Women Leadership in Immuno-Oncology Issue 2022

Celebration Issue

2022

Women Leadership in Immuno-Oncology

The official newsletter of the Immuno-Oncology 360° Conference

www.io360summit.com
Welcome to the Immuno-Oncology 360° third annual “Women Leadership in Immuno-Oncology” Issue, celebrating women leaders in the IO space and the upcoming 2022 meeting, March 16-18, 2022 in New York City.

We created this Q&A series to highlight the inspiring work these IO360° women speakers are leading in the field. We touch upon their career journeys, get their perspectives on a wide range of immuno-oncology topics, and encourage younger generations entering the space. These women are CEOs, directors, heads of department, development leads and investment partners.

We are honored to highlight the IO360° women speakers ahead of the Immuno-Oncology 360° Summit, and thank them for participating in our ongoing series.

Enjoy the interviews.

Sincerely, the IO360° team,

Danny McCarthy, Multimedia Editor
Kate Woda, Conference Director
Valerie Bowling, Executive Director
BreAnna Bugbee, Senior Marketing Manager
Meredith Sands, Executive Director, Business Development

If you would like to nominate a woman leader in the immuno-oncology space to be featured in the 2023 issue, write to us at service@tcflc.org with the subject headline “IO360° Women Leadership Nomination.”
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OUR SERVICES & OUR APPROACH

We take a personalized and integrated approach to help our clients position their pipelines and companies for success offering a full range of development and commercialization services.
Adrelia Allen, PharmD, Director, Clinical Trial Patient Diversity, Global Clinical Trial Operations, at Merck Research Labs.

Can you tell us about the work you’re currently leading?

As the Director of Clinical Trial Patient Diversity, I am responsible for driving the execution and implementation of activities to support the enrollment of racial and ethnic minorities in Merck clinical trials.

What made you passionate about entering the field?

In my past role as a Clinical Research Manager overseeing the operations and the enrollment of patients in clinical trials, I witnessed how participation in a clinical trial represented hope and the possibility of changing the trajectory of a patient’s life. I also recognized many patients that looked like me were often not represented in clinical trials to benefit from the novel scientific medical advancements.

As a double minority, I have made it a personal priority to increase the awareness about the barriers that limit diverse participants and engage colleagues to bring solutions to bridge the diversity gap in clinical trials.

What has surprised you about working in immuno-oncology?

The speed of novel medical developments and the scientific advancement in immuno-oncology has offered hope for many in the fight against cancer. This paradigm shift has changed the approach to making new cancer treatment available for patients.

Because of the important role cancer clinical trials play in making new medical discoveries available, broadening the participation of racial and ethnic minorities is critical to create equitable access and to address health inequities in cancer treatment.

What are your thoughts on how to encourage young women entering STEM?

Although women make up nearly half of the US workforce, we are still underrepresented in STEM careers. We are more than capable to lead and drive innovation to develop solutions to our most simple and complex problems.

We are great problem solvers and critical thinkers, which are useful skills in STEM. Take charge to educate, explore and increase your exposure to STEM opportunities. Your GIRL POWER is needed for developing the next innovation to change how we live and play.

Is there anything else you would like to share with our readers?

In developing drugs for everyone, we must be proactive and intentional to drive change to bridge the diversity gap in clinical trials. The time is now to address and resolve this long-standing medical issue.

“Your GIRL POWER is needed for developing the next innovation to change how we live and play.”
Sarah Anderson is Executive Director, Oncology, Therapeutic Strategy Lead, in the Oncology franchise at Worldwide Clinical Trials. With more than 18 years of oncology-focused industry experience, she has provided global project development/oversight and clinical management for both CROs and pharmaceutical companies.

Can you describe your role at Worldwide and the work you’re leading?

My role as on Oncology Strategy Lead is quite interesting as I am able to take my 18 years of oncology development work and meet with sponsors to evaluate their study/program in the early stages and provide strategies along with risk mitigations to both them and our internal teams to successfully start and complete a study. Key here is out-of-the-box thinking as oncology trials are complex and can potentially pose many challenges that require key strategies.

How did you enter into this field?

Early in my career I had the opportunity to work at a small biotech company where I was immersed in the drug development process which fueled a passion in me. I saw the work we were doing day-to-day was positively impacting patients’ lives, I knew then it was something I wanted to do for the rest of my life.

What is so special or surprising about oncology to you?

The number of biotech and pharma companies dedicating their passion to providing patients advanced treatment options, and the rise of personalized medicine, is awe-inspiring. Our strong awareness that each patient’s cancer diagnosis and journey is different but understanding how the advancement of treatment options is impacting people’s lives for the better is the soul of our work.

How have you witnessed the evolution of what an oncology trial was when you started in your career versus what you’re dealing with now?

Oncology study designs have become much more complex with accelerated designs focusing on precise dosing against patient’s earlier response, especially in Phase I trials. When I began my oncology career as a Clinical Research Associate the trials I worked on were heavily chemotherapy based with exploring supportive care options to help balance patient’s treatment adverse events. What we are seeing now is a movement to personalized medicine where we are able pin-point effective treatment options based on patient’s tumor tissue and genetic analysis. Majority of patients now have advanced treatment options that expand into immunotherapies, target therapies and many fewer toxic options where possible.

What are some of the challenges that prevent a successful early stage trial?

Understanding of the complexities of the clinical trial landscape in the early stages at the sponsor, CRO and site levels are imperative. The biggest issue we are all tackling right now globally is balancing the COVID landscape against limited resources industry wide to run any phase study. These resourcing constraints have a domino effect as it can potentially delay the activation of new early phase studies for patients who are in desperate need of an additional option.
How do you mitigate or plan for a challenge as fundamental as staffing?

You must think out of the box from the very beginning. What we’re having to do now, is evaluate the number sites we are utilizing and then focus on the global landscape holistically. This holistic approach allows us to thoughtfully balance a proposed country mix while proactively risk mitigating potential hurdles with restrictions and/or staffing concerns without timeline implications.

What is the root cause of that lack of experience from rising clinical staffers?

I think it’s awareness. If you ask people about how they entered clinical research, the majority will tell you they just happened to fall into it. When I was going to college, I always knew I wanted to do work in medicine but at that time careers in clinical research were not even discussed.

At the college level and even within the CRO industry now, there are programs that focus on careers in clinical research including training to become a Certified Clinical Research Associate. What we need to think about now is, about bringing awareness earlier about what clinical research is, but also jobs that are available which have potential to positively change a patient’s life; which is the heart of all our work.

What are your thoughts on how to encourage young women to enter STEM and to help them in their careers?

My children have the privilege to go to a great public school that is STEM-certified. It’s amazing, at an elementary level, to have science, technology, engineering, and math as their focus every single day. I’m a mother of two boys and have friends who are mothers of girls and I listen to their daughters talk about wanting to be doctors, nurses, astronauts, etc. Coding is a big thing for these kids now.

I am a big advocate in encouraging education in STEM, I even do this with my own family members who are going through college and high school express an interest in science. I tell them whether they want to be a nurse, doctor or even lab technician. There’s so much available.

It’s great because I feel like younger generations, especially women, have such a phenomenal opportunity to advance in science, technology, engineering, and math.

Is there any piece of advice that you come back to often in your career?

I once had a boss who said to me, years back, “There will be very long days. There will be very hard days, where you are dragged down, and you find yourself emotionally drained. You must be able to dig in deep and do what the majority of people are unwilling to do, and that is the hard work. Not only to change your life, but the lives of patients and their families.” That is something to live by.

Where do you see the areas of growth in oncology?

Personalized medicine is a big one, absolutely. Not every patient’s cancer journey is the same. If you take a look back at when cancer medicines first evolved, especially in the 1990s, patients were diagnosed with cancer to which the majority were treated with chemotherapy. Now it’s much more targeted therapies. If you think about it from this perspective, we’re able to take patients’ tissue samples and be able to genetically look at them to understand what treatment options are going to work for them, which ones are not, and then from there specifically treat them for the way they treat them to help their disease. You’re not just running the gauntlet to hopefully get a response.

How does that shift to personalized medicine change your work with biotechs?

The shift to focus on personalized medicine and evolving advanced cancer treatment options means that I must continue to understand the detailed logistics but also complexities of incoming treatment options and multi-tiered diverse testing requirements but also be able to balance where and who can successfully activate and enroll at the country and site level.

What would be your parting message?

