

The 2022 generation

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Twelve early career investigators share experiences from the process of starting their laboratories throughout the past year, and reflect on the challenges faced and the opportunities seized.

A surgeon–scientist’s perspective on establishing a laboratory



Mautin Barry-Hundeyin:

I made the unconventional decision to become a surgeon–scientist after spending three transformative years completing a postdoctoral research fellowship in tumor immunology.

As much as I enjoyed taking care of patients, it became increasingly clear to me that to make a broader impact, the most difficult oncological problems must be tackled in the laboratory. My ongoing pursuit of impactful discoveries continues to be inspired by my patients.

Earlier in 2022, following completion of surgical oncology training at Memorial Sloan Kettering Cancer Center, I accepted a position as a surgeon–scientist at the University of Kentucky Markey Cancer Center. Clinically, I specialize in gastric and hepatopancreatobiliary malignancies, and my laboratory focuses on understanding innate immune regulation of the tumor microenvironment. We seek to leverage the plasticity of tumor-associated macrophages in pancreatic cancer and gastric peritoneal carcinomatosis to identify novel vulnerabilities for immunotherapy.

As an early career surgeon–scientist, it can be challenging to balance the duality and intersection of the operating room and the laboratory. Building a clinical practice while simultaneously developing a research program may seem insurmountable. In anticipation of becoming a principal investigator, I formulated short- and long-term goals, potential projects and specific

aims 1–2 years before the laboratory’s inception. Similar to my favorite dessert, a tiered wedding cake, I organized my professional priorities into six tangible tiers. Tier 1 is comprised of the foundational components typically negotiated during the hiring process. This includes protected time for research, departmental financial support with the provision of start-up funds, and establishing institutional commitment. Tier 2 consists of building an academic village – a symbiotic ecosystem of mentors, collaborators and laboratory staff. Actively cultivating relationships, building collegiality and selecting compatible team members with a shared vision for excellence have been invaluable. Tier 3 involves building the laboratory infrastructure, obtaining regulatory compliance and budgeting. Tier 4 encompasses the core of the scientific process—performing experiments, gathering data, writing grants and preparing manuscripts. Tier 5 is comprised of participating in professional development opportunities to facilitate scientific growth and national visibility. Finally, and often overlooked, is the ubiquitous tier of maintaining a healthy work–life balance. It is important to recognize that this journey is a marathon, and prioritizing well-being is crucial to make it to the finish line.

Increasing diversity in cancer genomics



Jian Carrot-Zhang:

When I opened my lab at the start of 2022, I asked the same question as many principal investigators: “where have all the postdocs gone?”. Undoubtedly, the pandemic impacted the research trajectories of many

PhD students, increasing the reluctance of many to take risks for a faculty position that could not be guaranteed. But postdocs are essential for junior faculty to explore new research directions. In addition, when faculty struggles with hiring, this is likely to reverberate and subsequently affect decision making

for PhD students to stay in academia – thereby generating a vicious circle.

I started my group with a bioinformatics engineer and a computational biologist. I am fortunate that I was able to recruit several brilliant minds quickly, thanks to my colleagues – the computational oncology group here at Memorial Sloan Kettering Cancer Center. They created a collaborative, interactive, creative, inclusive and friendly environment that convinces young researchers, like myself when I accepted the junior faculty position a year ago, that this is the place to do great science. But it took me almost a year to find postdocs. I cannot remember how many conference poster sessions I went to and how many PhD students I spoke to – as a mother of two children, traveling is challenging. But what I remember well is that when my first postdoc signed the offer, I was incredibly happy that I could now expand the research horizon of our group.

I am also thrilled that the people who joined my lab are there for the research that we are doing. They are curious about why we still do not know the genetic and environmental determinants of acquiring different somatic alterations in tumors. They see one of the biggest gaps in the field, namely that we are not sequencing enough patients with cancer of non-European ancestries, and want to be part of the work to improve diversity in the field of cancer genomics. Our goal is to ensure precision oncology for all, and the biology revealed from cancers with non-European ancestries is not only fascinating in its own right, but also essential. After my first year as a principal investigator, I realize that I am not just a mentor or supervisor – everyone in my group is my inspiration.

