Program in Cellular and Molecular Medicine
at Boston Children's Hospital

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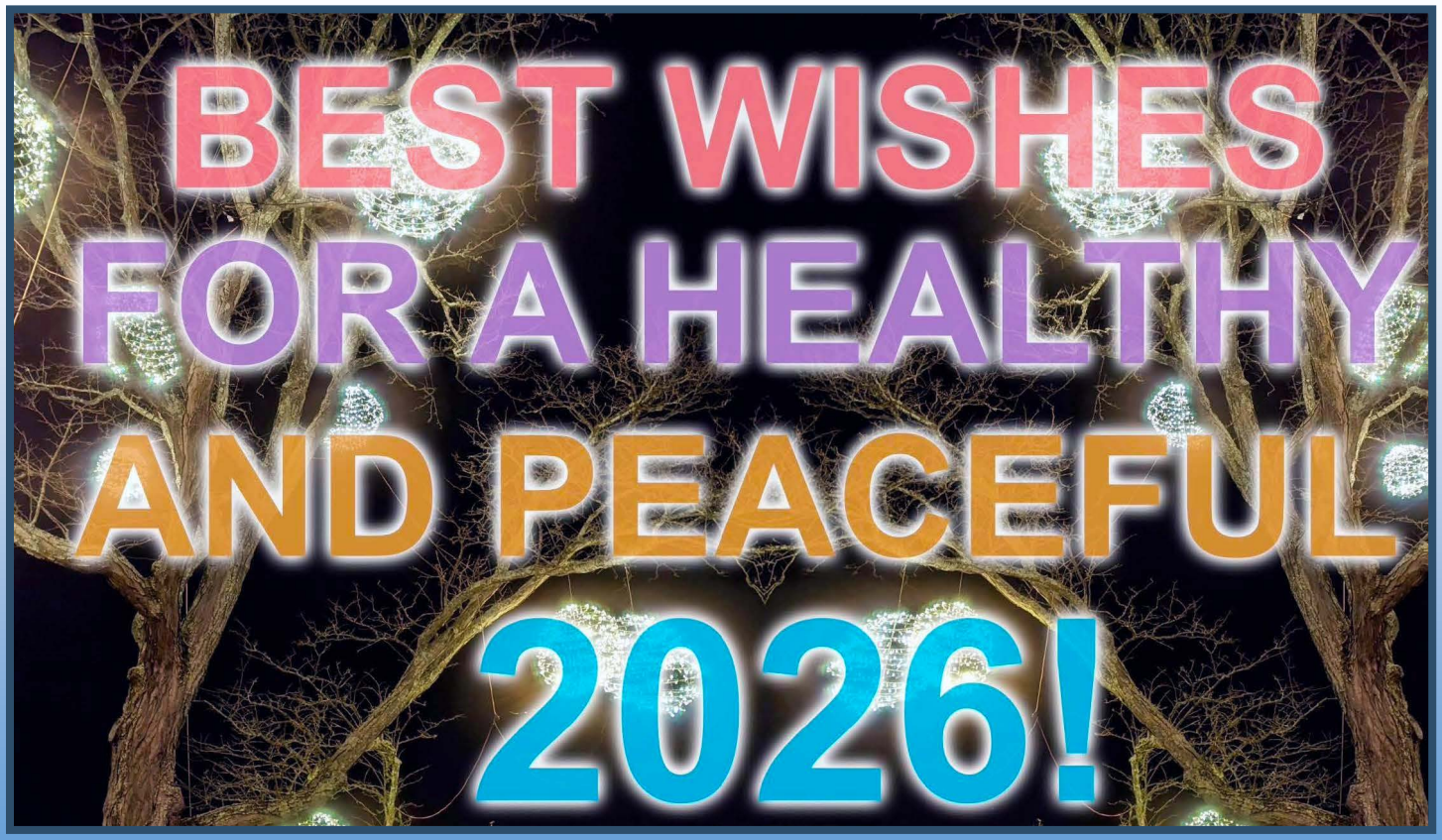
Greetings, PCMM,

We hope that everyone has a good end of the year! In this issue, we'd like to start featuring visiting seminar speakers and the insights they share during lunches with PCMM trainees. We start with Dr. Feng Zhang of MIT.