I would say that the opportunity for women – for anybody, quite honestly – is so great right now. I feel like there are limited barriers and a lot of growth opportunities and advancement at all levels. Working in the CRO industry, especially at my company, we are over 70% women with strong female executive leadership where a culture of diversity and inclusion are embraced and promoted, it is encouraging and such a great privilege.

To all young women, I would say not to let the long days and the hard work stop you from pushing forward and being passionate for change.

To learn more, visit www.worldwide.com
Can you tell us about the work you’re currently leading?

I am the Head of Cell Therapy Research for the Immuno-Oncology and Hematology Disease Area at Novartis Institutes for BioMedical Research (NIBR). NIBR is the R&D division of Novartis and my work focuses on the early discovery and development of novel cell therapies for heme malignancies and solid tumors.

As part of the team that brought the first T cell therapy to approval, I’ve had the privilege of working across the larger NVS organization with clinical development, technical development, regulatory, quality and commercial to create a new path for personalized medicines.

What made you passionate about entering the field?

Making a difference in the lives of patients and their families has always been my source of passion and motivation. Having worked at NIBR for over 17 years, I continue to be impressed by the quality of the science and the consistent drive to do better for patients and develop truly transformative therapies. When we saw the CAR-T cell data published by Carl June and colleagues in 2011, we were astounded by the clinical benefit and the hope it could bring for many more.

Since then, I have been personally touched by friends and colleagues who we’ve lost to cancer while working on cell therapies that could have potentially impacted them if we were further along in the field. The transformative nature of this personalized medicine is unprecedented and the difference it makes in the lives of patients and their families inspires me to keep pushing for more innovative approaches to expand the reach to those who may benefit.

What has surprised you about working in immuno-oncology?

How much we know and yet how little we know. The immune system is complex and as an immunologist, I understand the yin and yang of immune regulation. However, this creates tremendous complexity in translational research as we attempt to uncover biomarkers of response or resistance.

We can see the power of the immune system in promoting durable remissions in select patients with the right immuno-oncology agent but our ability to predict these outcomes is still quite limited and key to better identifying markers for patient selection and stratification.

What are your thoughts on how to encourage young women entering STEM careers?

Follow your passion and listen to your inner voice as you explore new areas. Think about what gives you energy and excites you to come to work. This will provide much needed fuel throughout all the challenges along the way. And look for strong mentors and leaders who can help guide you. I have been blessed with amazing female and male mentors over the years, starting as early as high school and continuing to my current role. They provided numerous opportunities to explore and nurture my curiosities in the early days of my career and have become important role models as I sought to grow my own leadership skills.
Can you speak about your ongoing CAR-T cell therapy clinical trials?

It’s an exciting time at City of Hope and in the field of CAR-T cell therapy for both primary brain tumors and tumors that metastasize to the brain. These are very difficult to treat tumors. Most other therapies fail. There is a huge opportunity to improve outcomes for patients using cell-based therapies. Oftentimes when I give presentations, I start off by showing that CD-19 CARs can traffic to the brain and eliminate leukemia and lymphoma in the CNS. That was a surprise to all of us but it gave hope that this type of therapy can make a significant impact in these really difficult cancers.

I think City of Hope has more trials treating malignant brain tumors than any other institution at this point. We’re running seven clinical trials. Six of those are in primary brain tumors, either pediatric brain tumors or glioblastoma (GBM) or grade III gliomas. One is for HER2 malignancies that have metastasized to the brain. My laboratory is focused on accelerating learnings from the bench through City of Hope’s translational infrastructure to the clinic and to patients as quickly as possible. We have been doing that in many exciting ways since we started this program.

We have been looking at optimizing the route of CAR-T cell delivery for patients based on my preclinical research. We are also evaluating combination therapies and new CARs. We now have trials testing CARs that recognize three different antigens: IL-13 receptor alpha 2, HER2 and a chlorotoxin-directed CAR. We are also looking at different agents that modify the tumor microenvironment. We are combining CAR-T cells with checkpoint inhibition. We’re looking at CAR-T cell therapy with and without lymphodepletion.

What are some of those recent learnings from the bench that you’re translating to the clinic?

One important learning goes back to a New England Journal of Medicine publication from 2016. We had a patient with multifocal GBM. At that same time, my research laboratory was investigating different routes of administering CAR-T cells and how best to address the challenge of multifocal tumors. In mice, we were implanting tumors on each hemisphere of the brain and looking to see which delivery routes were most effective. We found that if we delivered these cells to the cerebrospinal fluid (CSF) we got better trafficking to multifocal tumors.

When one of our patients seemed to have a local response but his tumors far from the injection site progressed, we were able to meet with the clinical and research teams and show that the data in mice suggested the utility of delivering these cells in the CSF, which no other group was doing. We went to the FDA and asked for permission to administer CAR-T cells into the CSF in that patient and this individual had a dramatic clinical response where all of his lesions regressed and the therapy mediated a complete response in that setting.
Now there have been publications from other groups looking at other types of brain tumors and they are finding that administering CAR T cells into the CSF has clinical advantages. Many institutions are now using this route of delivery for their clinical trials. That is one example where we pivoted for a specific patient based on learnings from the research bench.

What are some of the challenges with taking an allogeneic approach for brain cancer?

We’re really excited about moving toward an allogeneic approach for brain tumors. These patients can’t wait. Median overall survival at first diagnosis is just a little over a year and a half. Once those tumors recur, which is the setting we’re treating at, it’s six months. Waiting 3-4 weeks for your autologous therapeutic product to be manufactured is a critical time for these patients. Off-the-shelf therapies will be important for all cancer types but will have a real opportunity for brain tumors. Also, the brain is an immunospecialized organ and so you might potentially have a greater therapeutic window before the allogeneic cells are rejected. Quite a while ago, City of Hope was one of the first institutions to evaluate an off-the-shelf approach for CAR-T cells in collaboration with Sangamo Biosciences.

The iPSC platform gives us a new opportunity. We have really encouraging and exciting preclinical data for our ability to differentiate these iPSCs into a T-cell lineage but we now need to scale-up the process and make this GMP compatible so it can be administered to patients. There are some unique aspects to the cell product. Our publication will show that these cells look very T-cell-like. They have a conventional T-cell phenotype but the majority of cells are more CD8 in the product versus CD4. We’re trying to use that to our advantage to build out a potent therapy and combination therapies that will be geared to promoting the therapeutic activity of a CD8 CAR product.

What are the biggest challenges to have a meaningful clinical impact on brain tumors?

The first is how to get the cells there. That is a huge challenge in brain tumors because these are regional cancers protected by the blood-brain barrier. How do you get these cells to infiltrate and penetrate these tumors? A lot of our work has been focused on that question and we have started out by focusing on optimizing the route of delivery to address this challenge. We are now looking at other ways to promote trafficking of the cells and creating an environment in the tumor to better recruit these immune cells. That’s true of all solid tumors but brain tumors represent a unique challenge because of its location.

The second key challenge for solid tumors is figuring out how to safely target without compromising or targeting normal tissue. At City of Hope, we are evaluating three novel CARs for GBM and hoping to build out trials combining them to have a multitargeted approach to address the challenge of heterogeneity. You want specificity but also broad targeting. A year ago we published in Science Translational Medicine a novel CAR using the chlorotoxin peptide, and are now looking to evaluate the utility of this CAR in the clinic and whether it will be tolerated by patients and if it will broadly target tumors as our preclinical data has suggested.

Lastly is the tumor microenvironment. How do you co-opt the microenvironment to become more anti-tumor? Our publication that is coming out and is online shows how CAR-T cells not only kill the tumor but through production of inflammatory cytokines like IFN-gamma can reshape the tumor microenvironment and actually promote endogenous immunological memory. That is really exciting because it shows that the CAR-T cells can kill and, under the right conditions, stimulate a host immune response. I think that the engagement of endogenous immune cells will be critical as we try to develop therapies that are highly effective against solid tumors. There is evidence that CAR-T cells can convert a tumor from “cold” to “hot” and recruit in more immune cells.

What will the next generation of therapies for GBM or brain tumor in general look like?

Most of our trials are focused on GBM. If you can crack the nut of curing GBM, you have a good likelihood of helping patients with any type of malignant brain tumor. Most of my studies and research has focused on GBM as the model for malignant brain tumors. It’s the most common and it’s an intractable tumor with few efficacious therapies.

