Challenges and opportunities in 2021

Twelve early-career investigators share their thoughts on the challenges faced by their teams and communities during the past year, and look ahead to new opportunities for 2022.

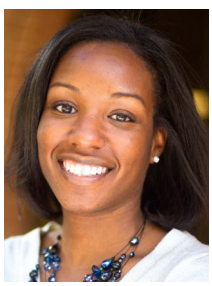
Leila Akkari, Stacey D. Finley, Ping-Chih Ho, Misty Jenkins, Barbara B. Maier, Nicholas McGranahan, Miriam Mutebi, Rushika M. Perera, Carla Daniela Robles-Espinoza, Santosha Vardhana, Liling Wan and Meng Michelle Xu

Leila Akkari: plasticity — where challenges and solutions lie

Choosing a career in academic research always involves the development of a remarkable capacity to accept challenging situations and adapt to them, whether it is when planning and performing experiments or building novel lines of research as a junior principal investigator (PI). It involves passion, commitment and patience — in all steps of this journey, we grow, learn and evolve.

This process of growth and change is not unlike the one observed within tumors, in which the plasticity of tumor and immune cells is a crucial source of heterogeneity underlying the dynamic features of malignancy. Tumor-associated macrophages (TAMs), the most abundant immune cells in nearly all solid cancers, exhibit a beguiling level of versatility. This past year further revealed the layers of complexity underlying TAM heterogeneity, ontogeny and education, which we now appreciate are far from static and orchestrated in a tumor- and tissue-specific manner. TAMs co-evolve with cancer cells often to the advantage of the tumor — all thanks to the tremendous plastic nature of what are, originally, housekeeper cells of organ homeostasis. This hallmark of macrophage biology is now at the core of myeloid checkpoint blockade approaches and the therapeutic potential may be tremendous, although several challenges remain in understanding how to best equip these cells to boost anti-tumor immunity rather than support malignancy.

Thus, enduring harsh environments requires plasticity, which, in the case of macrophages, often leads to thriving. This concept very much applies to our experience of the past 18 months, when we had to wield a lot of flexibility to keep ourselves sane, physically and mentally healthy and somewhat productive. These unprecedented challenges fostered different forms of bounds — more focused, personal and caring. We appreciated that that every lab member had different needs to cope with the sudden halt of regular lab life. To support each other, we made use of online casual meetings and remote celebrations, and kept a more attentive eye to each other's mindsets and vulnerabilities. It took time, but altogether this experience allowed us to grow into a more united and efficient group. It taught us that we could still be scientists without being at the bench all day; and in the case of early-career PIs, such as myself, it showed that being a leader did not only entail directing the pace of our research, but also keeping the team connected and reassured. Consequently, we forged forward and grew scientific networks enriching our research questions, taking more time to think and discuss, while slowly re-initiating experiments. The resilience we had to build will eventually be a formidable asset to the careers of the next generation of scientists, and we now relish the simple joys of sharing lunches and coffees, strengthened by the challenges we turned into opportunities.



Stacey D. Finley: resilience in research and life

I work in the area of computational systems biology, leading a research group that develops mechanistic mathematical models. My group applies such models to answer unresolved questions about how cells behave, and to identify new ways to control their behavior. We particularly look to these models to help us better understand pathological conditions, with a focus on predicting tumor growth and response to treatment. Collectively, we are engineers and computational biologists that get really excited about modeling approaches that allow us to generate new insights about biological systems.

Understandably, excitement about my science has waxed and waned over the past 18 months. I readily admit that leading a research group during a global pandemic has been hard. As a group, we faced health challenges, experienced the loss of loved ones, dealt with mental health issues and handled dependent-care responsibilities, all while trying to make progress towards research and career goals. More personally, it has been hard to lead my research group while managing home life that includes a spouse who is also in academia and three young children. Additionally, as a Black woman in the United States, I acutely felt the burden of the racial unrest in this country. At one point, the goal became to just make it through 2020. Then I realized that many of the difficulties from last year would (literally and figuratively) bleed into 2021.