As a community, we still have a long way to go to take better care of our postdocs, students and staff scientists – we need to help them cope with stress, practice work–life balance and achieve their career goals. Yes, academia can be competitive, but every postdoc deserves to enjoy being a postdoc. The pandemic reminded us that the core of research is the people, and that we need to appreciate each other’s contribution and support one another more than ever.

Getting comfortable with being uncomfortable



Talya Dayton: On 31 October 2021, I submitted my first application for a position to lead an independent research group, with a focus on the use of organoids to study neuroendocrine cells and cancers. At the time, I did not know

what to expect and I certainly could not have imagined what lay ahead of me. Between faculty interviews, preparing manuscripts from my postdoctoral work, moving to a new country and transitioning to my role as a group leader at EMBL Barcelona, 2022 has been a whirlwind.

Throughout this past year, we have all faced many challenges, and I am sure that 2023 will have its share of new ones – many undoubtedly related to the energy crisis being experienced by many European countries, and to lingering supply chain and public health issues related to the COVID-19 pandemic. But as I reflect on the past year, I want to focus on two key ideas that have held true for me.

The first idea is that discomfort is a sign that I am learning and facing new difficulties. When reflecting on starting my research group this year, the challenges that stand out to me include negotiating for the resources that I need to run a successful lab, embracing a new form of visibility, and building confidence in my ability to make the decisions that will shape the future of my group. I am learning to get comfortable with being uncomfortable, and this has been empowering.

The second idea that has held true throughout this year is that, beyond our science, so much of what we do is about the people – fomenting positive interactions and collaborations is a strong driver of progress. When I reached out for help with navigating the faculty application process, I was struck by the generosity of time and advice of not only my mentors and colleagues, but also of other researchers who, in some cases, did not know me well at all. I was also struck by the confidence that I gained from seeing and interacting with successful group leaders and principal investigators who I identify with – especially women of diverse backgrounds. Representation matters.

As my lab begins to take shape, I find myself inspired by the excitement of my new lab members. Their curiosity is such a strong motivator. It is a privilege to have the opportunity to

lead a research group, and I look forward to what the future holds.

A year in flux



Shila Ghazanfar: I wrapped up my postdoc in Cambridge, UK, and started my independent career as a group leader at the University of Sydney, Australia, in May 2022, with a mission to use technical capacity and methodological

creativity to solve emerging data problems in biomedical research. Key projects in my lab include the development of statistical approaches and computational tools for multiscale data integration of spatial genomics at single-cell resolution.

While we collectively dealt with the pandemic, technological advances in biotechnology powered along. Currently, there is an urgent need to develop novel analytical techniques and data infrastructure to examine high-dimensional spatial genomics beyond single samples, especially in the context of characterizing tumour microenvironments in complex experimental scenarios.

There has never been a more exciting time to do global science. Online workspaces lower the barriers to communication with existing and potential collaborators, and virtual conference options make it easier to keep up with the latest research. However, these pandemic-inspired solutions have also exposed a key problem, namely that researchers in the Asia-Pacific region still lose on the timezone lottery more often than not. This presents a dilemma of compromising on a work-life balance to join meetings scheduled for North American or European attendees, or to simply miss out. As it is so easy to lose momentum just by being 'out of sight, out of mind', this is a real challenge – especially for newcomers in the field.

At some points, setting up my lab has felt like an uphill battle. For several months, when recruiting trainees, I was 'my own best postdoc' while simultaneously navigating new research and administrative landscapes. I have lamented that there are not enough hours in the day more often than I care to admit. I am incredibly grateful to my peers and mentors for the support and advice during this time, especially with keeping perspective on what is important: the people and the science.

As I lay the foundations for my research group, I recognize that it takes a village to train and mentor the next generation of scientists. Science is done by people and I highly encourage all trainees in my vicinity to be involved in student and Early Career Researcher-run networks – for example, COMBINE, the student subcommittee of the Australian Bioinformatics and Computational Biology Society and the official International Society for Computational Biology Regional Student Group for Australia. Such support networks make us more creative, more resilient and more fulfilled while tackling important societal challenges in biomedical data science.