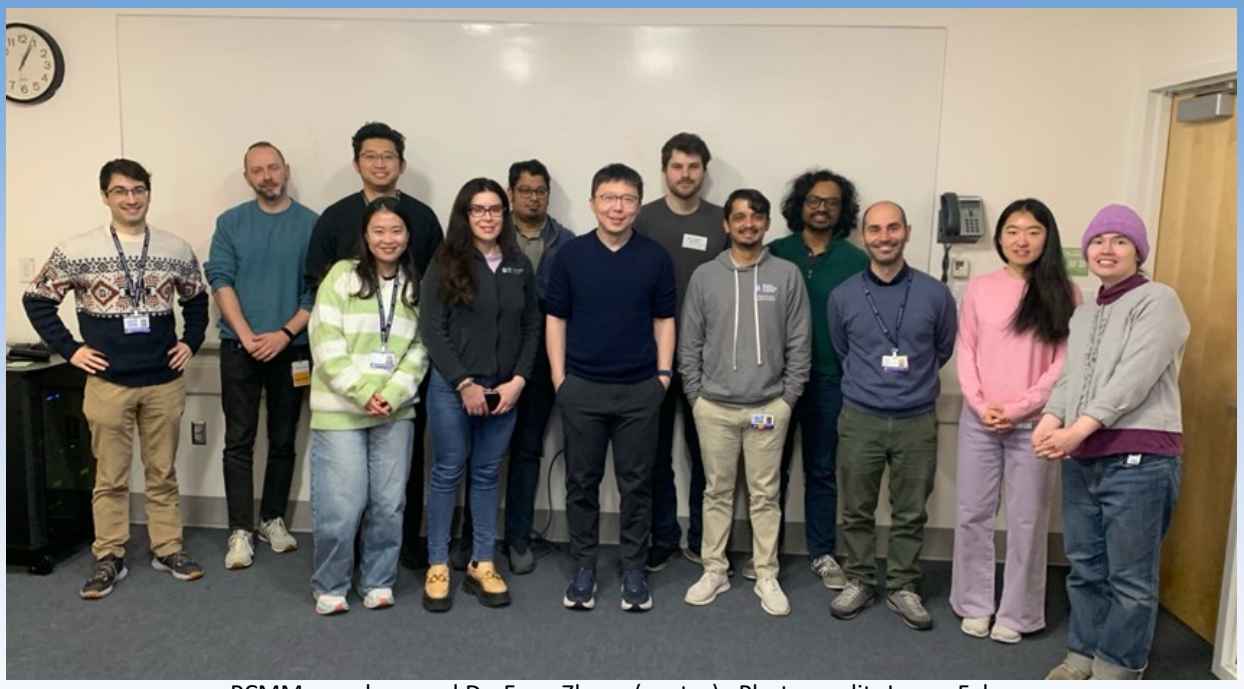
As always, if you have any suggestions for the newsletter, please contact us at vera.gaun@childrens.harvard.edu.

In this issue

Happy New Year!



Lunch Conversations with Seminar Speakers



PCMM members and Dr. Feng Zhang (center). Photo credit: James Falvo.

On November 20th, Dr. Feng Zhang of MIT and Broad Institute visited PCMM to give a seminar titled "Exploration of Biological Diversity." As part of his visit, he had lunch with PCMM trainees and shared his thoughts on a variety of topics:

On his scientific journey: Dr. Zhang conducted undergraduate research at Harvard in Dr. Xiaowei Zhuang's lab and went on to Stanford for his PhD. Initially, he was looking to join Dr. Steven Chu's lab, however by that time Dr. Chu became the U.S. Secretary of Energy and moved his lab. Coincidentally, when Feng Zhang stopped by Dr. Chu's office, Dr. Karl Deisseroth occupied that office. They discussed potential research topics, and the rest is history (of optogenetics' origin). Dr. Zhang describes this meeting as a "serendipitous moment." However, might we also suggest this as a case of "luck favors the prepared mind?"