At the same time, I am prouder of myself and my trainees than I have ever been. We have displayed great strength, fortitude and courage. We grew together as a group and worked to sustain a welcoming and healthy lab culture. We talked about diversity and equity issues that individuals from minoritized groups face. For the first time, we connected with cancer patient advocates, who give purpose and urgency to our research. We also celebrated amazing feats this year — three PhD students graduated in the spring (all now gainfully employed!), two students passed their qualifying exams and an undergraduate researcher submitted a first-author paper, just to name a few.

The circumstances of 2021 magnified the highs and lows of leading a research group, but it allowed me to witness firsthand how resilient we can be. As a perennially optimistic person, I believe that both the difficulties and successes of this year will propel us to greater heights.

Ping-Chih Ho: metabolic cross-talk in the tumor microenvironment

Our understanding of immunometabolism and how the metabolic stress imposed by the tumor microenvironment (TME) disarms anti-tumor immunity has increased dramatically in recent years. Building on the lessons we learned from the success and failure of cancer immunotherapies, including checkpoint blockade and cell therapy, we now enter a new era of unraveling the complexity of metabolic crosstalk between immune, stromal and tumor cells in the TME. Although, we gained a tremendous understanding of how metabolic stress imposed by the TME hampers anti-tumor functions and orchestrates differentiation of tumor-infiltrating T cells and natural killer cells by perturbing their metabolic program, it remains challenging to therapeutically target metabolic machineries in cancer cells and alleviate the microenvironmental stress. Adapting engineered cell therapies, including T cell receptors and CAR-T cells, by rewiring their metabolic program may allow immune cells to better handle metabolic stress in tumors. However, the complexity of the TME caused by heterogeneity and specialized metabolic programs of tumor cells could represent major hurdles for developing a one-size-fits-all strategy.

In the path to address those issues, similar to many other investigators worldwide, the lockdown of laboratories during the COVID-19 pandemic and the resulting supply-chain issues significantly hampered our progress. Moreover, travel bans restricted the interactions and brainstorming within the scientific community. These challenges caused mental stress and anxiety for junior investigators and trainees, resulting from a lack of in-person communication, support by team members and the uncertainty in securing funding or employment. However, we were also able to regroup, refocus the core values of scientific research and reorganize the format of scientific communication and collaboration in the past year. As we see an increase in hybrid meetings, we witness a more robust dissemination of knowledge. Looking forward, the lessons and new solutions we learned and built in 2021 will strengthen the links within the scientific community and will enable us to conduct scientific research in a more sustainable and less stressful format.

Misty Jenkins: pandemic exposes our tenuous grip on gender equality

The COVID-19 pandemic continues to dramatically shape the way we work and live. Despite hard-won improvements in gender equity and inclusion in the past decade, this pandemic has had a serious regressive effect on the participation of women in the workforce, including in the medical research sector. The pandemic has compounded existing inequities, culminating in reduced authorship roles and publication rates for women, especially for women of color and those from minority groups.

I lead a productive team of 11 researchers at The Walter and Eliza Hall Institute (WEHI), Australia, where we are generating new immunotherapies for brain cancer. Here in Melbourne, we hold the unenviable record of being the most locked-down city in the world (with our lockdown lasting a total of 262 days by the time restrictions were lifted in October 2021). Government stay-at-home orders limited on-site activities and made it impossible to train young and enthusiastic scientists. For myself and my colleagues, school closures also meant working from home while home-schooling our children for more than a year. It has been challenging, to say the least.

We have witnessed the widening intersectionality gaps and COVID-19 has only exacerbated the gender equity gap in medical research, with long-term consequences. Research shows that male academics are four times more likely to have a partner engaged in full-time domestic care compared to their female colleagues, and female scholars are overwhelmingly bearing more of the domestic load during COVID-19. As a result, the gender equity gap in medical research has widened, potentially with long-term ramifications.

However, there are silver linings. It has taken a global pandemic for society to truly embrace the cultural change required to incorporate flexible ways of working. Even though much of our work as scientists cannot be done outside the laboratory, there are some real lessons to be learned about how we build stronger, more inclusive and innovative medical research workplaces.