Timing is never perfect



Lillian M. Guenther: In three years, I have birthed three babies – two of the human variety and one scientific entity. All have elicited a similar range of emotions, from excitement and anticipation

to rushes of pride and protectiveness, with many feelings of fear and unworthiness in between. Although the idea of opening my own laboratory has been percolating for over a decade – much longer than the notion of the small children who arrived first – my status as a new principal investigator is somehow the biggest jolt.

While the lingering pandemic and its associated challenges have led many oncology physician-scientists out of the academic arena, I was offered an extraordinary chance to flourish. I recently started a laboratory at St. Jude Children's Research Hospital that is focused on the investigation of genomic targets in osteosarcoma, a rare pediatric tumor that has fascinated me since my early medical training. Unique among pediatric cancers, this aggressive malignancy is characterized by a scrambled genome and diverse oncogenic drivers that make it challenging to target. We aim to improve therapies by understanding key unmutated dependency genes identified through CRISPR screening and other modalities. Within my growing team, bolstered by the incredibly rich scientific community in Memphis, the possibility for discovery seems limitless.

Although my scientific vision was always strong, I admit that when this door first opened, I was more focused on infant feedings and stable childcare than on starting a research program. I thought I could not

possibly make the transition with all that life had delivered – an infant and a toddler would have been enough, but the pandemic made everything seem impossible. Thankfully, my grounding forces swept in. First and foremost, this includes my extraordinary mentor – a brilliant physician–scientist, leader and female role model who nurtured my scientific growth and pushed me to consider that I might be ready. The unmatched academic environment in Boston supported me as a trainee and young attending, which enabled me to be confident about my abilities as a physician and a budding investigator. My incredible partner, family and friends propped me up, urging me toward what they recognized as the opportunity of a lifetime. So, although my babies were small and there were projects to finish and papers to write, I took a leap.

This constellation of circumstances is not how I imagined the start of my independent scientific career. I have realized, though, that in science and medicine, timing is never perfect or ideal. Now, as my children – including my nascent laboratory – grow, I can see the steps ahead. From my daughter's first words to my son's first days of preschool, to hiring a postdoc and writing my first R01, I am ready to embrace it all.

Recruiting as the top priority



Diu T. T. Nguyen: RNA-binding proteins (RBPs) are the key players of post-transcriptional processes, modulating RNA stability, modification, localization and translation. They have recently been revealed to be critical

regulators in cancer development, which has led to rapid development of RBP-targeted drugs. Despite the therapeutic potential, the role of most RBPs in cancer is not well understood. My research group is committed to fill this fundamental gap in our knowledge and to exploit post-transcriptional pathways to find opportunities for novel anticancer therapies.

Compared to many colleagues who struggled to start their labs during lockdowns and travel bans, I have been fortunate to establish my team in 2022, where the immediate effects of the COVID-19 pandemic are less evident. However, the lasting effects of the pandemic and Brexit have provided plenty of challenges. I started the year in New York, wondering how

I was going to establish my young family life in the UK while also starting a new role as a group leader. I often told myself that there are so many scientist mothers, and if they can do it, why shouldn't I? Come April 2022, this optimism started to evaporate. Suddenly I found myself struggling to play multiple roles – mother, CEO, CSO and accountant of my own lab, immigration consultant for my employees and even estate agent while doing house viewings for my first technician.

Although my instinct as a scientist is to start doing experiments as soon as possible, the top priority when setting up a new lab must be to recruit. COVID-19, but Brexit even more so, have caused a severe shortage of labour in the UK and has driven overseas talent away. When I arrived, I was shocked to hear that a senior group leader at our institute had received only six applicants for a postdoc position in their lab. After a challenging couple of months, I now feel proud to have assembled a group of highly driven young scientists, with different ethnic and cultural backgrounds. I am very grateful that they chose my lab and believed in my mentorship. Together, we have troubleshooted our initial experiments and celebrated our first successful grant application, and we continue to cultivate an open and collaborative team environment. I am also incredibly grateful for the support of my senior mentors and many faculty members at the Barts Cancer Institute, who always provide invaluable sources of advice and inspiration. Throughout this eventful year, I have treasured friendship and family support more than ever. Being a principal investigator can feel quite lonely, and I feel fortunate to have a close circle of peers who have been through the same experience and with whom I share the same concerns. The past year has been a steep learning curve, but these challenges have helped me to uncover new abilities and a renewed sense of optimism. I now have great confidence that my team and I can realize our potential and together tackle new scientific challenges.