The next generation of therapy will be a multipronged approach that targets tumors in a way that engages the host immune system. We hope these therapeutic cells will act as micro-scalpels that are able to go throughout the brain parenchyma and other areas and eliminate these sites of malignant disease. It’s not going to be easy. We spoke about the challenges. But I am optimistic. I think that there are a lot of exciting innovations going on in the field and bringing together other fields to make a meaningful impact for this patient population and other solid tumors.
Tina Cascone MD, PhD
Assistant Professor, Thoracic and Head and Neck Cancer at MD Anderson Cancer Center

Tina Cascone MD, PhD is an assistant professor in the Department of Thoracic, Head and Neck Medical Oncology at The University of Texas MD Anderson Cancer Center, Houston, TX. The overarching goal of Dr Cascone’s research program is to identify mechanisms of response and resistance to immunotherapies and develop novel therapeutic strategies to improve the cure rates of patients with operable non-small cell lung cancer (NSCLC).

Can you tell us about the work you are currently leading?

As an assistant professor in the Department of Thoracic/Head and Neck Medical Oncology at The University of Texas MD Anderson Cancer Center, I am leading clinical trials investigating perioperative immune checkpoint therapies in patients with early-stage non-small cell lung cancer who are candidates for surgery with the goal to prime the immune system when the intact tumor is still in place, enhance pathological tumor regression at surgery and minimize the risk of disease relapse.

My laboratory has established preclinical non-small lung cancer mouse models to evaluate different combinations of immune checkpoint inhibitors and study the mechanisms of resistance to immune-based therapies. Our goal is to use the preclinical findings to inform new clinical trials that investigate novel targets and biomarkers of clinical benefit.

What made you passionate about entering the field?

As a physician scientist, the results of the research that I do can have a direct impact on the patients that I see and care for in my clinic, and that is extremely rewarding. I have always been excited by the process of discovery and I was fortunate to participate in cancer research when I was in medical school.

Those initial studies were focused on examining cancer cell responses to different targeted therapies and I knew at that time that I wanted to pursue medical oncology as my profession. During my postdoctoral studies, my passion for cancer science and medical oncology grew tremendously and I focused my research efforts on studying mechanisms of lung cancer resistance to antiangiogenic therapy.

During my tenure as medical oncology fellow and instructor at MD Anderson, I decided to concentrate my research work on understanding how lung cancers become resistant to immunotherapy. Unfortunately, many patients with lung cancer do not respond to immunotherapy and my laboratory is studying the molecular basis of this immune resistance in order to develop more effective treatment strategies for our patients.

What has surprised you about working in immuno-oncology?

Perhaps most surprising has been the speed at which advances are being made for different types of cancer with the use of immunotherapy. This is certainly the case for non-small cell lung cancer. Immune checkpoint therapy has transformed the treatment landscape for early-stage resectable, unresectable locally advanced and metastatic non-small cell lung cancers.

We are trying to sustain the momentum by working in partnership with teams of physicians, researchers and trainees from several institutions to perform groundbreaking translation research work. This team science-driven research approach will allow us to expedite the investigation of more rational and effective combinatorial treatment strategies in the next-generation of clinical trials.

What are your thoughts on how to encourage young women to enter STEM?

One of the ways that we are trying to do this at MD Anderson is by going out into the community to local high schools and speaking to students about our research and the personal satisfaction one can receive through a career in science and medicine.

We have also established a research program for rotating college and medical students who are considering a career in biomedical science, including those who are under-represented in science and medicine. This program provides trainees with a hands-on experience in research laboratories and also exposes them to patient care. We hope that connecting female students with strong women role models and mentors can motivate young women to pursue a STEM career.
Vikki Cerniglia is Senior Director, BioPharma Business Development at Natera. Natera is a global leader in cell-free DNA (cfDNA) testing, dedicated to oncology, women’s health, and organ health.

What is your role at Natera?

I’m with the business development team working with our oncology pharma partners at Natera. I joined the company a little over four years ago. We collaborate on retrospective testing of completed clinical trials, testing in prospective trials and companion diagnostic (CDx) co-development. For example, last year we announced a Phase III trial and CDx collaboration with Roche/Genentech in muscle-invasive bladder cancer, using Signatera with their IO therapy, atezolizumab.

How has your career led to your current role?

I’ve always been a curious person. And I have always loved science. I feel very fortunate that I had several mentors that really steered and guided me along the way. I started out as a nursing major in college. And then after a series of scientific classes that I took, I was more excited and motivated in the scientific component, and I switched my major to microbiology. I started my career in a technical role in research. While I was a “lab rat”, one of my bench-mates mentioned they knew someone who was interviewing for a company and passed it along to me. I said, “Why not? Why not just talk to people and see what’s out there?”

Throughout my career, I had the pleasure of working with many sectors in science, anything that was related to DNA, RNA, and genomics. A former manager asked me to join Natera, and I was thrilled at the opportunity to join a cutting-edge team and cause. I was the first person to join Natera for their oncology business development group to help launch the pharma oncology team, and it’s been an amazing experience.

What is the work in business development you’re leading on a day-to-day basis?

As a key leader in driving Natera’s pharma business, I am in constant communication with our clients, and monitor their satisfaction with our services. It’s my responsibility to understand and identify the needs of the pharma and campaign for their initiatives at Natera.

In working with retrospective analysis projects, pharma typically has a question that they want to answer about a cohort of samples. They would say, “We want to send 500 patient samples with five time points and see how, for instance, if our immunotherapy performance changes in this cohort of cancer patients in a particular histology.” Was the Signatera test able to track molecular residual disease over time and how much earlier was it able to detect that over something like imaging?

For prospective studies, there is a lot of coordination, identification with the pharma partner on what criteria need to be in place, and what systems we must set up. And then, ensure the testing assay components are coordinated for booting up the trial to receive that pivotal first patient sample.
Can you describe how pharma clients are using Natera tests?

From the Pharma studies’ perspective, they are asking 1 of 2 questions: 1) In earlier stage cancers, is there tumor still present? And 2) Is the treatment working?

The Signatera test itself is a personalized, tumor-informed assay that’s used for detecting very low levels of ctDNA. In a patient’s blood, they may have circulating tumor DNA coming from residual tumor or micro-metastases after definitive surgery or therapy. The Signatera test is used to answer that question, “Is cancer still present?”

We use the test as a serial monitoring technique to see over time if the treatment is causing ctDNA to decrease. When we look at immune checkpoint inhibitors, and in the IO space, only 20-30% of those patients really respond. And in some cases, you have segments of patients who are super responders—those who clear their ctDNA very rapidly, versus one that takes a little bit longer but is still responding, versus the population of the non-responders.

In the INSPIRE trial published last year, collaborators at Princess Margaret Cancer Center and Merck were able to detect at six weeks into treatment if patients treated with pembrolizumab were responding or not. Early insights into treatment efficacy can have huge implications clinically and for pharma drug development. By understanding very early into treatment which patients are responding, it can allow for more rapid evolution of drug development strategies, as well as opening opportunities for new combinations or investigational treatments for patients who aren’t responding.

How does the work Natera is leading help us to better understand and treat cancer?

The whole goal of using something like a molecular residual disease test is to be able to provide information earlier and augment the current tools that are out there. Radiological and other established clinical metrics are great, but they may not be as sensitive as detecting low levels of ctDNA in a patient’s blood. The goal is to have a positive impact on the patient’s treatment journey by identifying residual disease or treatment relapse months to years ahead of clinical symptoms or radiologic progression.

It’s not only giving real-time methodologies for oncologists and cancer care and treatments going forward, but you’re able to intervene sooner. And by having that earlier intervention, the patients have a better outcome. We are constantly innovating and driving growth into emerging areas like our expansion into early cancer detection and screening. Those are the types of tools that Natera is trying to empower pharma companies, oncologists, and even patients: to ask more questions and to dive deeper.

Is there a piece of advice you’ve given or received over your career that you often come back to?

Have a vision of your career. It doesn’t have to be a detailed plan but have a vision of what you want for your career. Life is long and careers are often a crooked path that you are winding down. It’s not necessarily in a succinct, forward line. I was once told your career should be like visiting a foreign country: have an itinerary but be open to things that happen along the way. Sometimes that means changing your path. Don’t feel like you must be handcuffed to the choices that you made. Be open, be flexible, and be persistent.

What are your thoughts on how to encourage young women to enter STEM careers?

First off, we’re always getting feedback from innumerable sources. And as you go through life, whether it’s your parents or your teacher or your manager who is giving you feedback, focus on those positive comments. Too often we get tied up with negative comments. But when you get positive reinforcement, that’s something to think about as a budding scientist and as you’re trying to figure out what is your career path.