In 2021, we all had to adjust to new circumstances and I hope we can use this experience to create a more even gender-equitable playing field, both at work and at home. As Australia begins to re-open its economy, my immunology colleagues will continue to work responsibly inside and outside the laboratory to improve public health literacy, connect our teams, support each other and drive positive social and cultural change. WEHI has implemented initiatives to address some of the additional pressures on working parents and created a new approach to flexibility to harness positive change the pandemic has accelerated. During the past 18 months, we have demonstrated our resilience at work and at home — we must continue to drive change and make discoveries in a culturally supportive way, where everyone can innovate. We have been taking small steps in recent years, but there is nothing like a crisis to teach us to leap.

Barbara B. Maier: building a lab in pandemic year 2

Starting my own lab in January 2021 was, and continues to be, both the most exciting and most humbling experience in my professional career so far. The last year marked a glorious year for science with the race to beat a global pandemic unlike anything we have witnessed before. At the same time, many scientists still suffered from temporary lab shutdowns and the lack of professional interactions.

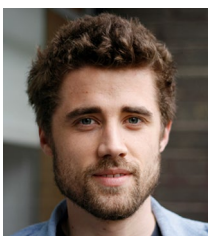
Planting the first seed to grow a team and a research program in the midst of a raging pandemic presents multiple obstacles. How to successfully hire the first team members without in-person interview options? How to establish shared values and create a constructive atmosphere within the team without social activities and in-person meetings? How to build a professional network and foster creativity without attending conferences or being able to invite other scientists? Even if there is no one-size-fits-all approach to face these challenges, scientists around the world have become increasingly innovative in finding alternative, mostly virtual, approaches. As I learned to adapt to this new reality, my more experienced mentors were an invaluable source of advice in navigating these processes. They supported me in online interviews, introduced me (virtually) into the local tumor immunology scene and encouraged me to reach out to scientists

whose work I admire. In fact, I experienced enormous kindness and generosity from colleagues that I have still, to this day, never met in person!

Despite all these uncertainties, the last year was also a productive year for cancer research. We are now beginning to understand mechanisms of cancer immunotherapy resistance, including suppressive immune microenvironments and adaptations of aberrant cancer cell signaling pathways. These advances have been made possible due to continuous immune monitoring of patients on immunotherapy through the use of in-depth multi-omics approaches, paired with rigorous mechanistic dissections in exceedingly clever disease models. This progress motivates the curiosity of many young scientists, such as me. Especially when we face great challenges, it can be inspiring to focus on our common goal of moving science forward to shape the future of cancer care.

Among the most positive developments of the past year is the fact that the fight against racial and gender inequality has finally arrived in many major research institutes, which promises a welcome change in attitude and more opportunities for early-career scientists. Many young group leaders feel empowered to take part in these societal changes.

However, in the coming years, cancer deaths are likely to increase due to missed opportunities of early diagnosis during the pandemic with screening programs temporarily halted and patients suspending regular health check-ups. It is therefore crucial that we continue to identify therapy resistance mechanisms and develop improved cancer immunotherapies to impact the disease trajectories of millions of cancer patients.



Nicholas McGranahan: rethinking priorities

In March 2020, when it became clear that we would have to start working from home, I anticipated a short period of minimal disruption. My group is computational, so, in theory, working from home is straightforward. Perhaps a change would be good. Perhaps it would provide the opportunity to grapple with the big issues. In the end, the disruption of our life and work has been a lot more substantial than anticipated, which is why 2021 has forced me to confront what is important, both from a personal and scientific perspective. Rethinking these priorities, I identified several key elements.

First, communication and collaboration. As a lab, we cannot function without staying connected. When lockdown began, we instigated virtual catchups every morning: 15 minutes to discuss plans for the day (or, in case of those on the other side of the world, what they had already achieved). This quickly became a cornerstone of each day, and even as we move back to the lab, our catchups have remained. Likewise, while our lab-meetings were initially necessarily online, we now have adopted a hybrid approach that allows us to invite external collaborators and share ideas across the world.

