important to take a step back and remind ourselves that cancer research is much more than our benchwork; it behooves us to learn about the greater field of cancer research, explore the ethics of our work and its evolution through history, and remind ourselves of our ultimate goal to improve and save the lives of cancer patients. One of the best and easiest ways to expose ourselves to these ideas is through books. Here are a few books to learn more about the greater world of cancer:

The Emperor of All Maladies: A Biography of Cancer (Siddhartha Mukherjee)

No list of books about cancer would be complete without first mentioning Mukherjee's sprawling, comprehensive guide to the history of cancer. Starting with the first known observations of cancer in antiquity, Mukherjee, a hematologist-oncologist himself, leads the reader through centuries of cancer history before ending with a look into the modern standard of care and what future therapies may look like. Woven in among the biographies of cancer pioneers are anecdotes of Mukherjee's own experiences working on a cancer ward. The juxtaposition of his memories of patient suffering with the timeline of cancer discovery reminds the reader of the pain of all cancer victims through time, and why we spend long hours working for a cure.

The Immortal Life of Henrietta Lacks (Rebecca Skloot)

In this enlightening biography, Skloot reveals the uncredited woman behind the first immortalized cell line. Henrietta Lacks, a poor tobacco farmer from Virginia, developed and eventually succumbed to metastatic adenocarcinoma originating in her cervix. During her treatment, biopsies of her tumor were taken and cultured without her knowledge or consent. Her cells became the HeLa cell line which is used in research to this day. Tragically, Henrietta's family was not aware that her cells were being used until twenty years after her cancer was first sampled. Her family fought for compensation for many years after her death, and only received compensation in August 2023. Through her exploration of Henrietta Lacks' life, Skloot recognizes the importance of HeLa cells in research while also prompting the reader to grapple with the many ethical questions raised by the usage of those cells.

When Breath Becomes Air (Paul Kalanithi)

When a neurosurgeon on the cusp of finishing his training is diagnosed with stage IV lung cancer, he must face death the same way his former patients did. In this eloquent, heart-wrenching memoir, Kalanithi explains how he was diagnosed, reflects on his tragically short life, and discusses coping with the knowledge of his own impending death. Sadly, Kalanithi

passed during the production of this book, but he was survived by his wife, who completed the work and ensured its publication. This book serves as a powerful reminder that tomorrow is not promised and our greatest legacies are preserved in the people we love.

Being Mortal (Atul Gawande)

After his father was diagnosed with brain cancer, Gawande, a doctor himself, became curious about the nature of end-of-life care for all kinds of patients. He found that healthcare has become so focused on preventing death that it no longer embraces a graceful end of life. In “Being Mortal”, Gawande explores the most difficult questions surrounding end-of-life care: when should treatment for a failing patient stop? What should be done when a patient is in intense pain but not yet close to death? How does the cost of prolonging life influence the decision to do so? Although this book is not cancer focused, it is filled with lessons on empathy and gentleness in the face of hard decisions.

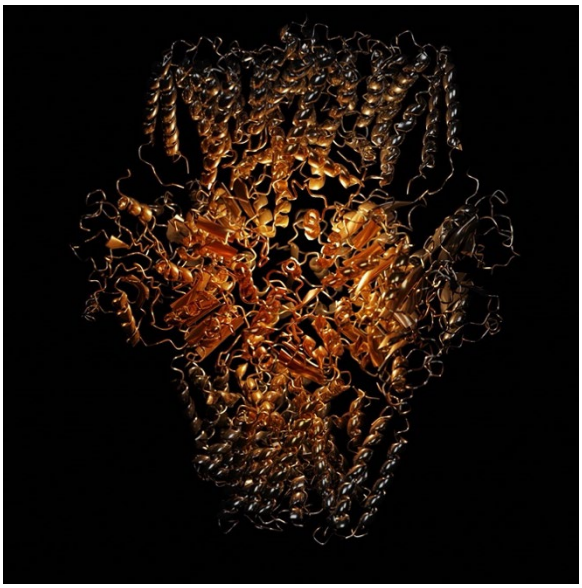
Dr. Folkman's War (Robert Cooke)

