

## Supporting the Next Generation of Scientists to Lead Cancer Immunology Research



Elise Alspach<sup>1</sup>, Ryan D. Chow<sup>2</sup>, Shadmehr Demehri<sup>3</sup>, Jennifer L. Guerriero<sup>4</sup>, Shashi Gujar<sup>5</sup>, Felix J. Hartmann<sup>6</sup>, Beth A. Helmink<sup>7</sup>, William H. Hudson<sup>8</sup>, Won Jin Ho<sup>9</sup>, Leyuan Ma<sup>10</sup>, Barbara B. Maier<sup>11</sup>, Vivien I. Maltez<sup>12</sup>, Brian C. Miller<sup>13</sup>, Amy E. Moran<sup>14</sup>, Erin M. Parry<sup>15</sup>, Padmini S. Pillai<sup>16</sup>, Sarwish Rafiq<sup>17</sup>, Miguel Reina-Campos<sup>18</sup>, Pamela C. Rosato<sup>19</sup>, Nils-Petter Rudqvist<sup>20</sup>, Megan K. Ruhland<sup>21</sup>, Idit Sagiv-Barfi<sup>22</sup>, Avinash Das Sahu<sup>23</sup>, Robert M. Samstein<sup>24</sup>, Christian M. Schürch<sup>25</sup>, Debattama R. Sen<sup>26</sup>, Daniela S. Thommen<sup>27</sup>, Yochai Wolf<sup>28</sup>, and Roberta Zappasodi<sup>29</sup>

### ABSTRACT

Recent success in the use of immunotherapy for a broad range of cancers has propelled the field of cancer immunology to the forefront of cancer research. As more and more young investigators join the community of cancer immunologists, the Arthur L. Irving Family Foundation Cancer Immunology Symposium provided a platform to bring this expanding and vibrant community together and support the development of the future leaders in the field. This commentary outlines the lessons that emerged from the inaugural

symposium highlighting the areas of scientific and career development that are essential for professional growth in the field of cancer immunology and beyond. Leading scientists and clinicians in the field provided their experience on the topics of scientific trajectory, career trajectory, publishing, fundraising, leadership, mentoring, and collaboration. Herein, we provide a conceptual and practical framework for career development to the broader scientific community.

### Introduction

The inaugural Arthur L. Irving Family Foundation Cancer Immunology Symposium took place on March 22 to 24, 2021 (<https://irvingcancerimmunologysymposium.com/>). The mission of the symposium is to create strong ties between young scientists and senior

faculty mentors in the field of cancer immunology. Further, the symposium aims to provide the community with practical lessons about different paths to success in cancer immunology research. The faculty mentors who participated in the inaugural symposium are all highly regarded scientists and clinicians in the field (**Table 1**). Symposium attendees were selected through a highly competitive

<sup>1</sup>Department of Molecular Microbiology and Immunology, Saint Louis University, St. Louis, Missouri. <sup>2</sup>Department of Genetics, Yale University School of Medicine, New Haven, Connecticut. <sup>3</sup>Center for Cancer Immunology and Cutaneous Biology Research Center, Department of Dermatology, Center for Cancer Research, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts. <sup>4</sup>Department of Surgery, Division of Breast Surgery, Brigham and Women's Hospital, Boston, Massachusetts. <sup>5</sup>Department of Pathology, Microbiology and Immunology, and Biology, Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada. <sup>6</sup>Department of Pathology, School of Medicine, Stanford University, Palo Alto, California. <sup>7</sup>Department of Surgery, Washington University School of Medicine, St. Louis, Missouri. <sup>8</sup>Emory Vaccine Center and Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, Georgia. <sup>9</sup>Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, Maryland. <sup>10</sup>Koch Institute for Integrative Cancer Research and Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts. <sup>11</sup>CeMM—Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria. <sup>12</sup>Lymphocyte Biology Section, Laboratory of Immune System Biology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda; National Institute of General Medical Sciences, National Institutes of Health, Bethesda, Maryland. <sup>13</sup>Department of Medical Oncology, Dana-Farber Cancer Institute, Boston; Department of Immunology, Blavatnik Institute, Harvard Medical School, Boston; Evergrande Center for Immunological Diseases, Harvard Medical School and Brigham and Women's Hospital, Boston; Broad Institute of Harvard and Massachusetts Institute of Technology, Cambridge, Massachusetts. <sup>14</sup>Department of Cell, Developmental and Cancer Biology, Knight Cancer Institute, Oregon Health and Science University, Portland, Oregon. <sup>15</sup>Department of Medical Oncology, Dana-Farber Cancer Institute, Boston; Harvard Medical School, Boston, Massachusetts. <sup>16</sup>Koch Institute for Integrative Cancer Research and Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts. <sup>17</sup>Winship Cancer Institute and Department of Hematology and Medical Oncology, Emory University School of Medicine, Atlanta, Georgia. <sup>18</sup>Division of