Second, a new outlook. The change of circumstances also forced us to adapt and to re-think our approaches to the science we do. This year we developed a new way to exploit existing DNA sequencing data to explore the immune landscape of tumors. We have renewed our efforts to integrate different data types and to focus our analysis beyond the cancer genome to understand the cancer transcriptome and beyond.

Third, science and society. The year 2021 has also raised important questions regarding the role of science in society, and how we can promote scientific literacy. Despite the scientific success of vaccines developed at record speeds, so many avoidable deaths were not avoided, posing evident questions. What is the best way to ensure science gets communicated beyond scientific journals? How can science communication be harnessed to ease vaccine hesitancy and leverage its successful creations?

Science is often presented as cold and calculated, an entirely rational endeavor, devoid of emotion. However, while in theory science itself may be rational, scientists are human and scientific progress requires communication, collaboration, creativity and a good dose of social proximity. The year 2021 has made this abundantly clear.

Miriam Mutebi: the renaissance of the African scientist

The last year has given us pause to reflect on the process of producing good science in our respective regions. As an academic surgical oncologist and scientist working in low- and middle-income countries in Africa, the constant aspiration is to produce impactful, culturally sensitive and resource-appropriate research. Further, there is a strong drive to translate this research to actively improve our health systems and ultimately facilitate better patient care.

At the start of the pandemic, with the global focus rightfully on COVID-19 research, there was an initial slowdown in most cancer care and research. Due to regional lockdowns and poor access to cancer centers, many research projects ground to a halt, along with the loss of funding opportunities. In addition, several institutional research boards put the processing of non-COVID-19 studies on hold. While licking our collective research wounds, we suddenly realized that despite our research slowing down, there were suddenly many more opportunities available to us! Conferences that were frequently out of reach due to large registration fees and travel expenses were now available at the click of a mouse. The subsequent explosion of online webinars and courses had us dashing to accumulate new knowledge and different perspectives.

As we settle into the 'new normal', we have come to realize that in the middle of adversity there is always opportunity. We have now integrated online learning into our mainstream educational activities for oncology and surgery residents. Grand rounds, morbidity meetings and other research and educational activities have all shifted to online models with more faculty engagement. Initial feedback from our residents has shown a satisfaction with this model as they now have access to local, regional and international faculty and more shared learning with global peers. This has also percolated down to patient care with virtual tumor boards, treatment planning and online patient consultations.

We have also had to innovate and pivot our research focus. Despite the speed bumps, I now have a vibrant online research community from across the world, interested in pursuing collaborative research. In addition, we are part of a global taskforce conducting research on the impact of COVID-19 on cancer care. We are also seeing increasing interest and engagement from the diaspora in addressing challenges in our health systems. My colleagues and I are now working locally on projects aiming to leverage telehealth to improve care provision for our patients with cancer. As we strive to enhance systems through practical research, I am pleased that the renaissance of the African scientist is here!

Rushika M. Perera: getting back to business

When I first stepped into an empty office and lab space at University of California, San Francisco, as an incoming assistant professor back in the fall of 2015, I did not anticipate the rollercoaster ride I was about to go on. Six years later, I have learned much of what it is to be an effective mentor, teacher and role model, while also developing the confidence and perseverance to pursue my own 'brand' of science. Of all the unexpected surprises I have encountered, a global pandemic is one that I, or perhaps anyone, could not have anticipated or prepared for. As we moved to shift work, physical distancing, virtual teaching, online seminars and — most bizarrely — rationing of plasticware, the concept of perseverance took on a new meaning. The past year has challenged us to find new ways to remain curious, engaged and motivated. Day to day, teamwork and collaboration has been essential for enabling progress and maintaining productivity despite the hurdles of the past year. Our studies focus on how the lysosome — a key degradative organelle — confers a growth and survival advantage to pancreatic cancer cells. My fascination with the lysosome stems from a long-standing interest to understand how alterations in cellular trafficking and processing pathways contribute to disease onset and progression. Our most recent findings have uncovered how the lysosome has a central role in diverse cellular processes from regulation of cancer cell metabolism and escape from immune-cell-mediated killing and have highlighted the extraordinarily robust mechanisms in place to protect this key organelle against damage and dysfunction. As we slowly move towards re-establishing many of our pre-pandemic norms, I am hopeful that we can incorporate opportunities and new lessons learned from our most recent past. For instance, virtual lab meetings have enabled us to host trainees from different labs who are exploring lysosome function in different contexts, as well as corresponding authors of research papers for in depth Q&A sessions. The increased prevalence of free webinars in our respective fields featuring a diverse array of speakers has provided an important opportunity to remain engaged and up-to-date in the absence of in-person meetings. With renewed motivation, I am excited to embark on a new era for my lab as we explore more complex questions relating to lysosome function at different stages of cancer progression, and continue to unlock the fascinating biology of this organelle.