My final recommendation to my fellow cancer researchers is a deeply personal one. I read “Dr. Folkman’s War” as a young high schooler with a strong interest in science and the impression it left on me was so profound that I decided to pursue cancer research as a career. This incredible biography chronicles the life and scientific journey of Dr. Judah Folkman, the man behind the discovery of tumor angiogenesis. While the idea that tumors must recruit blood vessels to feed themselves is well established and accepted today, this was not always the case. Pulling from a massive collection of original documents and personal interviews with Folkman himself, Cooke describes Folkman’s struggle not only to conduct his research, but also to establish the basic credibility of his ideas with his fellow scientists. This book is a thorough introduction to the field of tumor angiogenesis, a motivational tale for all of us struggling with our own research, and, above all, a beautiful tribute to a persistent, unfailing scientist. I hope the reader will find this story as inspirational as I have, and have their passion inflamed by its message.

Molecular Graphics in Blender

By: Kailin Guo

Hello, Kailin here! I led the Molecular Graphics in Blender workshop at the NIH Research Festival this year. In case you missed it, Blender is a completely free and open-source 3D software! It's a generalist program that can handle not only modelling and animation, but also simulations, video editing and compositing, and more. Its power is boosted by a wide range of both free and paid add-ons which are written by various third parties. These enable all kinds of functions that don't "come stock," from allowing you to better organize your workspace, to simulating more realistic fluids. In particular, the Molecular Nodes add-on is useful for biochemists and structural biologists—it allows you to import Protein Data Bank (pdb) files, the standard file format for atomic coordinates, as well as a range of other structural biology file types directly into Blender. By directly utilizing the atomic coordinates, you save hundreds of vertices which would otherwise have been used to define the curvature of a ball or ribbon—which makes life much easier. In addition, it gives you the ability to dynamically select representation styles in Blender without having to reimport 3D objects from ChimeraX or Pymol, which can be computationally demanding and time consuming. Blender can also display electron density maps generated from cryoEM or X-ray crystallography, and it can even play and render molecular dynamics (MD) trajectories or morphs between different states to give realistic motion to your protein of interest. By better representing motion and relation in 3D space, you can help your audience more intuitively understand the unique challenges and implications of your work. If you haven't already, I highly recommend giving Blender a go! I'll be posting the recording of the workshop to the NIH 3D Youtube channel soon, so please check it out if you're interested! Brady Johnston is the creator of Molecular Nodes, and he has a very detailed guide on his GitHub as well.



Render of a crystal structure of the TrkH-TrkA complex (PDB: 6V4K), colored by distance from an arbitrary point and lit in Blender, offering ability to focus your audience's attention on structures or interactions of interest.

As for the workshop itself, I think it went well! It's really important to hit the ground running when approaching a software with a steep learning curve, or it's easy to lose momentum and motivation. When I first started using Blender, it used to take me hours to set up the most basic scene—loading some proteins into a nanodisc, and a quick spin to show off the assembled complex. What I didn't know was that there were easier ways to move things in

3D space than dragging them around in the plane of the screen, then rotating the viewport to change the directions available for manipulation. I also didn't know that instead of haphazardly dragging objects together and hoping you didn't make a mistake when keyframing, you could just have one object "parent" the others, and tow them around. Though the more complicated programmatic aspects of Blender are exactly that, complicated, they are also incredibly powerful. The use of nodes, Blender's built in drag-and-drop coding system, gives you the ability to automate and procedurally generate many complex effects that would be difficult to manually create. While Blender is quite resource-intensive for final renders, it also provides a lot of less demanding options as well for rapid prototyping of materials and animations. I did manage alright on my government-issued laptop (no GPU in sight), the renders just took a while to complete. If you have any questions about using Blender for your work, please feel free to reach out at kailin.guo@nih.gov!