On the makeup of his lab: As it's more difficult to recruit postdoctoral fellows upon starting one's lab, originally Dr. Zhang's lab consisted mainly of graduate students, and he worked alongside them while also training them - he emphasizes the importance of training your nascent lab well. Now he has a roughly 50/50% makeup of grad students and postdocs. Dr. Zhang appreciates the "different" energy of graduate students and the deep expertise of his postdocs. Idea generation comes naturally to Dr. Zhang – he connects ideas by reading research in different fields, and he welcomes collaboration in his lab.

On choosing the right people: Dr. Zhang did acknowledge the difficultly of this aspect, mentioning that "bad hires" do happen from time to time, and it's important not to hire more people just for the sake of hiring more people – there needs

to be a good fit. The dynamics of a research laboratory are important, and one person that's not a "good fit" can negatively affect the whole team. Thus, for the recruitment process, Dr. Zhang spends a considerate amount of time with each applicant, first on Zoom, and then in-person. He asks them how they would approach certain problems, to gauge how they think. He also considers reference letters and has the entire lab meet with the candidate. Additionally, Dr. Zhang mentioned that for him, a few good papers on the applicant's C.V. might outweigh having just one top tier paper - this shows that the applicant has mastery of going through the scientific method.

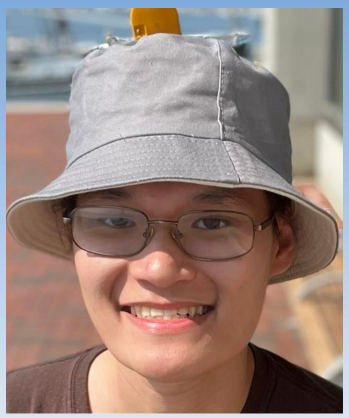
Dr. Zhang also added that biotechnology company investors [just like the Howard Hughes Medical Institute in the academic world] often value "people over project," meaning that a project idea can be excellent, but if the team is not "gelling" together, the project might not get anywhere. Conversely, the project idea might not be the greatest, but great team members can elevate the outcome.

On helping his trainees choose postdoctoral labs: Dr. Zhang meets with his trainees twice a year to go over career goals (in addition to the regular scientific update meetings). For quite independent graduate students, he advises to join a well-funded lab for a postdoc. Also, a lab's track record of producing faculty is indicative of potential future success: i.e. a lab that produces a new faculty member every year might be more favorable than a lab minting new ones every 5 years. For graduate students who might need a little bit more guidance, he suggests joining a smaller lab, where they can receive additional mentoring and training to enhance their skills and C.V. Additionally, working on a mechanism-based project can be a good choice.

On future innovations: Having significantly transformed the field of CRISPR-based genomic editing and seeing the field having matured, the Zhang lab is now wrapping up genetics research and shifting focus to research on tissue and organismal homeostasis maintenance. While Western medicine places a heavy focus on treating diseases as they have developed, another viable angle is a more of an Eastern medicine/holistic approach, i.e. maintaining homeostasis to begin with. One current focus in the lab is "boosting" the immune system, which declines with age, to hopefully enhance overall systemic function.

We thank Dr. Zhang for taking time out of his busy schedule to meet with PCMM trainees and share his insights! We'll be collecting more perspectives from visiting PCMM speakers in the future.

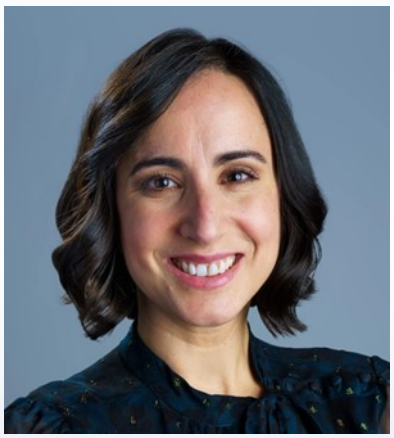
PCMM Researcher Wins a Prestigious Fellowship



Xincheng Yuan, a graduate student in Sua Myong's Laboratory, has been awarded an NIH F31 Ruth L. Kirschstein Predoctoral Individual National Research Service Award. Xincheng's research focuses on Fused in Sarcoma (FUS), an RNA-binding protein implicated in several age-dependent neurodegenerative disorders, including amyotrophic lateral sclerosis (ALS) and frontotemporal lobar dementia (FTLD). His work investigates the molecular mechanisms governing FUS nucleolar translocation during transcriptional stress and DNA damage, and how disease-associated ALS/FTLD mutations disrupt these stress-response pathways. Ultimately, his research aims to provide insight into how impaired FUS dynamics contribute to the pathogenesis of neurodegenerative diseases.