Carla Daniela Robles-Espinoza: a challenging year with a silver lining

The pandemic arrived in Mexico in 2020 in an atmosphere of uncertainty, but somewhat guarded optimism. Staff at the International Laboratory for Human Genome Research, part of the National Autonomous University of Mexico, where our lab is based, were told to work from home for what would probably be a couple of months. As COVID-19 cases and deaths accumulated, however, the seriousness of the situation became evident and drastic measures were applied. We had to completely stop patient recruitment for our protocol investigating melanoma genomics, were forced to sacrifice animals that were part of our project on liver cancer transcriptomics and were not allowed to enter offices or laboratories. Bench work was postponed, and as all in-person meetings were cancelled and classes moved to an online format, video conferencing became the norm. Sequencing pipelines became saturated with SARS-CoV-2 samples (as they should have been), delaying our projects for months. This meant that plans for some students' thesis work had to be revised from generating new data to thinking of novel ways to analyze previous experiments. We had to amend our proposals and write to our funders, explaining that we would probably need an extra year or two to fulfill our objectives. With the arrival of 2021 not much changed — regulations continued to prohibit our lab from meeting in-person and doing any clinical or experimental work. Doubt and insecurity creeped in, and I wondered if I would be able to survive as an early-career researcher, with so little progress and a performance evaluation underway. But in this time of need, the scientific community really came together. People around us were kind and understanding, funding agencies extended our projects, dissertation changes were accepted and senior colleagues offered their support (and even data to work with!). As the second part of 2021 began, and as vaccines became available in Mexico to the wider population, we were able to slowly re-start our paused projects. As I look back on an undoubtedly challenging year, I also see the opportunities it brought, sometimes hidden within struggles — novel collaborations with scientists that can use our data in different and creative projects, the development of coding skills by bench researchers in our lab, an easing of the bureaucratic burden at the university as most operations moved from paper-based to online, or the optimization of online teaching technologies that can now be used to reach more people. There is no question that measures need to be taken to alleviate the burden that this pandemic brought on early-career scientists and other vulnerable researchers, but I am optimistic that, as we adapt to this new reality, the lessons we learned during this time will help accelerate the pace of science and its reach to many people worldwide.

Santosha Vardhana: the scientist at the bedside

"This half of the unit is all lymphoma" — those words hung in the air as I walked into the intensive care unit in April 2020 to take care of patients with COVID-19 for the first time. Although I had been there numerous times before, this time I entered with a feeling of unfamiliarity. The pandemic had created a constant feeling of uncertainty in so many aspects of life — a sensation that we all experienced. I had taken to describing this as a loss of 'proprioception' — the sense of knowing where you are in the world so that you can perform coordinated and meaningful movements. That loss of meaningful movement for me was occurring as I approached a crossroad in my scientific career. I had been interviewing for independent laboratory positions up until the few weeks before the shutdown. Now, as I read e-mail after e-mail lamenting the current hiring freeze, my scientific future felt similarly frozen.

However, one of the many gifts of being a physician-scientist is the ability to switch roles when needed. With my scientific future on indefinite hold, leaning into my role as a physician simply felt right — the most consequential role I could play in that moment. I volunteered for extra hospital shifts, took off my lab coat, put on my N95 respirator and went to work.