Biological Sciences, Section of Molecular Biology, University of California, San Diego, La Jolla, California. <sup>19</sup>Department of Microbiology and Immunology, The Geisel School of Medicine at Dartmouth College, Lebanon, New Hampshire. <sup>20</sup>Department of Thoracic/Head and Neck Medical Oncology and Department of Immunology, The University of Texas MD Anderson Cancer Center, Houston, Texas. <sup>21</sup>Department of Cell, Developmental and Cancer Biology, Knight Cancer Institute, Oregon Health and Science University, Portland, Oregon. <sup>22</sup>Division of Oncology, Department of Medicine, Stanford University, Stanford, California. <sup>23</sup>Department of Data Sciences, Dana-Farber Cancer Institute, Boston, Massachusetts. <sup>24</sup>Department of Radiation Oncology, Precision Immunology Institute, Icahn School of Medicine at Mount Sinai Hospital, New York, New York. <sup>25</sup>Department of Pathology and Neuropathology, University Hospital and Comprehensive Cancer Center Tübingen, Tübingen, Germany. <sup>26</sup>Department of Medicine and Center for Cancer Research, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts. <sup>27</sup>Division of Molecular Oncology and Immunology, The Netherlands Cancer Institute, Amsterdam, the Netherlands. <sup>28</sup>Evergrande Center for Immunologic Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts. <sup>29</sup>Weill Cornell Medicine, Weill Cornell Medical College, New York; Parker Institute for Cancer Immunotherapy; Memorial Sloan Kettering Cancer Center, New York, New York.

**Note:** All the authors contributed equally to this article.

**Corresponding Author:** Shadmehr Demehri, Dermatology and Cancer Center, Massachusetts General Hospital, 149 13th Street, 3.215, Charlestown, MA 02129. E-mail: SDEMEHR1@mgh.harvard.edu

Cancer Immunol Res 2021;9:1245–51

doi: 10.1158/2326-6066.CIR-21-0519

This open access article is distributed under Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0 International (CC BY-NC-ND).

©2021 The Authors; Published by the American Association for Cancer Research

Alspach et al.

**Table 1.** Faculty mentors.

James Allison, PhD	The University of Texas MD Anderson Cancer Center
Philip Greenberg, MD	Fred Hutchinson Cancer Research Center
Nir Hacohen, PhD	Massachusetts General Hospital/Broad Institute
Elizabeth Jaffee, MD	Johns Hopkins
Matthew Krummel, PhD	University of California, San Francisco
Tak Mak, PhD	University of Toronto
Ira Mellman, PhD	Genentech
Miriam Merad, MD, PhD	Mount Sinai School of Medicine
Robert Schreiber, PhD	Washington University School of Medicine
Padmanee Sharma, MD, PhD	The University of Texas MD Anderson Cancer Center
Shannon Turley, PhD	Genentech
Jennifer Wargo, MD	The University of Texas MD Anderson Cancer Center
E. John Wherry, PhD	University of Pennsylvania
Catherine Wu, MD	Dana-Farber Cancer Institute

application process based on their scientific creativity, productivity, and potential for leadership in the field of cancer immunology. In future years, new trainees will be selected for the symposium and introduced to previous cohorts through planned events and meetings, with the goal of forming a cohesive community of young cancer immunologists throughout the world. Herein, we report the key lessons discussed during the inaugural symposium with the aim of supporting the advancement of the community of young investigators in the field of cancer immunology.

## Scientific Trajectory

The symposium provided mentees with the unique opportunity to learn from established experts in cancer immunology research how their scientific journeys have evolved. Here, we highlight a few of these incredible stories and the lessons they impart.

### Reflection 1: Robert Schreiber

Robert Schreiber's scientific career began in basic immunology, marrying his interests in chemistry and medicine. During graduate school, he studied alternative pathways of complement activation. Dr. Schreiber's career is full of examples demonstrating the importance of establishing mentorship and collaboration in any scientific field. Schreiber's early faculty career was focused on the cytokine IFN $\gamma$  and its downstream signaling pathways. While at Scripps Research, and during a sabbatical at Harvard University, where he formed an influential relationship with Emil Unanue, he began studying this molecule and its downstream signaling pathways in detail, developing antibodies blocking a variety of cytokines, and characterizing mice deficient in IFN signaling pathways. At that time, cancer immunology was still a developing topic within the broader fields of both immunology and cancer biology, with skepticism about the value of pursuing a career in this area. Later, in collaboration with Lloyd Old, Dr. Schreiber's interest in cytokines took him toward cancer immunology as the two demonstrated the critical role of IFN $\gamma$  in driving antitumor immune responses. These early experiments gave way to the now well-known experiments that established immunosurveillance and immunoediting as key processes in cancer immunology. Recently, his work has focused on predicting neoantigens capable of driving antitumor immune responses and the generation of tumor-specific peptide vaccines.