When you start to identify those positive components, you start to see trends. You think, “My teacher said I was good at this. My dad said I was good at this. My mentor said I was good at this. Maybe I should do something that’s in this area.” And then, does it help invigorate other areas of my life?

I have two sons, and their schools have started to insert an A for “art” into STEM. It’s a creative component that has significance. In my older son’s STEAM class, projects had to satisfy all five components. Not only science, technology, engineering, and math, but it also had to be artistic.

And when you satisfy the art, you touch on the creativity of who you are, and it provokes that deeper level of curiosity and contentment. And so, when I think about women in STEM, and how it can change and impact the world for the better, we need to keep fostering these budding scientists so that their ideas will grow. Be curious, ask questions, trust that doors will open. And we should celebrate each other’s achievements so that we continue to empower these women, not only now but into the future.

To learn more, visit www.natera.com
Can you tell us about the work you are currently leading?

At Lyell, I am the SVP Corporate Strategy and Business Development. In addition to Corporate Strategy and Business Development, I am also responsible for Alliance Management, Competitive Intelligence and New Product & Portfolio Planning.

Lyell Immunopharma is a T cell reprogramming company dedicated to the mastery of T cells to cure patients with solid tumors. We believe the key to effective cell therapy is the mastery of the identity, fate and function of cells to create living medicines, and we seek to overcome what we view as the two major barriers to successful adoptive cell therapy – T cell exhaustion and lack of durable stemness – through the application of our novel and proprietary genetic and epigenetic reprogramming technologies, Gen-R and Epi-R.

Our technologies are designed to be applied in a target and modality agnostic manner to CAR, TIL and TCR therapies to fundamentally improve the properties of T cells needed to outlast and eradicate solid tumors. Our first IND for LYL797 was cleared by the FDA in December 2021. LYL797 is a ROR1-targeted CAR T-cell therapy that incorporates Gen-R and Epi-R. We expect to begin screening patients for our Phase 1 clinical trial of LYL797 by the end of the first quarter of this year. We expect to submit three additional INDs by the end of 2022.

What made you passionate about entering the field?

I’ve worked in oncology for over 15 years, mostly on the diagnostics side at Genomic Health (now Exact Sciences), Illumina and GRAIL. Genomic Health developed the Oncotype DX™ test to help breast cancer patients navigate their journey and determine how likely their cancer was to recur as well as whether they would benefit from chemotherapy.

Together with targeted therapies, these kinds of innovations have driven better treatment options and outcomes for patients, while also adding value to the patients’ families, physicians and the healthcare system. Immuno-oncology is in many ways a culmination of five decades of research and development to elucidate the complexity of cancer’s biology and its interactions with our immune system.

It’s the ultimate personalized and precision medicine, using living cells to treat a patient’s cancer. We still have a long way to go especially for solid tumors but the glimmers of potential curative treatments beyond the sporadic cases we’ve seen are emerging.
Like so many others, I’ve been affected by friends and family who have struggled and succumbed to their cancer diagnoses, and this is what made me passionate about entering the field, and to keep going. In the past year, my friends and family have been impacted by breast, pancreatic, renal, multiple myeloma, and ovarian cancers. Patients are waiting for better and more effective therapies. I’m constantly inspired by the brilliant minds and personalities who take on this endeavor to improve care for cancer patients, and I hope we will see dramatic progress through IO in the next 5-10 years.

What has surprised you about working in immuno-oncology?

Coming from the diagnostics side of things, the expense to develop cell therapies surprised me. However, I also understand that we are in the early stages of testing and hopefully demonstrating that our therapies will work in people.

If we can do that, there are many engineering solutions we need to explore and develop to reduce cost and increase scalability and access. This is often how innovation is achieved and disseminated. Twenty years ago it cost approximately a billion dollars and many years to sequence the first human genome. Now, it costs a few hundred dollars and less than a day, and sequencing is ubiquitous in both research and clinical settings.

What are your thoughts on how to encourage young women entering STEM?

There is a remarkable convergence of many different areas of science which is accelerating our understanding of not only cancer but other challenging areas of medicine at unprecedented rates. Just look at how quickly we can characterize and respond to new Covid variants.

We need all the bright, creative, curious minds out there who can embrace and leverage amazing capabilities like DNA sequencing, DNA editing, data science and machine learning to solve the biggest healthcare, and in fact – global, technological and societal, challenges we face. Entering STEM is the gateway for doing that.

As women leaders, and as leaders in general, we can support girls and young women in this. There are great organizations to get involved in like Young Women in Bio to expose more cross sections of our communities to the exciting potential of life sciences, and as the mother of a young daughter, I love seeing the increasing focus of STEM starting in elementary education and am an enthusiastic supporter.

“Like so many others, I’ve been affected by friends and family who have struggled and succumbed to their cancer diagnoses, and this is what made me passionate about entering the field, and to keep going.”
Rachel Haurwitz, PhD, is a co-founder of Caribou Biosciences and has been its President and Chief Executive Officer and a director since the company’s inception in 2011. She is an inventor on patents and patent applications covering multiple CRISPR-based technologies.

What is the application of CRISPR for cancer treatment that Caribou is trying to pursue?

Caribou is advancing the development of allogeneic CAR-T cell therapies for hematologic malignancies and allogeneic CAR-NK cell therapies for solid tumors. We believe the key to developing successful allogeneic cell therapies is persistence, and we are using our proprietary technologies to enhance persistence by preventing rejection or rapid exhaustion of our cell therapies.

Can you tell me about the development of chRDNAs and how much more specific they’re able to make genome editing?

Caribou’s proprietary, next-generation CRISPR technology is called the chRDNA (pronounced “chardonnay”) technology. It stands for “CRISPR hybrid RNA-DNA” and it describes the guides we have invented here at Caribou that contain both DNA and RNA. chRDNA guides yield genome edits that are orders of magnitude more specific (fewer off-target edits) than first generation CRISPR-Cas9 (using all-RNA guides). The Cas12a protein guided by chRDNA guides can carry out very efficient multiplex editing including multiple gene insertions into the same cell.

Especially coming into the role of CEO at a young age, and from the lab, how did you develop your leadership style and your approach to leading a company?

By learning! I have been on a steep learning curve for the past decade, and I expect to be a lifelong learner over the course of my career. People are the most important part of a company. I have learned so much from the many talented people with whom I have worked at Caribou over the years, and I’m grateful to the many fantastic people who are my colleagues today. It’s inspiring to be on a collective mission to deliver promising therapies to patients who need new approaches.

What were the challenges in developing an allogeneic product?

Although allogeneic cell therapy is positioned to unlock the broader potential of engineered immune cells as a leading therapeutic modality, allogeneic cell therapies emerging in the clinic today have yet to achieve the same rates and durability of response as autologous therapies. We believe there are multiple key elements to successfully developing an allogeneic CAR-T cell therapy. One key element is safety. Caribou uses healthy donor T cells, not a patient’s own T cells, to make each batch of product. Therefore, we have to use genome editing to remove the T cell receptor (TCR) in order to prevent the risk of graft-versus-host disease (GvHD). A second key element is targeting. We use our chRDNA technology to site-specifically insert a CAR into the T cell genome in order to direct the T cells to a tumor-specific antigen. Another key element is persistence. Allogeneic CAR-T cells are foreign to the patient’s immune system and are therefore rapidly rejected. This is quite different from autologous, or
patient-specific, CAR-T cells which can persist for years after the delivery of only a single dose.

At Caribou, we use our genome editing to enhance persistence in different ways in our programs. For example, in our lead program (CB-010), we knock out PD-1 from the CAR-T cell to prevent rapid CAR-T cell exhaustion, and in our second program (CB-011), we immune cloak the CAR-T cells to blunt CAR-T cell rejection. We plan to apply the experience from these programs toward the future development of additional allogeneic CAR-T and CAR-NK programs.

Are there hurdles utilizing CRISPR, as a newer technology, for commercial applications?

New technologies may encounter manufacturing challenges as products approach commercialization. Currently, we rely on CMOs for the manufacture of our product candidates for clinical use, and most of these CMOs have demonstrated capability in preparation of materials for commercialization. We conduct our own process development internally prior to transferring our methodologies to the CMO that manufactures our cGMP cell products. While we are seeing an expansion in manufacturing capabilities and capacity for cellular therapies, we may build our own manufacturing facility in the future to provide us greater flexibility and control over our clinical and/or commercial manufacturing needs.