Office of Intramural Training & Education Resources for Pre-med Postbacs at the NIH

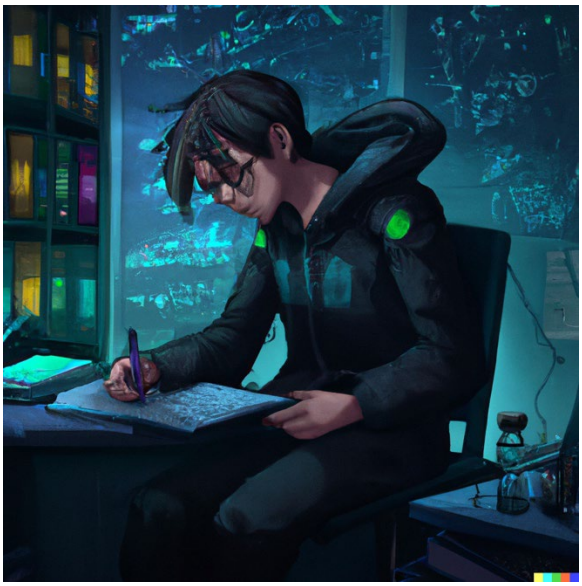
By: Varvara Folimonova

The Office of Intramural Training & Education (OITE) offers informed guidance and useful training opportunities for fellows and trainees in the NIH Intramural Research Program. They offer many resources for career readiness, communication, ethics and responsible conduct, teaching and mentoring, leadership; management; and diversity, equity, inclusion, and accessibility, as well as well-being and resilience. Further details can be found on their website: https://www.training.nih.gov/.

When I started my postbac at the NIH, I hadn't realized how great of a resource the OITE would be for my journey to medical school. Applying to medical school is an arduous process that involves taking the Medical College Admission Test (MCAT), filling out the medical school application and submitting a personal statement, writing multiple secondary essays for each school, and participating in interviews. This application process starts in May and lasts roughly one year until applicants receive

decisions from schools. The guidance I received from OITE pre-med advisors and workshops helped me to understand the specific steps of applying to medical school and the qualities that admissions committees may look for in applicants.

I highly recommend meeting with an OITE pre-med advisor as early as possible. By meeting with an advisor, I received informative feedback on my resume, and I realized that I needed to gain additional experience in community service and shadowing physicians. I was able to gain such experiences in parallel to my research position.



DALL-E 2 output for 'pre-med student studying for an exam, cyberpunk, digital art'.

Halfway through the first year of my fellowship, I attended the "Choosing and Applying to Medical and other Professional Schools" workshop. I was taken aback to discover the differences in acceptance rates for medical school between applicants from within the state and those from out-of-state. This workshop also assisted me in identifying crucial criteria for selecting medical schools that align with my priorities as I prepare my list of prospective applications for the upcoming year.

The personal statement writing course is another resource offered by OITE pre-med advising that I would recommend for every pre-med to participate in. This course was especially helpful in training prospective applicants in writing impactful personal statements. At the end of the course, an advisor read my

statement and gave me crucial feedback to refine my writing.

In addition to this, I also participated in a few additional workshops to receive guidance on each step of the medical application process – these included, “Tips on Filling Out Your AMCAS (American Medical College Application Service) Application,” “Secondary Applications,” and “Interviewing for Medical and other Professional Schools”. During these workshops, I learned about specific submission deadlines to be aware of, strategies for writing effective secondary essays, and common topics to be prepared to discuss during interviews. The OITE advisors have been very supportive and offered helpful insight for my application. I hope that sharing my experiences with the OITE pre-med advising services will encourage other pre-med postbacs to seek out these useful resources as well, which can be found at: https://www.training.nih.gov/career-services/educational-advising/pre-medical-and-professional-school/.