### Reflection 2: Catherine Wu

Catherine Wu started out interested in harnessing the graft versus leukemia (GvL) effect in hematopoietic stem cell transplantation to treat chronic myeloid leukemia (CML). At the time, there was no effective therapy for CML, and GvL seemed a promising strategy. However, in 2001, the small-molecule tyrosine kinase inhibitor imatinib was developed, and its success was described as a magic bullet against blood cancer. Numerous pharmaceutical companies and funding bodies shifted their support toward small-molecule inhibitors and targeted therapy. Wu, at that moment, was preparing a grant application to seek funding for a clinical trial in CML. After finding no support, she rebranded the idea for a different type of leukemia, which cannot be treated with imatinib, chronic lymphocytic leukemia (CLL). After a successful clinical trial, she pivoted again and sequenced samples to map somatic mutations specific to CLL, working with the newly formed Broad Institute. These mutations brought Wu back to her original interest in immunotherapy research, but with a new research direction on cancer neoantigens.

### Reflection 3: Ira Mellman

Ira Mellman's scientific trajectory has been anything but predictable. Following an undergraduate project looking into cell wall composition in algae, Mellman did his doctoral work with molecular biologist Howard Schachman. Interested in human disease, Mellman transferred to Yale to work with geneticist Leon Rosenberg. He discovered an enzyme involved in methionine synthesis often mutated in disorders of vitamin B12 metabolism. Inspired by cell biologist George Palade, Mellman sought to further explore the inner workings of cells, specifically the machinery involved in protein trafficking. As a postdoc at Rockefeller University, Mellman studied how proteins were shuttled within cells and investigated the role of membrane-bound vesicles before heading back to Yale to start his laboratory. Having been exposed to immunology as a postdoc, Mellman then began to study the role of dendritic cells in antigen presentation, discovering how these cells regulate the transport of MHC class II during maturation. Eventually, his investigation of cellular trafficking mechanisms in immune responses led to his current interest, cancer biology. In 2007, he left Yale to join Genentech to lead cancer drug discovery, ushering in a new cadre of cancer drugs for the treatment of a wide range of cancers.

Schreiber advises his mentees to "follow the science; follow the data," a key lesson also highlighted by these scientific journeys. Career-shaping opportunities can seem like serendipity, but "fortune favors the prepared mind" (Louis Pasteur). These stories also emphasize that early research directions are not always the ones that eventually bring success. Often roadblocks or changes in the field can alter the landscape, making resiliency a necessary skill. Flexibility can be equally critical, knowing when to switch directions or pivot can prevent stalling out. Finally, it is important to remember that although the data can and should dictate many critical decisions for the future, science does not exist in a vacuum. Scientific trajectories are inherently linked to other aspects of one's personal and career development, which we explore in the next section.

## Career Trajectory

Young faculty and late-stage trainees are not often exposed to the very early steps of established investigators. For many, the laboratories they join for training are helmed by established researchers who are well beyond, both by time and by physical distance, their initial starting point as junior faculty. Conversations surrounding career trajectory

can also be scarce; scientists often prefer to look to the future of their careers rather than what is behind them. Therefore, trainees and young faculty sometimes struggle to develop a perspective on the multitude of different paths that can lead scientists to success. When faculty mentors at the Irving Cancer Immunology Symposium were asked to discuss their unique career trajectories, it quickly became apparent that all researchers take very different journeys, and many do not start off big and just get bigger. For example, James Allison, who achieved one of the major pinnacles of scientific success when he was awarded the Nobel Prize in Physiology or Medicine in 2018, grew up in a small town in Texas and started his faculty career at an offshoot campus of MD Anderson in Smithville. Other faculty members shared how their early-career decisions were shaped by factors such as family and caregiving responsibilities or availability of mentorship. Small group discussions provided opportunities for interactions between attendees surrounding unique career trajectories, with younger trainees being able to absorb additional knowledge from junior faculty. These discussions demonstrated that career trajectories are unique in part because they are shaped by the personal backgrounds and past experiences of each individual scientist. The career trajectory of one scientist will be different from the trajectory of another, and these differences should be acknowledged and supported because success can be achieved at different rates and in many different ways.