Can you tell us about the ANTLER study?

The ANTLER study is a phase 1 clinical trial to evaluate CB-010, Caribou’s allogeneic, anti-CD19 CAR-T cell therapy, in patients with relapsed or refractory B cell non-Hodgkin lymphoma. We announced in July of this year that we had dosed the first patient in this study, and we expect to share initial data from this trial next year. To the best of our knowledge, CB-010 is the first allogeneic CAR-T in the clinic with a PD-1 knockout. We believe that removing PD-1 from the CAR-T genome will prevent rapid CAR-T exhaustion, thereby keeping the CAR-T cells in an active, antitumor state for a longer period of time.

How does Caribou hope to make progress in solid tumors using NKs?

Natural killer (NK) cells are emerging as an increasingly important cell type for therapeutic development, as they play an important role in ridding the body of cancer as well as viruses. Solid tumors are particularly challenging to treat, and CAR-T cells have largely underperformed in the solid tumor setting. In contrast, NK cells inherently target both primary solid tumors and metastases. This is a promising approach and we are developing CAR-NK therapies for the treatment of multiple solid tumor types. We are able to differentiate NK cells from induced pluripotent stem cells (iPSCs) that we first edit in multiple ways to address targeting, trafficking, proliferation, and overcoming the immunosuppressive tumor microenvironment.

What are the North Stars guiding your work, and where do you hope to see CRISPR technology, or Caribou, in the next 3-5 years?

Caribou’s mission is to develop innovative, transformative therapies for patients with devastating disease through novel genome editing. Over the next 3-5 years, I hope to see Caribou advance multiple additional programs into the clinic and I hope that those programs demonstrate promising safety and efficacy data in patients with unmet medical need. CRISPR technology holds tremendous potential for patients.

Your most developed product is CB-010; on your website, you describe the specific edits made to that product. What was the process of picking those things to edit/change, to optimize its potential?

We believe enhancing the persistence of our cell therapy product candidates is the key to unlocking the broader potential of off-the-shelf cell therapies. There are multiple ways to enhance persistence, and we are evaluating two different strategies in our first two programs. As described in more detail above, we are removing PD-1 from CB-010 in order to prevent premature CAR-T exhaustion. We understand from the literature that the PD-1/PD-L1 axis is important in NHL and the majority of NHL tumors are PD-L1 positive, so we felt that NHL is an appropriate disease setting in which to evaluate the safety and efficacy of a PD-1 knockout. CB-011, Caribou’s preclinical allogeneic CAR-T for multiple myeloma, is on track for an IND filing next year. In CB-011, we enhance persistence by a different method: we immune cloak the cells to prevent their rapid rejection by the patient’s immune system.
How did you get involved in science?

I think I was pretty much born to be a scientist. And my mom will tell you that, like when I was a kid, I would take everything apart, much to her chagrin. And as I got a little older, I started putting things back together. I always had a project that I was working on. My dad bought me a book called “The Way Things Work,” which showed detailed diagrams of a refrigerator, or a manual transmission, and I had an insatiable drive to figure out what makes something work.

That drive led me to explore biology and genetics, and, ultimately, tool development.

Can you describe the work you’re leading at 10x Genomics as Senior Director, Cell Biology and Applications?

We invent and build high-resolution tools for oncology research. This requires innovation and collaboration across many different disciplines. The focus of my department is biological samples and scientific applications.

And what is the work you’re doing in biological samples?

10x Genomics is known as a leader in single-cell genomics. And that really means we enable scientists to profile the transcriptome, cell surface proteins, chromatin structure, and immune receptors for every individual cell in a sample. And to do that, you have to start with a very high quality sample, whether that’s a tumor biopsy, a vial of blood, an organoid, or a mouse model of disease. That sample needs to be prepared in a very specific manner.

The scientists in our department have expertise in tissue dissociation, flow cytometry, and handling clinical samples. This is really a critical part of product development. We make sure that our customers will be successful, because sample processing is that make-or-break step of our workflow. If you get the first step wrong, and you’ll have poor quality results at the end.

What does current tissue sampling look like?

We’re building the next generation of research tools. Previously, you’ve been able to take a biological sample process with perhaps a standard technology, and you can look at the transcriptome of all the cells combined together. When you think about what we’re trying to do to enable single-cell analysis, every single cell is important.

Therefore, you want your sample to have very high viability, very high quality with very low amounts of debris or decomposition occurring. That’s what our group thinks about, and that’s how we build our advice, our protocols and how we work with our customers.

In what part of the research lifecycle are you working with clients?

Our customer base is incredibly broad, so we’re finding that our customers are using our tools for everything from drug screens using cultured cells, to working in mouse models of disease, and working with patient cohorts and clinical samples. The diversity of biological samples that our customers use runs a complete gamut of everything.
that’s happening in oncology research. And we need to make sure that all of those different sample types are compatible with our assays.

In what capacity are you working with clinical teams on their trials?

My department really has two functions. The first is biological sample processing. The second function of the department is applications: what scientific questions can you unlock using our technology? The scientists in our department manage collaborations and work with key opinion leaders to make sure that our products are doing what they’re supposed to do in the context of those clinical trials. We don’t necessarily process sample cohorts on site, but we work closely with our key customers.

We also perform smaller scale demonstrations in house that show the maximum potential depth of information you can get from a sample or set of samples, and then we will publish that data for free on our website so other scientists can download and make discoveries within those datasets.

What are the hurdles or opportunities of growth that you’re coming across in your work?

Some of the challenges include transitioning from being involved in every experiment to now leading a big team of individual scientists who have more expertise than I do in a lot of these different fields. My challenge is learning how to step back and really appreciate all of the growth and all of the development that’s happening within the team.

How does the work you’re leading help us to better understand cancer, and therefore how to treat it?

I’m a tool builder, and I love opening up possibilities for other researchers and enabling them to move more quickly. My north star is to make other scientists better. And how our technology fits in with that is we enable scientists to look at a biological system, and measure every single cell in that sample on an individual basis. It’s fundamentally the right way to characterize a biological sample or system.

What we’ve seen is that the products are used across the board in oncology research, from looking at basic mechanisms of disease, new breakthroughs in how to stratify patients, as well as deeply understanding CAR-T mechanisms of action and off-effects, and being able to characterize the tumor microenvironment at an unprecedented level of resolution.

As I look towards the future, what I think is exciting about the tools we develop is that they’re not just used by the top-tier institutions, or well-funded large consortia. Individual grad students and individual postdocs are all applying our technology to their own research systems. To me, it makes the future of immuno-oncology research fundamentally democratized and accelerated.

What are your thoughts on how to encourage young women entering STEM?

I think the key to being successful and remaining engaged is not to think of that as a linear progression, but to scramble it up. Especially for young women going through school, coursework can be intense or competitive or routine. So it’s crucial to make sure you have that connection to the spark that made you interested in science in the first place, and always making sure you have an outlet. It’s still STEM, but it’s light-hearted and fun, and positions you to be in this for the long haul.

Is there advice you’ve given or received over the course of your career that you come back to often?

The piece of advice that I go back to most often is the importance of being both correct and helpful. As scientists, we’re trained to pursue the truth with all abandon. And sometimes that can lead us to be competitive with each other, whether it’s fighting for authorship or grants when you’re in school, but when you’re out in a career, your success is about building bridges with others, and realizing that as a team, you accomplish much more.

So not only do you need to be correct in what you’re doing, you have to apply that knowledge to help others around you. There isn’t a place for competition, at least not in our company.

What are you looking forward to being able to accomplish in the IO space in the next few years?

I’m really excited about seeing not only our technology, but any high resolution technology, one day to make it into diagnostics. That’s very far in the future. But for all of the advanced research that we do in a laboratory research setting, when it comes to patients and getting their own diagnoses and receiving treatment, those tests tend to be quite simple or based on imaging. They are not based on a host of molecular information specific to their unique tumor.

I know this is a long journey, but the breakthroughs we’ve seen at the bench from customers using our technology, I know will be included into the patient treatment ecosystem one day.

To learn more, visit www.10xgenomics.com
Vassiliki Karantza, MD, PhD
Associate Vice President in Global Clinical Development at Merck

What is the work you’re leading at Merck?

I am the Breast Cancer Sub-Section Head within the Women’s Cancers Section at Merck. Our mission is the development of more effective treatment paradigms for all breast cancer subtypes in all settings, including both metastatic and early-stage disease.

How did you first enter science as a career?