Exploring the connection between IFITM3 and the mTOR pathway

By: Isaiah Wilt

In Dr. Alex Compton's lab, much of our work centers on understanding the mechanics of innate immune factors that work to restrict viral entry. Interferon-induced transmembrane proteins (IFITMs), a subclass of the CD225 superfamily, consist of five members: IFITM1/2/3/5/10 [1,2]. Of those, IFITM1/2/3 are of great interest to us. These IFITM proteins are front-line defenders that restrict membrane fusion between incoming virus particles and cellular surfaces, including the plasma membrane, early endosomes, late endosomes, or lysosomes [1]. A recent project looked at IFITMs in cells where mechanistic target of rapamycin (mTOR) activity was inhibited by rapamycin or rapalog treatment. This work was led by Dr. Guoli Shi and found that cells treated with rapalogs led to the degradation of IFITM2/3 resulting in increased cellular susceptibility to SARS-CoV-2 and influenza A infections [3,4].

In the Compton lab, my research focuses on exploring regulatory roles of IFITM3 on the mTOR pathway. We have data showing knockdown of endogenous IFITM3 results in a decrease of Akt phosphorylation at Ser473, a known phosphorylation site of mTROC2 [5], suggesting an involvement of IFITM3 in the activities of mTORC2 and Akt. My on-going work will center on further elucidating the direct and indirect effects IFITM3 may have on upstream players (eg. mTORC2 and Akt) and downstream targets (eg. mTORC1).

Under homeostatic conditions, the mTOR signaling cascade functions to regulate healthy levels of cell growth and survival [6]. Following an influx of amino acids, oxygen, and/or growth factors, Akt (Protein Kinase B) is phosphorylated by either PI3K-PDK-1 or mTORC2 kinases [6]. Active Akt in-turn inhibits the activity of the tuberous sclerosis complex, resulting in inhibition of Rheb [6]. This leads to the release and activation of mTORC1 on lysosomal surfaces and the promotion of downstream anabolic processes, including lipid, nucleotide, and protein synthesis [6]. With mTOR having such intricacies and a high level of importance to the cell, what are the implications if something goes wrong?

On the Chilean island of Rapa Nui (Easter Island), a compound was isolated with immunosuppressive and antiproliferative properties of which was later found to inhibit the activity of mTORC1, this is where mTOR takes its name (mechanistic target of rapamycin) [7,8]. Rapamycin binds to two host proteins (FK506 binding protein (FKBP) and mTOR) resulting in a three-way mTOR-FKBP-rapamycin complex that renders mTOR inactive [7,9]. The mTOR pathway has been extensively studied in the context of cancer [7]. Hyperactive mTORC1, a phenotype associated with tumorigenesis and cancer progression, has been found to be caused by mutations in upstream players, such as PI3K or Akt, or factors associated with nutrient sensing [6,7]. Various rapamycin analogs, also known as rapalogs have been developed and are being used clinically to treat cancers linked with abnormal mTOR function [3,7]. With the mTOR signaling cascade being an optimal target for cancer therapy, a scientific quest has begun to better understand this signaling cascade and key regulators. It will

be interesting to further explore this relationship between IFITM3 and the mTOR pathway in a cancer model.

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Being a clinical fellow in Bethesda

By: Dilara Akbulut

When I moved to Bethesda to embark on a career as a clinical fellow, the only connection I had to the city was that the guidelines we use in our daily pathology practice was named after it. I did not anticipate how pretty this small town would be in all seasons and what a rewarding experience awaited me on this journey.

Located in the heart of Maryland, Bethesda is home to not only the National Institutes of Health (NIH), but also other prestigious medical institutions such as the Walter Reed National Military Medical Center, Holy Cross Hospital and the Joint Pathology Center. Being part of the NIH opens the doors to rotate in not only these institutions but also other nearby academic centers (such as George Washington University and Johns Hopkins University). After medical school, following a residency training is the standard way to pursue a subspeciality. In most instances, fellowship training would be the next step to further focus on one's interested niche area. The NIH has many clinical fellowship programs, including specialties such as internal medicine, surgery, neurology, psychiatry. They also provide a few residency programs, including my specialty, pathology. The NIH is world-renowned for being at the forefront of groundbreaking research, so clinical fellows here naturally find themselves becoming a part of exciting medical breakthroughs. Medical school graduates choosing to be trained here have the chance to follow the most updated treatments and clinical trials.