Building a congenial microenvironment



Jason R. Pitarresi: I study cellular plasticity in cancer and have often been astonished by the remarkable ability of tumor cells to adapt to challenges during tumor evolution. My focus is on pancreatic cancer,

where tumor cells are vastly outnumbered by a harsh microenvironment that forces them to find ways to survive in the toughest conditions. Over the past year, while interviewing for tenure-track faculty positions and balancing a young family at home, the plasticity and resilience of my tumor cells inspired me to endure this phase of personal adversity. Starting a lab during a global pandemic has been equally challenging, but my group has persevered, and I am incredibly proud of them for helping me to build a successful research program.

I started my lab at the University of Massachusetts (UMass) Medical School in 2022. In some ways, establishing my research group during the pandemic has many parallels to a tumor cell adapting to a harsh environment. One of the most important elements for the success of a young principal investigator is to build a supportive network, both within and outside of the lab, and I knew that this would be more difficult during a pandemic. I have, however, been fortunate to have a supportive network of scientists who have helped me along the way to create a congenial 'microenvironment' where I can thrive. My extremely supportive postdoctoral mentors have been critical to my prior success and now continue to support me after leaving their tutelage. Similarly, my new colleagues at UMass and my network in the larger pancreatic cancer community have proven invaluable and have contributed directly to the lab environment by sending people my way that have proved to be true assets.

As a father of two young boys less than five years in age, I have experienced several of the most challenging aspects of the pandemic – from months-long daycare shutdowns to finding ways to navigate the re-opening of society while my kids were still too young to be vaccinated. I feel that I have come through this transformative experience as both a better scientist and group leader, as well as a better father and husband. During the pandemic, my wife, who is also a busy PhD scientist working in the biotech sector, and I often struggled to balance my demanding interview schedule with home life. I relied on her during this critical point in my career to keep me grounded and focused on building a better future. Much like a strong family unit, I want to build a community within my lab where trainees can feel valued and supported, no matter what is happening around them. Thus, the pandemic has forced us to change the way that we do research and, in some ways, has strengthened our sense of community. I, for one, would not

have survived and thrived were it not for the community of scientists – at my university, in the pancreatic cancer field and in my household – that have empowered me during these unprecedented times.

Becoming a stem cell in your niche



Sheerien Rajput:

The road to my career as an independent investigator offered me several firsts. My first grant application, first collaboration, mentoring the first researcher, creating the first budget and signing off the first

consumable bill as an independent investigator. While going through these humbling experiences, I realized that the pandemic is not only a health concern, but that it has heavily shaken every aspect of our lives so much so that research and funding were divided into two categories: (1) COVID-related; and (2) others.

So, we primarily belong to the ‘other’ side conducting basic research. The role of stem cells in cancer and tissue repair is the primary focus of my team. Recently, we have started to investigate these interactions by employing three-dimensional (3D) culture technologies and incorporating 3D bioprinting techniques.

Despite its bedrock value, basic science in Pakistan has never been recognized and is not well funded. Extensive investment in COVID-related research further reduced the already limited resources for basic science. Additionally, funding body regulations regarding the economic or commercial impact of research, budgetary constraints and supply-chain bottlenecks further limit the resources for basic research. Due to insufficient financing, individuals in our part of the world are disinclined to pursue a career as a basic research scientist and, therefore, recruiting and retaining researchers is a big challenge. However, these limitations encouraged us to be more vigilant in planning experiments and developing collaborations to maximize our output.

Our Centre for Regenerative Medicine & Stem Cell Research at Aga Khan University, Pakistan, is probably unique in that it had not closed for a single day during the pandemic. Thanks to the marvelously cooperative team members who scrupulously followed policies, we advanced with a commitment to science, despite the challenging circumstances.

We worked hard to keep the lab environment accommodative and healthy and grew as a team. Leading a group during that time, with researchers under mental stress and facing health issues, made me realize that being a principal investigator means evolving as a scientist and as a human being.