It all started with a great chemistry teacher I had in high school. I loved chemistry, and so when I did my undergraduate in Greece, I majored in Chemistry. I then came to the US for a PhD in biochemistry. During that time, I realized that being in the lab was not enough. I needed to do something more practical, like being involved in direct patient care. So, at the age of 30, I went to medical school.

It is quite interesting that when I went to medical school, I did not want to do any further lab work. However, I realized that basic science is very relevant to health and disease, and my interest in it resurfaced. I decided to do a medical oncology fellowship, as cancer research is a very active and potentially impactful field. I also decided that I would go back to the lab, where I did postdoctoral basic research focused on breast cancer at Rutgers and the Cancer Institute of New Jersey. I then stayed on as an Assistant Professor and a physician scientist. My primary responsibility was running a basic research lab and my clinical responsibilities were in the Phase I clinic of Experimental Therapeutics.

What led to the transition from academia to industry?

After several years, I decided that it would be great to do clinical trials on a much bigger scale, and potentially have an impact on the lives of many more patients. So, I transitioned to industry and joined Merck. When I first started my higher education studies, I could not foresee where this journey would ultimately take me. I have been very fortunate, and I am grateful that I was at the right place at the right time. I certainly had the opportunity of a lifetime to play a major role in the clinical development of pembrolizumab in breast cancer from the very beginning of Phase I data interpretation all the way to bringing it to patients as a component of more effective treatments for triple-negative breast cancer.
What is the process of developing a new paradigm treatment?

I was very fortunate to join Merck at the time when the first data using Keytruda for the treatment of breast cancer became available in 2014. It was a small cohort of patients with heavily pretreated metastatic triple-negative breast cancer in a bigger multi-cohort study looking for proof-of-concept signals in different malignancies. Based on promising data from the breast cancer cohort of 32 patients, we started investigating pembrolizumab as a treatment for triple-negative breast cancer with a Phase II clinical trial, and then expanded the Breast Cancer Program to three Phase III trials.

In two of these studies, KEYNOTE-355 and KEYNOTE-522, the regimen that included Keytruda did better than what was standard-of-care treatment at the time of study start for patients with previously untreated metastatic disease and for patients with early-stage disease, respectively. In KEYNOTE-355, the addition of pembrolizumab to chemotherapy extended the overall survival for patients with metastatic triple-negative breast cancer compared to chemotherapy alone.

In KEYNOTE-522, pembrolizumab in combination with chemotherapy given before surgery and then continued as a single agent after surgery, for a total pembrolizumab administration of one year, resulted in longer survival without disease progression before surgery or a recurrence after surgery. These two studies led to approvals of pembrolizumab for the treatment of metastatic and early-stage triple negative breast cancer by FDA in 2021. Pembrolizumab plus chemotherapy has now been approved in 30+ countries for patients with PD-L1-positive triple-negative breast cancer, whereas the early-stage regimen is under review by multiple regulatory agencies in the world, including the EU and Japan.

We started the process in 2014, and we got our approvals in 2021.

What did using a previously approved immunotherapy for other cancer types, such as melanoma and lung cancer, in a new indication elucidate about how breast cancer operates?

A drug like pembrolizumab re-activates the immune cells in the tumor and ultimately leads to cancer cell death and tumor shrinkage. We have found that tumors infiltrated with more immune cells are more responsive to immunotherapy. As a result, pembrolizumab can potentially work in many tumor types, so long as there are immune cells present, but the effectiveness may be different. It is not a coincidence that pembrolizumab was first approved in melanoma and lung cancer, which are inflammatory tumors with many immune cells.

Breast cancer is not a very immunogenic cancer and is generally not so responsive to single agent immunotherapy. However, when combined with chemotherapy, pembrolizumab becomes more active in breast cancer as the killing of cancer cells by chemotherapy brings more immune cells into the tumor. Triple-negative breast cancer was the first breast cancer subtype to be tackled with immunotherapy, as it is considered more immunogenic than the other two main breast cancer subtypes. It is also a cancer with a high unmet medical need, as patients with triple-negative breast cancer generally have poor prognosis and short overall survival after their disease becomes metastatic.

Is there a piece of advice you often come back to over your career?

The first piece of advice I was given was to do something that really interested me. Because no matter what one works on, there are always difficulties. And one needs to remain involved, focused and committed even during a time of adversity. Doing what one truly likes and is deeply interested in is paramount.

Another advice I was given when I joined Merck was to be very good at what I did. I was told “find your niche and be very good at it to be considered an expert”. It wasn’t too difficult for me to do well in breast cancer, as I already knew it clinically and had done relevant research. However, I still strived for a deeper knowledge of the disease and a solid understanding of drug development in industry. Building a successful breast cancer program at Merck was due not only to a great drug, such as pembrolizumab, but also due to a dedicated team of many individuals who greatly enjoy what they are doing and are experts in it.

Do you have any thoughts on how to encourage young women entering STEM fields?

To any young woman who is contemplating entering STEM, I would like to say: “If this is the field that deeply interests you, you should pursue it. Do what you like most, as this will keep you driven and lead to success”.

Getting to the approval of Keytruda in triple-negative breast cancer was not an easy task. For seven years, we had a lot of ups and downs. A major reason we kept going and persevered despite the difficulties and setbacks was that the team members were working on what they mostly liked, were good at it, and remained committed to helping patients.
Can you tell us about the work you are currently leading?

I lead Allogene’s Biometrics team and am responsible for the study design, analysis strategy, statistical aspects of regulatory requirements and negotiation, analysis conduct, analytical programming, and data acquisition for Allogene’s clinical development programs. Additionally, my team oversees data curation and archival across Allogene’s functional platforms.

I began working in the CAR T field and the cancer immunotherapy field at Kite Pharma, where I built and led the Biometrics team beginning in mid-2014 up through the end of 2019. Working at the leading edge of the field at Kite, and now at Allogene, in our endeavor to bring accessible, quick-delivery CAR T cells to patients, is such an honor and privilege, and I am thrilled to make my contribution.

What made you passionate about entering the field?

As a person with a technical and scientific background, I am drawn to multiple facets of immuno-oncology. First, math and statistics applied to immunology, disease models, and clinical trial models is absolutely fascinating for me. I truly enjoy thinking about the mathematical modeling aspects. Secondly, immunology is wonderfully complex, and from a biological perspective, I am constantly learning new elements of the science.

From a mathematical perspective, immunology adds a wonderfully complex layer to the statistics and modeling. Thirdly, IO requires many different areas of expertise and fosters so much cross-functional collaboration. I have learned so much from my colleagues with different areas of scientific focus and enjoy working with such dedicated scientists. Lastly, and most importantly, if our collective work in IO can lead to better outcomes in patients, help improve survival, quality of life, and patients’ options, it is profoundly gratifying.

What has surprised you about working in immuno-oncology?

The complexity of the disease has always fascinated me, but working in IO, I have begun to learn how equally complex the immune response to cancer is. The depth and dynamics of the immune system and the ability of IO to improve outcomes in a meaningful way (with durability of response) surprised me.

I am also pleasantly surprised at the open-mindedness of regulatory agencies on the review and approval of IO therapies, including consideration of pan-tumor trials, novel endpoints, and smaller, more innovative trials; this makes my work very interesting and exciting. I am also pleased to see how quickly IO therapies have moved closer to the mainstream in a relatively short time. This motivates me to work toward improving access to IO therapies so that more patients can benefit.

What are your thoughts on how to encourage young women entering STEM?

Believe in your capability and expertise; your capability and place in STEM is not in question. STEM is much more than just being a technical expert, you will also need to bring skill in communication, listening, leadership, negotiation, and creativity to your work.

Develop these along with your technical expertise and bring your own personal strengths to the field. Be confident that there will be other women both in and outside of STEM to help you as you move forward in your career path. Actively find ways to help other women move forward on their career paths – network with them, nominate them for special assignments, roles, speaking engagements, internships, promotions.
Andrea Perrone, MD
AVP, Global Clinical Operations, Head of Clinical Scientists and Study Management, Oncology, at Merck

Can you tell us about the work you are currently leading?

My team of talented Executive Directors, Sr. Directors, Program Leads, Clinical Scientists and Study Managers support the development and execution of late stage clinical trials (180+) as well as early stage and External Collaborations (300+) in oncology.

What made you passionate about entering the field?