As a pathology resident, I'm part of patient care at the Clinical Center and my daily routine includes grossing specimens/biopsies from patients, reviewing the glass slides at the microscope, performing autopsies, and preparing diagnostic reports to guide treatment options. Here at NIH, we receive a unique set of rare cases which gives an opportunity to master diagnoses that would be a rare instance for everywhere else.

From the start, Laboratory of Pathology, including the clinical and research community, has been welcoming, collaborative, and generous in providing additional learning opportunities. As a member of this vibrant community, I have the privilege of working alongside the brightest minds in healthcare and gaining exposure to cutting-edge research and medical advancements. There are various occasions where I get to directly interact with other providers regarding a case in our daily routine; one of them is the tumor board which includes attendings, fellows and researchers who focus on a specific diagnosis and gather to discuss a patient in depth. Multiple tumor boards happen generally on a weekly basis and give the fellows the chance to meet with other clinical providers, to work with diverse patient populations, and to discuss possible research ideas. Clinical fellows may be assigned or choose a mentor within the department, who will guide them through their work, considering fellow's interest and skills. Mentorship acts not only during the training but also beyond it, by guiding fellow's future career options. NIH is the ideal place for academic thriving for clinical fellows who have already decided to pursue a career in this unique environment.

Not infrequently, it can be challenging to maintain the work-life balance while managing clinical duties and the research responsibilities. The NIH Office of Intramural Training and Education (OITE) provides fellows with

resources to deal with this hardship. They offer fun, non-work activities such as mindfulness meditations, monthly hikes, and more. Educational seminars related to managing workplace stress, job searching, applying to advanced degrees, and workplace communication are also available. Other than the official resources for managing clinical fellow life, living in or around Bethesda helps to deal with the stress of academic life. NIH campus, filled with lots of green, deer and duck families, and is walkable to downtown Bethesda.

Bethesda is also unmatched in its proximity to a vast network of professionals in the DC area, including clinicians, researchers, and policymakers. Many career fairs and scientific conferences are hosted here. This is especially relevant given the growing importance of networking for professional development in this era. After finishing training at NIH, many career paths are available in academia, private practice, pharmaceuticals, the FDA, and other government organizations. Being able to follow the most updated clinical practice gives the chance to develop skills valid in any other institution and one could carry those skills to anywhere based on their preferences.

As I reflect on my past year and a half in the NIH clinical fellow program, I remember how much I have learned with the support of my mentors and colleagues, who gave me the motivation to succeed here. Belonging to a community with a shared passion for science is indescribable and I have no doubt my training at the NIH will guide me throughout my future endeavors.

Katalin Karikó: A life devoted to science

By: Omar Jose

The 2023 Nobel Prize in Physiology or Medicine was awarded jointly to Dr. Drew Weissman and Dr. Katalin Karikó for the discovery of the mRNA-based technology that allowed the development of the two most effective vaccines against COVID-19. Millions of doses of these vaccines have been administered in the US and around the world, and countless lives have been saved.

The immigrant behind the scientist

Dr. Karikó was born in Hungary and from an early age she had a clear interest in nature. She earned her bachelor's degree in biology in 1978 and her doctorate in biochemistry in 1982 from the University of Szeged, where she later worked as a postdoctoral fellow at the Biological Research Center. In 1985, her lab lost its funding, and Dr. Karikó had to look for work at institutions in other countries. She accepted a position as a postdoctoral researcher at Temple University in Philadelphia in Dr. Robert J. Suhadolnik's lab. Thus, she left Hungary for the United States with her family. In 1988, she accepted a job at Johns Hopkins University and in 1989, she got another job as a research assistant professor with Dr. Elliot Barnathan at the University of Pennsylvania, where her research focused on mRNA. "In 1997, Dr. Barnathan left the university for a position at a biotech firm, and Dr. Karikó was left without lab and financial support. She could only stay at Penn if she found another lab" [1]. After Dr. Bernathan left, Dr. Karikó was helped by a colleague, David Langer, who convinced the chief of Penn's neurosurgery department to hire Dr. Karikó as senior head of research.