Alumni Careers

Principal Scientist in Biotech Industry: Dr. Ângela Crespo



This month, Dr. Ângela Crespo, a former postdoctoral fellow at Dr. Judy Lieberman's lab, shared some thoughts on working in biotech industry, from her current role as a Principal Scientist at Dragonfly Therapeutics.

Dr. Crespo is originally from Portugal and attended the PhD Programme in Experimental Biology and Biomedicine at the University of Coimbra, where she received a scholarship from the Portuguese Foundation for Science and Technology to travel anywhere in the world to work on her PhD thesis. Her interest in immunology of pregnancy led her to Dr. Jack Strominger's lab for her PhD, and subsequently to Dr. Judy Lieberman's lab for her postdoc. Dr. Crespo's postdoctoral work resulted in a *Cell* publication on the immune system during pregnancy, on which she comments: "This high-profile publication did help me land a job in the biotech industry. Although it's true that publications do not have the same weight in biotech and pharma job applications as they do in academic job applications, high impact publications are a testament to our scientific and project managing skills which are also highly regarded in biotech and pharma."

On the application process for biotech company positions: As mentioned, Dr. Crespo ultimately chose to go into biotech industry, since she wanted to have a more immediate effect on treatments for diseases. She started looking for an industry position in 2021, when the job market was strong (not as much at the moment, unfortunately). She interviewed with many companies and got many offers, and ended up at Dragonfly Therapeutics in a circuitous way. One of the companies at which she interviewed told her that a former postdoc

of Judy Lieberman's had worked there. Dr. Crespo has not previously met this person, but she reached out – this person ended up introducing a different company, Dragonfly Therapeutics, to her and gave her resume directly to Dragonfly. Thus, this is a great story of the power of networking!

On choosing the company: Dr. Crespo chose Dragonfly Therapeutics based on her background – she had expertise in Natural Killer (NK) cells, which fit well with the company's work. Additionally, the company's size fit her – she was interested in a medium-size company where she could interface with different departments (strategy, clinical, business, etc.) and learn non-bench aspects in addition to her research role. (A startup, on the other hand, would be very intense and all-hands-on-deck type of role, and a pharmaceutical company would probably present more of a specialized and siloed role with less learning opportunities across departments).

On the biotech-specific aspects of her role: In the company, Dr. Crespo learned a lot on project management and strategy aspects, such as derisking – figuring out potential drug pitfalls and designing experiments to address them at the beginning stages of basic research. Another important aspect Dr. Crespo learned was to not get too attached to different projects, as some projects get "killed," not because of unsound science, but a switch in company's strategy and direction. For example, a similar type of treatment/drug by a competitor might be further ahead in clinical trials, but is resulting in serious adverse side effects, so if the own company's drug focuses the same target, it could make sense to stop the project without wasting any further resources. Similarly, priorities change, so one might have to switch focus to more time-sensitive projects. Another different aspect is that while in academia each researcher is mostly responsible for their own project, in industry different teams interface for various projects. For example, a team can be responsible for protein generation only and provide necessary proteins for other teams. Finally, achieving work-life balance is often easier in biotech industry as compared to academia.

On Dr. Crespo's mentorship organization and similar resources at BCH: In addition to her research work, Dr. Crespo has created a Ciências Alumni Mentorship Program back at her alma mater in Portugal. Mentorship programs are very common in U.S., but not necessarily in other countries. With her program, Dr. Crespo is "importing" mentorship practice to her alma mater, where students get paired with alumni and learn about how the alumni got to where they are today.

While Dr. Crespo didn't go through a formal mentorship program herself, she did connect to the Office of Postdoctoral Affairs at Boston Children's to get help with her resume and interviews. Additionally, Dr. Crespo networked and conducted informational interviews, which are very useful in the career development process - informational interview coaching is also offered by the Office of Postdoctoral Affairs.

We thank Dr. Crespo for finding the time to share her insights! We will continue to connect to PCMM alumni for their perspectives.