Although available tenure-track faculty positions have diminished, the number of junior scientists competing for such positions has increased. The COVID-19 pandemic has added additional challenges for young scientists, including impacting funding and job availability, networking opportunities and the already difficult task of opening a laboratory. In this harsh climate of employment, the scientific community should be more supportive and resourceful in order to help trainees identify, navigate, and select their ideal career paths in science. As both the academic and industrial job markets are rapidly changing, new career opportunities are always emerging to complement the usual tenure-track faculty trajectory. Therefore, the community should invest in educating the next generation of trainees in the variety of career paths they can potentially pursue. In addition, for those trainees who do seek to become successful principal investigators, management skills (for example, leadership, mentorship, and budget handling) and soft skills (for example, grantsmanship and scientific writing) should be emphasized more throughout their training. Recognizing the responsibility of the community to guide its trainees will enable the trainees to better fulfill their potential and will reduce the number of excellent scientists who get “burnt out” and eventually drop out of academic science.

Finally, communication and mentorship remain essential for enabling a scientist to find the most satisfactory career path. In the end, a career trajectory is truly successful when it enables scientists to accomplish their scientific goals. However, for young investigators to project and mature these ideas on their own is difficult, and trainees may not even know about the existence of specific positions that would exactly fit what they enjoy to do or what they excel at. Connecting with peers and receiving guidance from senior/established mentors is critical to maximize the likelihood of successful career transitions and advancements. Scientific institutions should promote such interactions and programs to grow a happy and successful community.

## Publishing

Publications are important for all scientists, but they are essential for those with new laboratories. Although the main purpose of publica-

tions is to communicate scientific results, they serve additional goals for junior faculty. Most importantly, publishing articles improves a scientist's visibility within their field and establishes their independence. A consistent stream of publications may thus be superior to sporadic articles in high-impact journals. These early publications will demonstrate the data-generation capability of a scientist's laboratory, introduce the direction of their research, and establish their reputation as a scientist, all of which are critical for submitting successful funding proposals and advancing a scientific career.

In keeping with the goal of visibility, young faculty seeking to establish their independence should approach publishing as a charge to be led early and often. To this end, projects may be constructed within the framework of a scientific narrative from the very beginning with figure layouts existing as infinite iterations that adjust to accommodate incoming findings. This type of structured fluidity not only fosters focused experimental planning during the critical laboratory start-up period, but also facilitates prudent publishing timelines as every project moves somewhere along the pipeline toward publication. As for the difficult question of “when” a story is ready, caution needs to be exercised to avoid premature submission, or the practice of holding back key experiments in an attempt to predict or preempt reviewer comments. This pitfall can lead to an unfortunate rejection from a preferred journal outlet. It is far better to include all scientifically important experiments prior to submission and have confidence in a cohesive scientific narrative rather than attempting to predict the requests of reviewers. On the other hand, critical feedback from trusted colleagues can assist in gauging the maturity of a project as it approaches submission and thus help dodge the dangerous cycle of needing “just one more experiment.”

A key aspect of crystallizing a clear scientific narrative is having sufficient opportunity to refine the overall structure. Presenting the results regularly at laboratory meetings, departmental seminars, and conferences provides excellent opportunities to elicit critical feedback and establish the narrative structure. Generating a deck of data slides early on and working to distill the information into a logical narrative may also be synergistic. It is thoroughly expected that a great deal of time is spent on refining any given figure; thus, it is typical to have numerous versions of “Fig. 1A.” Beyond the data, it is key for the written narrative to be easily followed. Language is critical. Each word choice may influence how well the intended message is conveyed. Importantly, this includes creating a distinctive and engaging title, which could be the only element in the publication that a reader consumes. In the end, the goal is to guide the reader through the results in a seamless and logical flow, causing the reader to ask questions about one figure only to find the answers to those questions in the next figure.

When the writing of the manuscript is completed, the ultimate hurdle is to successfully publish the paper. Recently, preprint servers such as bioRxiv and others have emerged as a first step to make data swiftly available before publication in a peer-reviewed journal. Although preprints can bear some risks, the positive consequences may prevail, as this can be a good way to create additional exposure, highlighting the ability of the new laboratory to generate results. Engaging editors before submission to a peer-reviewed journal, for instance by sending a presubmission inquiry, may be helpful; editors can be allies in supporting the paper through the peer-review process and allow one to get an upfront impression of how the paper may be received. If the paper is not accepted, it is crucial to learn how to interpret rejection letters. Sometimes a rejection leaves room for discussion, and, if this is recognized, the editor can be utilized to find

Alspach et al.

possible ways to make the paper acceptable for publication. Finally, if one realizes that another competing group aims at publishing a similar or related story, copublication can be a rewarding approach. It not only helps both groups to successfully release the story but also strengthens the rigor of each group's findings, ultimately helping to move the entire field forward.