A ray of light shone through the darkness when we established the country’s first regenerative medicine lab, with Pakistan’s first 3D bioprinter. Travel constraints for the vendors enabled us to read and investigate more, to better understand and operate the instrument and to develop resources to replace expensive bioinks. The silver lining is that even in such challenging ‘hypoxic’ conditions, we adjusted and integrated flexible work practices without compromising work integrity. The pandemic taught us that turning challenges into opportunities requires resilience and refusal to admit defeat by becoming a stem cell in one’s niche.

Lessons learned and challenges ahead



Naiara

Santana-Codina: As we slowly resumed our activities in 2021, with pandemic-induced supply shortages restricting work and regulations limiting in-person meetings, I started looking for a

faculty job in the middle of a hiring freeze, a travel ban and a pregnancy. In the uncertain environment created by the pandemic, there have been challenges and even moments of defeat. However, the pandemic has transformed us in a myriad of ways and pushed us to be more resilient and persistent. We have learned to value the importance of in-person work, but we have also come up with creative alternatives to collaborate and interact with each other. While looking for positions, I have had the privilege to virtually engage with researchers around the world. I was interviewed for faculty positions online from my living room – an alternative that was crucial to balance my career with my recent motherhood.

Launching my laboratory at Aarhus University has been an exciting milestone. Our studies focus on targeting the oncogene-driven metabolic reprogramming of pancreatic cancer cells using combinatorial treatments to overcome drug resistance. We are just starting to witness a paradigm shift in the field with the development of selective inhibitors against KRAS(G12C) and KRAS(G12D) – a

target long considered undruggable – which have the potential to transform the care of patients with pancreatic cancer. However, our exponential understanding of the complex nature of the tumor microenvironment has also shown us that we cannot neglect the interactions between cancer cells and their surroundings. We are entering a new era for cancer metabolism where technological and biological advances will be critical to understand the contribution of the tumor microenvironment to metabolic changes that drive tumor progression and therapy response.

As a new group leader just starting to assemble my team, I look forward to the challenges ahead. How can I stay creative and find my own niche while working with rigor and curiosity? How can I be a good teacher and mentor for the next generation of students in the lab and in the class? How can I become a good leader who is able to motivate my students and colleagues every day? The pandemic has imposed tremendous pressure on early career investigators, and it has exposed existing inequalities in science but has also demonstrated that we can overcome hardship if we work together. Let’s use this newly acquired knowledge and resourcefulness to make science more sustainable and equitable.

Translating chaos into progress



Tanaya Shree: As the world ‘returns to normal’ after more than two years in a global pandemic, we are dealing with the aftermath of life disrupted. “Where are we now?” and “where are we going?” are the questions that defined life

in 2022 and produced curious juxtapositions. Large-scale public gatherings reconvened, prompting many of my immunosuppressed patients to retreat further into isolation. I flew to attend in-person faculty interviews, but spent half of my visit on video calls with faculty working remotely. Interviewing candidates for my new lab, I met highly experienced scientists recently out of work and recent graduates whose laboratory research opportunities had been constrained, each trying to find their bearings.

As an assistant professor starting both a lab and clinical practice at a new institution, I am finding these curious juxtapositions congruous with my own professional stage – a

soul-searching period of transition – in my case, from being a mentored to an independent physician–scientist. I am well prepared for many of the challenges (for example, patient care and experimental design), frustrated by others (procurement processes) and somewhat daunted by the need to advance on all fronts with immediacy while also prioritizing long-term research plans, not to mention the task of resettling two uprooted children. How to focus on the enormous possibility that my new position provides without being subsumed by the chaos of uncertainty?

I study human tumor immunology, attempting to understand the dynamics and function of immune networks in patients with cancer with a particular focus on lymphoma, which arises from an immune cell and alters immune networks ‘from within’. This area of research requires dealing with the complexity of immunology and the immense heterogeneity of patients and cancers and emerging with robust answers. I feel similarly engaged in translating the chaos of the current transition into bold forward progress. Just as I guide my research plans by asking how any potential line of investigation can improve patient care, we can use our core values to guide our emergence from the pandemic. What lessons should we take forward and what conventions can we shed? As I build my research team during this transitional time, I am focused on my first specific aim – to create a supportive scientific community with a shared purpose, hope and vision, asking not where we are going, but where it is we want to go, together, from here.