I had the privilege of leading Merck’s Clinical Imaging team for 8 years at Merck to formalize our imaging strategies in early and late stage oncology. As our IO portfolio continued to expand, I was passionate about taking on a new role in Global Clinical Operations where the impact of our new therapeutics was even more tangible and exciting. Now, my areas of passion now include strategies to improve diversity in our oncology clinical trials to ensure there is parity in access to so many novel and promising treatment options.

What has surprised you about working in immuno-oncology?

The immuno-oncology space has been rapidly evolving where many indications have replaced chemotherapy as a standard of care to an IO that is better tolerated and more efficacious. As treatment options continue to expand including combinations of IO as well as the opportunity to treat patients in the adjuvant and neoadjuvant setting, I have been surprised about the truly transformative nature of the impact of our industry. It is conceivable to consider potential cures for some cancer indications in our lifetime; that is not something I expected when I entered this field.

What are your thoughts on how to encourage young women to enter STEM careers?

There are many ways to encourage young women to enter STEM that can start at a very young age including being a Girl Scout Leader with a focus on related activities. As girls get older, it is ideal for women in STEM to support events such as science fairs or ‘Bring Your Daughter to Work Day.’ I have enjoyed going to my daughters’ schools with X-rays of animals and things that people have swallowed. It was always exciting to catch a spark of interest in a young girl. And, finally, as our children are growing and considering careers, it is important for business leaders to support internships that are accessible to young women as well as minorities in fields of science, technology engineering and math.

Do you have any advice that you come back to often?

My father brought up five daughters and his message was always clear: “Pick a career where you can leave the world a little bit better.” He used to make us all practice changing tires (before we knew about AAA) and would often tell us that we could do anything a man can. His guidance helped us all realize our true potential: two physicians, one engineer and two business executives, and I have tried to impart that spirit in my three daughters as well.
Can you describe the work you’re leading at Parexel?

My role focuses on the improvement of clinical trial design from strategic consulting to the execution of biomarker and precision medicine studies. Our global team across the US, Europe, and Asia-Pacific regions are specialized experts in biomarkers, genomics, computational biology, statistical genetics, and clinical pharmacology as well as other therapeutic areas. My team operates cross-functionally within Parexel and also externally with our partners to support clinical research, developing novel therapies to fill unmet medical needs faster, safer and better.

How did you end up in science and in your career now?

I like detective work, figuring out the why’s and the how’s. As a physician-scientist, I was involved in medical science about twenty years ago at Columbia Medical Center. We were working on the very first Human Genome Project. It was scientific research, but it was more like detective work. We needed to sequence the genome, putting the fragmented data puzzle pieces together in order to discover tumor suppressor genes and identify the root cause of the problem. We needed to do that in order to understand the mechanisms of tumorigenesis and figure out how to switch on and off this complex machinery in order to stop or reverse cancer progression.

How is your work in biomarkers and genomics being leveraged for immuno-oncology?

Immuno-oncology, as well as targeted therapies or cell and gene therapies, share a pivotal pillar: biomarkers, be it PD-L1 expression or driver mutations or novel neoantigens. We touch upon basically every component of biomarkers, from genomics and PK-PD biomarkers to immunogenicity biomarkers. The key for us is to think of it as an ecosystem. The common foundation is to focus on the leveraging of biomarkers to find the best treatment option for patients.

What do you see moving forward for the use of genomics and new biomarkers?

Oncology is a field devoted to both science and the art of creating second chances for patients. It’s quite broadly accepted in the medical community that cancer is a disease of the genome. Cancer progression and tumorigenesis involve the mutation of or change in the genome. So genomic medicine is a critical component for us to create scientifically sound, and also creative solutions, to tackle this complex disease of the genome. As medical researchers, we seek avenues to design clinical trials creatively leveraging genomics and biomarkers, how we can execute the clinical trials with maximum efficiency and explore what we can do to leverage both data and technology to reduce patient burden and clinical practice burdens. For those of us working in genomic medicine, we evaluate all of these factors in our quest to help the most challenging and vulnerable patients with life-threatening diseases. We are competing against time, so any forward step to identify patients sooner, and conduct clinical trials faster, is key in the success in the biomarker and genomic space.
Is incorporating and leveraging all the genomic/biomarker data you’re amassing into better trials a challenge in your daily work?

It’s all about how to integrate data and insights, from upstream to downstream, in order to move forward. Scientifically, the challenge of fighting cancer is similar to fighting COVID-19: it’s not a static problem, but highly dynamic. Cancer is a genomic disease. Similar to COVID-19 with variants and mutations, the tumor type also carries mutations that are constantly changing. That provides them some evolutionary advantage in either blocking or escaping from our treatment. That forces us to evolve how we tackle this challenge, to act more nimbly and creatively to find new solutions.

What career advice can you share with aspiring professionals?

To anyone seeking a role in this field, I would say that you need to have a genuine passion for your areas of focus. Engage in active learning, especially in a quickly evolving field such as innovative drug development.

Do your research. Identify and seek out a workplace that fits your core values. Connect with employees, follow the organizations on social media, take note which are winning awards for innovation, inclusion, and new discoveries. On the flip side, as leaders of a team, we should ensure that our workplace nurtures, supports, and accelerates equal opportunities for young men and young women in this area. This includes development opportunities and increasing representation and inclusion, from all segments across the organization, as well as providing mentoring and coaching programs to young scientists.

What would be your advice for young women entering oncology or STEM careers?

I always say to young female scientists, “Cherish your motivation and be bold about your good ideas.” You need to develop your confidence ideally early in your career. It’s also very important to develop and establish your competence and credibility. Specific to STEM, don’t be afraid of failure. It’s especially common in drug development – be ready to fail nine times out of 10. Be open to feedback and learnings, and always be willing to try and fail – and retry.

You are speaking about “From Tumor to Host Genomics: Rekindling Impact of Germline Variants in Immunotherapy Development” at the upcoming conference. Can you tell us a little bit about what that means for the IO space?

I use the word “rekindle” because having worked in this field for many years, I witnessed a shift of the paradigm and a change of perceptions, from germline variants to tumor variants and tumor genomic profiling. And now with our accumulated learnings, host genomics stands as one of the key pillars that shouldn’t be overlooked now that we continue to gain a better understanding of the whole omics field in the IO space, including the impact on drug responses and strategizing the IO trial designs.

What are you looking forward to in the next few years in the biomarker-genomics field?

I would expect to see more and more of the data offerings come to fruition as treatments, Not just genomics, not just clinical data, but also, for example, integrated real-world data, to help us gain new insights for improved trial design through to execution. Team-wise, I look forward to continuing to build and expand our global biomarkers and genomics teams, staying cutting-edge, strengthening our capabilities, as well as creating supportive working environments.

Speaking of big data, do you believe we’re making good use of the data that we do have already?

Yes. We are seeing more and more genomic data or genomic information being incorporated into the study protocols for patient selection and inclusion. On top of that, integrated omics or multi-omics data are being explored either in the biomarker discovery space or the drug mechanistic understanding space. Even more broadly, we have radiomics and digital pathology or other imaging data, phenotypic data, plus EHR clinical data and real-world data. The incorporation of those types of data modalities offers broader use applications. There are a lot of exciting efforts ongoing in integrating and analyzing the data to explore what we can learn from these big data offerings.

Is there a new development in your biomarker work that you are excited to apply in pursuing immuno-oncology?

There are a few areas that I consider that are playing an important role in immuno-oncology. One is spatial whole-exome/whole-genome sequencing. We’re leveraging them to paint a more comprehensive picture of the tumor and its interacting microenvironment. Jointly is the advancement of liquid biopsy biomarkers including ctDNA, which offers an opportunity to harvest tumor dynamics information in a less invasive approach. I feel quite excited about incorporating a new development like this to provide some additional insights in IO therapy development.

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Managing Site Operations and Sparking the Joy for Science

Chétna Rao, PhD
Head of Site Strategy and Operations at Bristol Myers Squibb

What is the work you’re leading at Bristol Myers Squibb?

I head the site strategy and operations in the Redwood City and San Francisco sites. In my role, I manage multiple functional areas, which include operational effectiveness by leveraging resources to allow science to operate in a more streamlined and innovative manner and removing barriers and tasks that prohibit scientists from spending more time in the labs. My job boils down to letting the scientists focus on the science because I can handle everything else.

Being a bench scientist in my previous role, I didn’t realize the important work that materialized in the background where I could do uninterrupted science. Now, from an operations perspective, forecasting the needs of the scientists ahead of time is the key. To me, sometimes it becomes a little easier because I know the journey of a scientist and a project, so I can anticipate what the needs are in advance.