Dr. Katalin Karikó with a statue of the fellow Hungarian Nobel Prize winner Albert Szent-Györgyi. Photo credit - Szegedi Tudományegyetem, Wikimedia Commons.

A breakthrough discovery

Even at the early stages of her career, Dr. Langer was confident that Dr. Karikó would eventually make substantial contributions in the field of mRNA because he esteemed her intellect and resilience. Not long after, Dr. Karikó met Dr. Drew Weissman, a professor of immunology at the University of Pennsylvania, and they initiated a collaboration to study mRNA technology. "Both researchers were interested in using mRNA to stimulate the development of immunity against viral pathogens in the body. While conducting experiments on dendritic cells, they discovered that *in vitro* transcribed mRNA is highly immunogenic and led to the activation and release of inflammatory signaling molecules. They wondered why the *in vitro* transcribed

mRNA was recognized as foreign while mRNA from mammalian cells did not produce the same reaction" [2]. Dr. Karikó and Dr. Weissman suspected that there must be some essential properties to differentiate both types of mRNA. They were aware that the mammalian cell RNA bases were frequently chemically modified. However, the *in vitro* transcribed mRNA is not. Could the absence of those modifications be responsible for the inflammatory reaction? "To investigate this, they produced different variants of mRNA with unique chemical alterations in their bases, which they delivered to dendritic cells" [2]. The results demonstrated that the inflammatory response was nearly eliminated when base modifications were included in the mRNA. "This breakthrough resulted in a technology known as non-immunogenic, nucleoside-modified mRNA, which was developed and patented in 2005 by Dr. Karikó and Dr. Weissman" [3]. Shortly after, the researchers founded RNARx, a company that aspired to commercialize this technology, and some years later they licensed the technology to the companies Moderna and BioNTech. "In 2013, Dr. Karikó took a position as a senior vice president at BioNTech, overseeing the company's work on mRNA. In the following years, although both companies had multiple RNA therapeutics in clinical trials, none had yet proved successful" [3].

The mRNA technology and the COVID-19 pandemic

During the COVID-19 pandemic, the scientific community faced the urgency to develop a vaccine that could decrease the symptoms produced by SARS-CoV-2. The mRNA vaccines can be developed relatively quickly, which is a major advantage over traditional vaccines. For that reason, shortly after obtaining the genetic code of the virus SARS-CoV-2, Moderna and Pfizer-BioNTech were able to generate mRNA vaccines ready for trials. Protective effects of around 95% were reported, and both vaccines were approved by the FDA as early as December 2020.

What's next? mRNA vaccines for every infectious disease

"While the first mRNA vaccines to be approved were used for COVID-19, similar vaccines are now being explored for many other diseases. Moderna is currently developing mRNA vaccines for RSV, HIV, Zika, and Epstein-Barr virus. On the other hand, BioNTech is exploring vaccines for tuberculosis, malaria, HIV, shingles, and flu. Both companies are working on treatments for cancer, and many other companies and labs around the world are getting in on the action" [4].

Dr. Karikó is now the head of RNA protein replacement therapies at BioNTech. She has received more than 130 international awards, including the 2023 Nobel Prize in Physiology or Medicine, and honors for her pioneering and globally significant work in biochemistry.

Resources

[1] The New York Times.

[2] The Nobel Prize

[3] Britannica

[4] MIT Technology Review

Katalin Karikó's autobiography "My life in science"

A phone call interview Karikó (her first reaction) right after she was awarded the Nobel Prize.