## Fundraising

Fundraising is a vital task for new investigators. Grants enable research continuation in an investigator's group and raise visibility as an independent investigator. The first step in fundraising is identifying funders. Grants from government agencies are one avenue of funds and are important for gaining tenure. For investigators in the United States, there are NIH K99-R00 and K08 awards for the transition from postdoc to independent investigator, early investigator awards from foundations, and NIH R21 grants that offer opportunities to start on the path of federal funding before applying to an R01 grant. European investigators can apply for ERC Starting Grants or country-specific awards. A second source of funding is smaller, topic-specific foundations, which often have funding opportunities geared toward young investigators and can be found through ProposalCentral, field-specific newsletters, or advertisements in scientific journals. Additionally, searching for foundations in a specific research area and contacting them directly can be a way to find funds that may not be widely advertised. Although perhaps harder to obtain for junior faculty, a third source of funding is from philanthropy and industry collaborations or sponsored research agreements. Finally, institutional intramural funding is often available, and many intramural awards are geared toward young investigators or pilot projects that may not have much preliminary data. It is also important to think about helping trainees to get their own funding for research projects and salaries, as this will not only advance their careers, but may also significantly support the laboratory as a whole.

The critical part of any application is the writing process. Here, "practice creates masters," which means starting writing for grants and fellowships in graduate school. There are numerous scientific publications and workbooks on the grant writing process (1–5). It can also be very helpful to attend grant writing courses, which are available at many universities. These courses are usually most effective when taken during the actual grant preparation. Grant writing tips that were discussed at the symposium included the following:

1. Identify the right call for your project and plan up to a year in advance. Start writing well before the deadline—ideas need time to develop.
2. Depending on the funding agency, grants need different levels of preliminary data. It can therefore be advantageous to write grants around experiments already performed, demonstrating the feasibility of the research approach.
3. The specific aims page needs special attention. Grant reviewers often only read this page carefully and skim through the rest of the proposal. Ground everything you want to do in the research question. Write an anchor sentence before each aim, "Why am I doing this?" "What question am I trying to answer?"
4. Strictly follow the formatting rules, do not overload the proposal ("less is more"), and make it appealing to read and easy to follow ("cosmetics matter"). Print out your proposal; text within figures should be easily readable when printed.

5. Have mentors, colleagues, and course members give feedback early in the process. Ask them if they understand what your hypothesis is. Make sure to have somebody read the grant who is not familiar with the technology applied or the specific subfield of biology because the grant should be comprehensible to a wide-ranging scientific audience.

Even after following all of this advice and having ample preparation, it is inevitable that some applications will not (immediately) get funded. Young investigators therefore have to learn how to deal with these setbacks in a constructive manner. Grant rejections are based on many factors, none of which are meant to be personal or a judgment of character. If reviews are provided, it can be helpful to set them aside for a couple of days to reflect on them and revisit them again later. For NIH grants, contact your program officer to discuss the summary statement. If no detailed reviews are provided, it might be possible to ask the funding agency for feedback. Participating in the grant reviewing process is a great way for young investigators to get to know the reviewer's perspective. Fair reviewers are always needed and specific programs seeking out junior faculty for this task exist (6). In any case, efforts to identify the reviewer's concerns are critical. Take the provided criticism seriously! Edit and amend the grant accordingly and resubmit at the next opportunity. If this is not possible, many parts of written grants can be reused for different funding opportunities. As with so many aspects of being a principal investigator, persistence is key!

## Leadership

What comes to mind when picturing an effective leader? An internet search for "leader" is peppered with images of cartoon people (mostly men) wearing suits and capes, pointing off into the distance, helping others get to the top of a mountain, even flexing some muscle (or all of the above). These images evoke the traditional view of leadership as one of authority, strength, and confidence. Throughout the symposium, however, the continuous themes of compassion and generosity reflect the fact that traditional ideals of leadership are giving way to effective leadership strategies that promote equality and inclusion. Leadership is not inherited by a job title, and postdocs transitioning to a principal investigator position have "leader" on a long list of roles they are expected to fill for the first time. During the symposium, there was substantial time devoted to discussing and learning about the "Dos" and "Don'ts" of being an effective leader. As such, with the list below we share with readers the major topics of conversation.

### Dos

#### Set a shared vision for the research program

Create and communicate the scientific vision to the team. Engage the team to tap into the collective intelligence of everyone and empower them with shared vision. When a team shares the vision of its leader, there is buy-in from them and a research group that is motivated to pursue the scientific discoveries envisioned by its leader is created.

#### Establish empowered culture

By definition, culture is a specific collection of values and norms that shape the actions of people. In simple terms, culture tells: "this is how things are done here." Having an appropriate culture established within the laboratory is conducive for promoting an inclusive, fair, and productive workplace in which laboratory members trust and

support each other at all levels. When the team aligns with the cultural values, it comprises empowered team members who then become leaders of their own and work toward the shared vision of the laboratory. Hence, promoting a culture of collaboration, excellence, accountability, well-being, and EDI (equity, diversity, and inclusion) is vital.