Yet all it took was seeing one COVID-19-infected patient with lymphoma to realize that being a scientist is not a job contained to a laboratory; rather, it is an identity. The core principles at the heart of being

a scientist are to observe, compare, hypothesize and test. Everything I had read about COVID-19 thus far described an over-aggressive immune system in need of extinguishing. But these patients with lymphoma were telling a different story — the sickest of my patients were the ones with absent immune responses. I was overcome by the desire to test a hypothesis: these patients were dying from immune incompetence, not immune excess. However, I had to acknowledge that I had nowhere to do experiments, and that I did not know where I would be employed by autumn. I tried to tell myself that the prudent move would be to stay focused on the research plan I had been developing for years.

But as meticulous as we scientists are in how we answer questions, what inspires us to ask them is often unpredictable. I found myself captured by this idea — that learning from some of the sickest patients in our hospital could teach us bigger lessons about the immune system. Over the ensuing months research facilities gradually reopened and I began building my own laboratory. Our first experiment — an ELISPOT (enzyme-linked immunosorbent spot) assay measuring COVID-19-specific T cell responses in patients — was conducted before we had even unpacked moving boxes. Now, less than one year later, I have the joy of watching new lab members begin to cultivate the ideas that were the foundation for my lab, including our ongoing forays in COVID-19 research. I have rediscovered my proprioception: I know where I am in the world.

Liling Wan: new beginnings in the time of COVID-19

I started my independent career as a group leader at the University of Pennsylvania in 2020. My group studies basic gene regulatory mechanisms and their dysregulation in cancer to leverage these insights for better therapeutics. Setting up a new lab during a global pandemic is undoubtedly challenging in many ways. However, the experiences of the past year also had a positive impact on myself and my group.

One of the most critical factors for the success of a research group is the people who comprise it. Recruiting, training and mentoring new students and postdocs during the pandemic has been particularly challenging. I have been very fortunate to have assembled a fantastic team of students and postdocs. All members of our group deeply care about and support each other as we all found ourselves at the beginning of new chapters of our lives that coincided with truly unprecedented times. As a group leader, I feel more than ever the responsibility to check in with everyone on my team and prioritize their safety and health above any research goals. Through virtual and in-person interactions, we established a highly supportive and collaborative lab culture that will have a long-lasting impact on each team member. A second challenge has been to stay connected with colleagues and to build a sense of community, which is critical for junior investigators, such as me who established their professional independence during restricted personal and social interactions. I am incredibly grateful for the support from many faculty members at the University of Pennsylvania. They have made themselves available to share experiences and offer help along the way and continue to be invaluable sources of advice, ideas and inspiration. The diverse research community of our university and nearby institutions also provide opportunities to receive scientific feedback and set up collaborations.

The hardships experienced during these unconventional times make every achievement and progress made more exciting and worth celebrating. For instance, we recently celebrated an undergraduate student's success in gaining entry to a prestigious PhD program to pursue a career in cancer research and the submission of our lab's first research paper, as well as multiple grants awarded to the lab. Through the experience of building a new lab during a pandemic, I have come to appreciate more than ever the true value of a supportive scientific community and the importance of mentoring beyond scientific and career development. The pandemic has reaffirmed the focus of my group on fundamental biomedical research and shaped, in a positive way, how I run a lab and mentor the next generation of young scientists.

Meng Michelle Xu: intratumoral T cells and beyond

Although sporadic COVID-19 cases were reported in China during the past year, there was no extensive outbreak in Beijing as most residents were vaccinated. Thus, similar to many others in the region, we did not face too many pandemic-related challenges, other than disruptions to the supply chains needed for laboratory work.

Despite these complications, in 2021, our team made some breakthroughs in understanding the mechanisms underlying T cell dysfunction within the TME. Our work demonstrated how an m^{6}A methyltransferase in tumor-associated macrophages promotes CD8$^+$ T cell fate divergence and tumor progression. We also elucidated how downregulating tumor-intrinsic m^{6}A demethylase could restore CD8$^+$ T cell function by impairing the glycolytic activity of tumor cells. Given that direct interactions with neighboring cells can influence T cell function, elucidating the composition of cell types surrounding intratumoral T cells and investigating whether specific cellular interactomes shape T cell phenotypes remain priorities. However, the immense complexity of the topography of intratumoral T cells makes detailed analysis challenging.