Being proactive



Zexian Zeng: My research group focuses on cancer immunology and immunotherapy, cell signaling and gene expression regulation. We have developed multiple algorithms to analyze high-throughput sequencing data, including gene expression data at the bulk and single-cell level, genomic data or spatial transcriptomics. When the data lead us to interesting results, we also design functional experiments to investigate the underlying mechanisms. In addition, we are developing several experimental platforms to perturb both immune and cancer cells and study their roles in the tumor microenvironment.

The long-term goal of my team is to leverage our interdisciplinary background to identify resistance regulators and effective combinatorial therapeutic strategies to overcome immunotherapy resistance. I started my independent career in February 2022. As well as being fulfilling, the past eight months have been turbulent. Looking back, I believe the key is to be proactive. I have identified three essential elements to this.

First, focus on people. I have been fortunate to have recruited a wonderful team of talented and motivated graduate students, postdoctoral fellows and technicians. Together, we have built a support system for one another. I have also found a few reliable collaborators, with whom we have held joint lab meetings and journal clubs, as we have complementary expertise and share the same research interests and passion. A few exciting projects are underway.

Second, increase exposure and seek resources. I gave presentations at many scientific conferences and offered talks at different institutions to become better known within the academic community. I have also identified several funding opportunities and submitted a few grants. In navigating these challenging aspects of starting a new lab, many mentors, including my doctoral and postdoctoral advisors, peer researchers and senior colleagues, generously offered their advice and support.

Third, ‘yes’ and ‘no’. When there seems no harm, people tend to say yes. But saying yes to something really means saying no to something else. The lockdown disrupted our work, but forced us to ponder our priorities. I have learned to say yes to things that align with our priorities. Yes to our important work, yes to our health and yes to our loved ones. Meanwhile, I have learned to say no unless excited.

Setting up a new lab during the global pandemic is undoubtedly challenging. But looking forward, I believe that the lessons learned during this time will strengthen us and enable us to transform challenges into opportunities.

Laying the foundation



Ying Zhang: The year 2022 has witnessed remarkable changes in my personal and professional life. After living overseas for more than a decade, I returned home to live close to family and started my

independent career as an assistant professor at Peking University, one of the most prestigious universities in China. Building a team with a focused research program has been a fresh, exciting and highly rewarding experience.

My group focuses on cancer immunology and immunotherapy. Specifically, we study how cancer cell pyroptosis, a highly inflammatory form of cell death, modulates the immune landscape within the tumor microenvironment to boost antitumor immunity, and try to find better drug targets to therapeutically harness pyroptosis. The primary executors of pyroptosis – the pore-forming gasdermin (GSDM) proteins – were identified in 2015. The discovery and application of the proteins in cancer immunotherapy, to which I am proud to have contributed, have just been recognized by the William B. Coley Award from the Cancer Research Institute. Yet, how GSDM expression and activation is regulated in different cancers remains largely unclear and other potentially essential functions of GSDM beyond its involvement in pyroptosis remain unexplored. Understanding these key questions could set the stage for new cancer treatments and so our group is keen to address them, with the goal of achieving long-lasting remission for patients with cancer.

Running a successful lab goes beyond asking good scientific questions and designing multipronged research plans. From designing a lab space and selecting equipment to recruiting lab members, I increasingly realize that all these decision-making steps may have a long-lasting impact. Team members are the pillar of a lab, and I prefer to choose people with different research expertise who often view scientific questions from a novel angle and help ignite new ideas. Besides, it is critical to create an inclusive and supportive lab culture to foster personal growth and scientific development. Inspired by many senior scientists, I drew on my own experiences and wrote a lab manual, laying out expectations for our daily work and interactions, on which each member could give feedback. By adapting these guidelines and adjusting based on what works best over time, we hope to build a healthy ecosystem where everyone can flourish and reach their full potential. Finally, collaboration is the key to many scientific discoveries. I am grateful that our research center brings together scientists with a diverse range of research interests, offering ample opportunities to share knowledge, develop new ideas and establish collaborations. With all the foundations laid at the initial stage, I am confident that our group is ready to conquer

roadblocks that dampen the efficacy of cancer immunotherapy and make meaningful contributions to the field.

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