#### **Strategize and be adaptable within scientific operations**

Science and technology are progressing faster than ever, so be adaptable by creating constant readiness for change. Strategically position the research program to undertake new scientific directions and incorporate technological advances. Collaborate with other scientists as well as research-supporting organizations (such as foundations). This will create sustainability by making it possible to pursue cutting-edge science and stay aligned with diverse funding opportunities.

#### **Lead by example**

Leadership is different from managing or authority over a team, so a young investigator needs to promote a culture that inspires their team to work and align with them, to value each other, and to develop trust across the laboratory. They need to recognize differences between people, in terms of both what they need and where they come from. A leader who institutionalizes EDI tenets within their program and practices them themselves will promote cohesion within their group and an understanding between team members from diverse backgrounds. Likewise, it is important to understand that different people have different strengths and weaknesses and thus require different mentorship approaches; be adaptable for every trainee's individuality and support their aspirations. Further, a young investigator must recognize that all team members do not respond to the same inspiration, know themselves—both their limits and strengths—and take care of their own well-being and that of their team. Leaders are made and not born; so, young investigators should keep on honing their leadership skills and be open to seek others' expertise and experience when they lack it.

#### **Embrace the Zone of Incompetence**

The Zone of Incompetence and Learning refers to leaving one's Area of Competence where one feels comfortable with their knowledge and skills. The Zone of Incompetence and Learning may provoke discomfort and anxiety, but it fosters important and necessary growth and leads to new discoveries. A period of mistakes, hard work with limited results, embarrassment, questioning of one's skills and knowledge are likely to occur. Therefore, it is vital that leaders support their team and/or mentees during the process of trying hard and failing and learning fast to try the next thing. For new principal investigators, embracing the Zone of Incompetence and Learning may be hard given the pressure to publish and obtain grant funding. As long as there is progress, it is okay for mentees to flounder in the Zone of Incompetence, but if movement stops altogether, it is the leader's responsibility to redirect. When leaders embrace The Zone of Incompetence and encourage their team to step outside of their Area of Competence, trainees will feel supported and safe in taking a risk to develop new and bigger ideas. Both leaders and trainees grow during this process, and, importantly, it helps move the science forward.

#### **Don'ts**

##### **Don't treat adaptive challenges as technical problems**

Before becoming an independent investigator, most scientists have spent their time developing expert skills in solving technical chal-

lenges. However, it is a mistake to think one can apply the same toolbox when approaching adaptive challenges. Where technical challenges often are more easily identified and can be solved in a linear process by a subject expert, adaptive challenges are less definable and demand a different perspective. Adaptive challenges are normally difficult to identify, partly due to an inherent resistance in recognizing them by the people involved. In contrast to technical challenges, adaptive challenges are more fluid and complex, have no "right" answer, cannot be solved by a subject expert, and the individuals involved likely have a set of different "truths" represented among them. This increases the complexity in addressing adaptive challenges, as the people involved need to be included in resolving them, often by recognizing, evaluating, challenging, and eventually changing cultural norms and values, and relationships within the team. When encountering an adaptive challenge, a leader has to take a step back to evaluate the situation and sometimes develop new theories and processes to meet the challenges with the right response. This can be difficult due to both political and personal reasons, and treating adaptive challenges as technical problems is one of the most common mistakes made by leaders, new as well as old.

##### **Don't put more than one person with the same competence on the same project**

Time as a new principal investigator seems to move faster than ever, but moving along new projects in a new laboratory, probably at a new institution, is naturally slow. The principal investigator needs to resist the urge to add two or more people with the same competence to a project with the idea that it will move along faster. It will not, and doing this more likely generate issues with ownership and creates tension between the individuals involved. Adding people with complementing competence may work, as long as each person can have their own goals met within the project.

##### **Don't put any person on a project; put the right person**

This "don't" relates to the previous one. New principal investigators want projects to move along faster; they are excited to see their new research program come to fruition. However, not only do they need to add the right person to the project to move it forward, they need to consider that adding the wrong person may make it move backward. Get the right individual, even if it means initiating the project takes additional time.

## **Mentoring**

### **Providing mentorship**

Being a good mentor is an important aspect of leading a group that will help a new principal investigator attract young talent to their laboratory. What unites all good mentors irrespective of their particular mentorship style is generosity. A good mentor is generous with their time, and let their trainees know and experience that they are available when the trainees need support. This attitude creates a sense of belonging within the laboratory. Furthermore, once the trainees are ready for their next career step, the mentor will send them off as allies and as their legacy in training the next generation of scientists.

It is important to respect the uniqueness of each trainee and their individual career goals. A good mentor supports and guides their trainees in achieving their goals, without pushing them in any particular direction. Not all trainees are hoping to pursue a career in academia; it is therefore important that a good mentor resists the urge to evaluate the success of their trainees primarily by whether

**Alspach et al.**

they become principal investigators. And throughout this process, remember the boundaries of the Zone of Incompetence and Learning. Both mentor and mentee will enter this zone throughout their training.