Excitingly, the latest approaches have demonstrated the possibility of overcoming this roadblock. For example, the advent of spatial transcriptomics has opened the door to a new era of context-specific and molecular-level dissection of cellular interactions within the TME. As part of our ongoing projects, we aim to use enzyme-based labeling approaches to validate transient ligand–receptor interactions used by subpopulations within tumor niches. We expect that the rapid development of spatial transcriptomics and proximal labeling techniques will allow us to uncover the spatiotemporal interactomes and the underlying mechanisms whereby subsets collaboratively govern T cell fate. The use of innovative approaches that combine information from tracking phenotypic specification of tumor-reactive T cells and their intraclonal differentiation trajectories might allow us to understand the contribution of T cells to immunotherapy better.

Furthermore, studies over past years have illuminated determinants of clinical response to various immunotherapies by integrating meta-analyses of single-cell omics data with datasets obtained through conventional methods. Comprehensive analysis of tumor-infiltrating T cells has further expanded our understanding of T cell subsets and their fate commitment directed by immunotherapy. As one example, a unique intratumoral population of stem-like CD8$^+$ T cells was found to contribute to the antitumor immune response by providing a pool for differentiated CD8$^+$ T cells in patients receiving anti-PD1 (programmed cell death

protein 1) checkpoint blockade, whereas the largest fraction of intratumoral T cells are non-tumor reactive 'bystander cells'. Our next ambition is to stratify the antigen specificity of intratumoral T cells and profile the full scope of antigens they recognize. With the foreseeable improvement of related techniques, such a once inaccessible goal will soon be within our reach. ❐

Leila Akkari[1]✉, Stacey D. Finley[2]✉, Ping-Chih Ho[3,4]✉, Misty Jenkins[5]✉, Barbara B. Maier[6]✉, Nicholas McGranahan[7]✉, Miriam Mutebi[8,9]✉, Rushika M. Perera[10]✉, Carla Daniela Robles-Espinoza[11,12]✉, Santosha Vardhana[13]✉, Liling Wan[14]✉ and Meng Michelle Xu[15]✉

[1]The Oncode Institute, The Netherlands Cancer Institute, Amsterdam, The Netherlands. [2]Department of Biomedical Engineering, University of Southern California, Los Angeles, CA, USA. [3]Department of Oncology, University of Lausanne, Lausanne, Switzerland. [4]Ludwig Institute for Cancer Research, University of Lausanne, Lausanne, Switzerland. [5]The Walter and Eliza Hall Institute of Medical Research (WEHI), Melbourne, Victoria, Australia. [6]Research Center for Molecular Medicine of the Austrian Academy of Sciences (CeMM), Vienna, Austria. [7]CRUK-UCL Lung Cancer Centre of Excellence, University College London, London, UK. [8]Aga Khan University, Nairobi, Kenya. [9]VP East Africa, African Organization for Research and training in Cancer (AORTIC), Nairobi, Kenya. [10]Department of Anatomy, Department of Pathology and the Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, CA, USA. [11]International Laboratory for Human Genome Research, National Autonomous University of Mexico, Queretaro, Mexico. [12]Cancer, Ageing and Somatic Mutation Programme, Wellcome Sanger Institute, Hinxton Cambridge, UK. [13]Memorial Sloan Kettering Cancer Center, New York, NY, USA. [14]University of Pennsylvania, Philadelphia, PA, USA. [15]Tsinghua University, Beijing, China.

✉*e-mail: l.akkari@nki.nl; sfinley@usc.edu; ping-chih.ho@unil.ch; jenkins.m@wehi.edu.au; bmaier@cemm.oeaw.ac.at; nicholas.mcgranahan.10@ucl.ac.uk; miriam.mutebi@aku.edu; Rushika.Perera@ucsf.edu; drobles@liigh.unam.mx; vardhans@mskcc.org; Liling.Wan@Pennmedicine.upenn.edu; michellexu@mail.tsinghua.edu.cn*

Published online: 21 December 2021
https://doi.org/10.1038/s43018-021-00294-6