Get to Know the Frederick Diversity Committee

By Hana Veler

The Frederick Diversity Committee (FDC) is an organization composed of a diverse group of fellows (postbaccalaureate fellows, graduate students, postdocs, and other research fellows) committed to fostering scientific excellence and empowering tomorrow's scientific leaders at NCI-Frederick. The FDC offers members valuable mentorship, networking, and career development opportunities to enable them to organize workshops, seminars, and social events that serve the broader NCI-Frederick community. The committee strives to unite fellows from different disciplines to broaden the research community and strengthen work-life balance. One way the committee accomplishes this is by hosting social events for NCI fellows, their families, and their friends.

Spring 2023 FDC hike at Sugarloaf Mountain.

Spring 2022 FDC hike at Maryland Heights, Harpers Ferry National Historical Park.

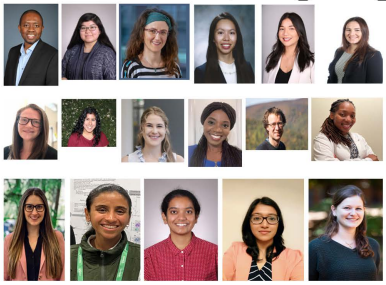
Activities include local hikes, bowling, meet and greets at downtown breweries, and potluck lunches. Our hiking socials are among our most frequent and most attended social events. Fellows are encouraged to bring their loved ones to social events to learn more about each other and their families; we think this is especially important for new fellows just starting to build their community.

If you are interested in attending one of our events, we host one social event bimonthly. We hope to enhance the committee activity by getting more fellows involved with the FDC. We welcome anyone who wants to either oversee or share their ideas for the upcoming activities to reach out to Hana at hana.veler@nih.gov. We are excited to see you all at our next social event in 2024!

Activities of Interest for Fellows

Join the Fellows and Young Investigators Steering Committee!

Are you interested in networking with other fellows, exploring careers in science, gaining marketable skills, or giving back to the community?



Who can participate?
We welcome postdocs, postbacs, graduate students, research fellows, and clinical fellows.

Meetings
The last Thursday of every month at 4:00PM via MS Team

Check out our website!

Open leadership positions!

- Outreach Chair
- FYI-Seminar Series Chair (Frederick)
- Frederick Social Chair
- E-Communications Chair

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SRK Program Elements

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For more information:

https://www.cancer.gov/grants-training/training/at-nci/srk

NIH NATIONAL CANCER INSTITUTE Center for Cancer Training

Frederick Diversity Committee FDC

Frederick Diversity Committee

Promoting Diversity

FDC Mission and Goals:

Celebrate diversity and inclusion on the Frederick campus

Promote productivity, work-life balance and career satisfaction

Meetings:

every 3rd Friday of the month at 1pm

Benefits:

Personal and Professional Development

Career Exploration and Enrichment

Networking

Mentorship

More information can be found at https://ncifrederick.cancer.gov/Diversity

NanCI by NCI – Connecting Scientists

NanCI is an AI-powered app that connects you to interesting science and scientists to build your career.

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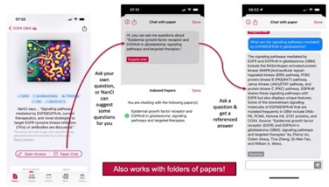
- Find and follow authors, and if they are on NanCI, connect with them.

Chat with Papers



- Interact with open-source papers or a folder of papers via an AI-driven chat: ask questions and see referenced answers based on the content of the paper(s).
- Select text in a paper and ask NanCI to explain it at different expertise levels (from five-year-old, to college student to expert)

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On NanCI's Roadmap

- Social - users interact on the app and easily form groups around shared interests, including closed groups with a private folders
- Expanded view of the world of science with other data sources, like grants
- Jobs: connecting job opportunities to the literature – imagine that when you see a paper you would also see the authors' lab have a postdoc position open.

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