Although mentorship styles must be adaptable to the needs of different individuals; it is nevertheless useful to follow some guidelines for cultivating an effective mentor–mentee relationship:

1. Make sure to schedule regular meetings to define and revisit “goals” and expectations and make detailed written plans. Reassess plans at regular intervals.
2. Every trainee profits from forming a professional network. Principal investigators can actively support their trainees by enabling networking opportunities with other faculty, journal editors, or industry collaborators as well as through public speaking at local, national, and international venues. This is especially important when a mentor is mentoring a trainee in a project outside their zone of competence.
3. Encourage collaboration within the laboratory and beyond, and actively work against a culture of secrecy.
4. Have a big picture meeting with trainees about their career goals and what they need to do to reach them once or twice per year.
5. Finally, be open and discuss trainees’ ideas; invite them to actively be part of the project planning and stay intellectually engaged.

For trainees who are considering a career as a principal investigator, engage them in transparent decision-making pertaining to laboratory culture and by highlighting the challenges and realities of your work as a principal investigator. The transition to independence is a jarring shift in responsibilities and priorities; when mentors share their everyday experiences, their trainees will be empowered to tackle these challenges themselves in the future.

**Navigating a conflict**

Conflict within teams often arises when expectations are not clear between mentor and mentee. Establishing clear expectations, such as through a Lab Compact, can reduce opportunities for conflict between laboratory members of all levels. Yet, even with the best of intentions, conflicts may arise within a team. It is important to be able to directly address and resolve conflicts in a professional manner and early (“nip it in the bud”). If a mentor senses that the mentee–mentor relationship is not optimal, they need to voice their observation and assess whether the mentee’s needs and goals are aligned with theirs. This could be a good moment to reevaluate the plans formed in the last mentee–mentor meeting and/or consider involving a co-mentor.

In case a conflict arises between laboratory members, one strategy is to reunite all involved parties to focus on the common goal: to move the project and science forward. Provide support to all parties involved, recognizing that there may be more complexity underlying the conflict than is readily apparent. Importantly, take the opportunity to guide the senior laboratory member in resolving the conflict; this could be a great mentorship moment! Be open to issues of mental health and guide people to institutional resources.

**Seeking mentorship**

Building a laboratory is an exciting time for many, launching an independent research program no longer under the mentorship of a

graduate or postdoctoral advisor. However, as with all new transitions, mentorship is key to success. A new principal investigator must build their “circle of trust” to include mentors of different backgrounds and personalities that can provide guidance. It is helpful to new principal investigators if they formalize a mentoring committee and find mentors who are invested in their success and have time to support their growth. Seeking mentorship outside their institution can also be helpful, providing an array of mentors for specific aspects of their career/work. In addition, peers can be fantastic mentors. They can help build a network and provide a sense of belonging with individuals in a similar transition.

Importantly, how one asks for mentorship is critical to the success of the mentoring. Senior mentors have limited availability; therefore, it is crucial to maximize quality and output of any one-on-one time. For example, it might be more feasible to obtain feedback in a quick, spontaneous meeting rather than asking a mentor to read a 25-page grant application.

**Collaboration**

Our goals as scientists are to advance fundamental understanding or to solve problems whose solutions are beyond the scope of our abilities. Positive and productive collaborations are rapidly becoming an essential component of research life, both in academia and in industry. Mastering all emerging technologies is unrealistic and counterproductive, as we can, and should, lean on each other to efficiently address our important research questions. Although collaborations between academic laboratories can lead to high-impact findings as well as short- and long-term dividends, there are some critical factors to consider before entering such an arrangement. First, it is important to put in effort to get to know any potential collaborator: talk to others the potential collaborator may have worked with to get a sense of their work ethic, trustworthiness, and approach to publications. Second, identify the personnel in each collaborating group who will be involved in the shared project. Have an open discussion with everyone potentially involved to make sure that they are excited about the project and share the same vision and goals. There is nothing worse than a project falling to the wayside because the principal investigators are excited, but the students/postdocs are not. Regular meetings between members can help guide the collaboration and provide a forum for informal and formal check-ins on progress. Third, collaborations are often most successful when the people involved have complementary skills and a shared vision for short- and/or long-term goals. In the age of big data, that could mean one laboratory has the computational expertise to handle the data produced by the other laboratory. Or perhaps one laboratory has extensive expertise in flow cytometry, whereas the other has it in microscopy. Last, there should always be a discussion about funding upfront so that no one is blindsided by costs down the line. Will there be an application for joint funding? Will each laboratory pay for just what it does in house? There is no one size fits all, but using these factors as a guide will hopefully help academic laboratories enter into positive and productive collaborations.

Many of the considerations detailed above also apply to collaborations between academic and industry laboratories, although there are some additional unique aspects to these relationships. Although rapid publication is a common goal in academia, industry partners often prioritize financial aspects including patents and competitive advantages. Often, industry laboratories have specific deliverables that must be met on time, with the end goal being a new technology or product rather than a research paper. This does not mean that they are not

interested in publishing, but it can result in delays due to concerns regarding intellectual property. Therefore, a clear discussion regarding publication timeline and restrictions before agreeing to the collaboration is important, considering the best interest of the academic laboratory and the students/postdocs who would be involved in the project. As with collaborations between academic laboratories, knowing who will fund the project, in part or in full, is key to outline from the beginning. Sometimes the industry side will want to fund the majority of the project, giving them more control over the timeline and expected deliverables. Again, this is something to consider in regard to investigative flexibility and project ownership for the involved personnel in the academic lab but should be decided on a case-by-case basis.

We strongly believe that the scientific community at large will benefit from increased collaboration and transparency in tackling the cutting-edge research questions of our day. Healthy competition will always be an integral component of scientific research, but hopefully so will healthy collaboration.

## Conclusion

In conclusion, the lessons outlined in this commentary encompass the major elements required for establishing a successful research career, which extend beyond the field of cancer immunology. Although we did not cover all aspects of running a lab (for example, hiring, training, communication, developing a research vision/statement, financial management), we hope that these lessons provide a practical guide for early-career investigators to build a resilient and bright scientific outlook as they navigate the

opportunities and challenges associated with setting up an independent research program.

## Authors' Disclosures

J.L. Guerriero reports grants and personal fees from GlaxoSmithKline and Array BioPharma, and grants from Eli Lilly outside the submitted work. W.J. Ho reports other support from Rodeo/Amgen, grants from Sanofi, and personal fees from Exelixis outside the submitted work. B.C. Miller reports grants from NCI during the conduct of the study, as well as personal fees from Rheos Medicines, Inc. outside the submitted work. E.M. Parry reports grants from Doris Duke Charitable Foundation and ASCO Conquer Cancer Foundation outside the submitted work. M. Reina-Campos reports personal fees from Pandion Therapeutics, a subsidiary of Merck, outside the submitted work. C.M. Schürch reports grants and other support from Enable Medicine, Inc. outside the submitted work, as well as a patent for anti-CD70 combination therapy issued and a patent for method for predicting patient response to immunotherapy pending. R. Zappasodi reports grants from Parker Institute for Cancer Immunotherapy and NCI during the conduct of the study; other support from Leap Therapeutics and iTEOS Therapeutics outside the submitted work; and a patent for WO2015184099A1 licensed, a patent for US20170081409A1 licensed, a patent for WO2018106864A1 licensed, and a patent for 62/582,416 pending. No disclosures were reported by the other authors.

## Acknowledgments

The authors thank the Arthur L. Irving Family Foundation for the establishment and support provided to bring the cancer immunology community together for the inaugural Arthur L. Irving Family Foundation Cancer Immunology Symposium. They thank the faculty mentors for sharing their experiences that have formed this commentary.

Received June 30, 2021; revised August 23, 2021; accepted September 13, 2021; published first September 20, 2021.

## References

1. Bordage G, Dawson B. Experimental study design and grant writing in eight steps and 28 questions. *Med Educ* 2003;37:376–85.
2. Inouye SK, Fiellin DA. An evidence-based guide to writing grant proposals for clinical research. *Ann Intern Med* 2005;142:274–82.
3. Koppelman GH, Holloway JW. Successful grant writing. *Paediatr Respir Rev* 2012; 13:63–6.
4. von Hippel T, von Hippel C. To apply or not to apply: a survey analysis of grant writing costs and benefits. *PLoS One* 2015;10:e0118494.
5. Grant Writers' Seminars & Workshops; [about 3 screens]. [cited 2021 Apr 5]. Available from: <http://www.grantcentral.com/workbooks/>.
6. Early Career Reviewer (ECR) Program; [about 6 screens]. [cited 2021 Apr 20]. Available from: <https://public.csr.nih.gov/ForReviewers/BecomeAReviewer/ECR>.

# Cancer Immunology Research

## Supporting the Next Generation of Scientists to Lead Cancer Immunology Research

Elise Alspach, Ryan D. Chow, Shadmehr Demehri, et al.

*Cancer Immunol Res* 2021;9:1245-1251. Published OnlineFirst September 20, 2021.

**Updated version** Access the most recent version of this article at:  
doi:[10.1158/2326-6066.CIR-21-0519](https://doi.org/10.1158/2326-6066.CIR-21-0519)

**E-mail alerts** [Sign up to receive free email-alerts](#) related to this article or journal.

**Reprints and Subscriptions** To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at [pubs@aacr.org](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, use this link <http://cancerimmunolres.aacrjournals.org/content/9/11/1245>. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.