How did you transition from your role as a scientist into your position now?

I’ve been working with oncology since 1999, when I joined my first start-up company. I attended university in India up to a master’s level. I came to California for my PhD program, did my postdoc and became a career research scientist. I had all these patents, and I brought three medicines to market. But in 2018, I actually stepped back. When this opportunity came through, I thought this change would actually help me provide others the ability to pursue education much like the opportunities I’ve been given. I changed positions and started seeing the site operations, and started honing in on my passion, which is the emphasis on furthering STEM education.

How has the pandemic impacted how you approach your work?

During the pandemic, this has been extremely challenging. I spearheaded the return-to-office initiative for both of the sites; and it was key to understand the project priority needs. This is a discovery site, so we may start with 20 projects, and two of them move into the clinic. But with those 20 projects, what are the priorities? What are the needs of the scientists?

To bring them back to work in a safe environment was challenging. From an operations perspective, to figure out the little things, it has to be a well-oiled machine. We can’t have scientists crowding in labs, but they still want to do their experiments. Trying to figure out how to keep that momentum going, despite the pandemic, was a learning experience for me and our teams.

I’ve lost my sleep over this sometimes, trying to figure out how we can get everybody together, and still keep the research moving forward so that our patients can benefit. And this has allowed the opportunity to rethink what our business continuity plan should be. Because the pandemic has taught me that: we need a plan. If this happens again, what is our plan going forward? That to me, was the biggest opportunity from an operations point of view.
Can you tell me about your role leading the R&D STEM Council?

The BMS R&D STEM Council aims to amplify and advance the company’s commitment to educating the next generation of STEM leaders. I spearheaded all of the company’s efforts in the Bay Area, where we are providing access to opportunities in education for students, especially in historically excluded communities, all the way from kindergarten to graduate school.

Under my leadership, BMS has helped schools in underrepresented areas to understand the importance of science on our society. Especially in the wake of the pandemic, it’s been a little difficult for people who have been historically excluded. During my time here, I’ve been instrumental in helping grow the BMS presence in the Bay Area, in terms of the expansion of the Redwood City campus, as well as the integration of the San Francisco site following BMS’ acquisition of Celgene.

Can you describe the STEM programs you’re leading in the Bay Area?

When I first started thinking about STEM, I felt we needed to look at the local environment, within our backyard. It’s very critical to expose young students to STEM and also provide role models so that you can empower them in a STEM career. And the only way we could do that was to provide these learning opportunities through various programs, where they can see what science is all about and hone their skills.

As an example, there is a small middle school just a stone’s throw away. It is 98% Latino students, and they had not had much exposure to STEM. I reached out to the principal and asked what we could do. From there, we put up a robotics lab where students applied their skills in coding and making these little robots. They were really excited about it, to the extent the science teacher said, “I’ve never seen students so quiet in any class.”

We also took some of our scientists who are women and who spoke Spanish to the students, to say, “This is what we are doing as our career.” When kids see role models, it makes a much bigger impact. That really ignited their curiosity and their passion for science.

We also partnered with a Black Excellence in STEM program at San Francisco State University. BMS provides funding to Black students for their undergraduate programs, and now some of them have graduated and moved on to PhD programs at different universities. We have multiple organizations we are supporting, and they’re all grassroots, which gives us an opportunity to actually connect with these students, as well.

How have you seen immunotherapy in oncology evolve since your involvement in its early phases?

It’s a world of difference. When I started working in oncology immunotherapy, around 2001/2002, there was no translational work. We went with almost a gut feeling of how things were going to work. We had great collaborations with academic institutions where they had done a lot of the basic research. We understood that harnessing the immune system was going to give us something. We ran mouse models. We did preclinical studies. We did clinical studies, and it worked.

We did not go in blind, because we understood the pathway. But knowing now how people living with serious diseases are responding or not, as well as how translational pieces and artificial intelligence (AI) are coming into place, creates the ideal combination of high-tech and biotech. Using, for example, AI, we can understand which patients may respond to a treatment, or not.

We didn’t have that information when I was doing basic research. And I’m not an immunologist; I’m a protein chemist. I generated molecules that were required by the immunologist to test. It is truly a different world, because we understand things a lot more now than we did back then. I don’t think we have the full picture yet, but we’re getting close to it.

Knowing which patients are going to respond based on their genetic makeup, depending on what gene they are expressing, from a translational perspective, is a game changer. That wasn’t available to us then, but it’s available now. The immuno-oncology field is definitely changing towards something better, which is really going to benefit patients in the future.

Is there a piece of advice you often circle back to over the course of your career?

As you mature, you look at things a lot differently. When I was a young scientist, I was all energy – and I still am – but over the years, I’ve had some really good managers and leaders to look up to and emulate their qualities. And one of the things that I’ve learned is, on a day-to-day basis, you have to practice humility. It’s very important because as scientists we can get carried away with what we’re doing. It’s game-changing, but practicing humility is extremely important.

Another piece of advice is never stop learning from anyone you meet, no matter how long you’ve been in this industry. Especially in our field, there’s always something you can learn and strive to achieve. I always say, “if you learn something new every day, that day is a good day.” If you shut yourself from developing your skills and knowledge, you’ll quickly fall behind.
Can you describe the work you’re leading at Catamaran Bio?

We are creating off-the-shelf engineered allogeneic CAR-NK cell therapies for solid tumors. I lead the strategy to leverage our TAILWIND platform to create a pipeline of innovative CAR-NK cell therapy product candidates that possess novel functionalities.

We use synthetic biology tools and transposon systems to engineer our NK cell therapies with new attributes to help tackle solid tumors. The significance of the transposon system is that it enables us to introduce larger genetic payloads into the NK cells than has been possible with the viral engineering methods being used in the field. With our approach, the sky's the limit for what we can put into these NK cells, and this enables us to empower them against the tumor in a way that is beyond their inherent capabilities.

How did you enter science as a career?

It was through school that I became interested. I liked math and I liked puzzles. Ironically, I didn’t like biology. It probably has a lot to do with the way it was taught. It just seemed like nomenclature and cutting things open. That just didn’t grab me. I had been interested in chemistry, what the world is made of, and how different principles work within the natural world. But then I did a summer course in high school, where I learned about the chemistry that underlies biology, and that was the hook for me. It was new to me that you could explain biology with principles of chemistry and physics, and that changed things for me. I ended up being a biology major in college, and then I earned a PhD in biochemistry.

How are you changing the power of NK cells?

The great thing about transposon engineering is that it allows us to provide our CAR-NK cell therapies with multiple functionalities. We are directing them more specifically to the tumor with the chimeric antigen receptors, the CAR. We are also arming them with biological switches so that they resist the suppressive effects of the tumor microenvironment. And what’s even more exciting is that some of our switches outsmart the tumor by converting those inhibitory or suppressive signals from the tumor into NK cell stimulatory signals. We also engineer our CAR-NK cells with factors that help their longevity. The cell therapy field is teaching us that those durable responses are related to the longevity of the cells, so we want to improve their pharmacology to last longer thus possibly enable durable responses.

What does Catamaran hope to achieve by utilizing CAR-NK cells, versus CAR-T, to treat solid tumors?

We are using our CAR-NK cell platform to develop allogeneic cell therapies to provide broader and immediate availability to patients.

NK cells are the first line of defense against tumors. They are wired to kill tumors and solicit other immune cell types to amplify tumor cell killing. They can also be engineered to improve their functionality in solid tumor environments.

A major advantage of CAR-NK cells over CAR-T cells is their improved safety profile. Allogeneic CAR-T cells carry the risk of GVHD, or graft versus host disease, where the T cells can start to attack the patient’s tissue, because they see it as foreign. NK cells don’t have that property. They are a safer way to deliver an allogeneic therapy.
Have NK cells been a large focus of your career?

My academic training was in cancer genetics, in other words, understanding what is going on in the tumor cells themselves. I started in the field of immuno-oncology during my industry career. Immuno-oncology comes in orthogonally, in that it’s not just about what’s going on in the tumor, but also about what’s happening in the whole body of the patient. I’m a lifelong learner; I love learning new things. It’s been great to enter this field through my work, as well as a lot of self-teaching and learning from conferences, to gain the appropriate background to be able to develop therapies in the IO space.

What can cell therapies achieve that is unique to their functionality?

Cell therapies can be considered as both a replacement for the patient’s immune system and as a catalyst for reawakening the immune system. They must change something in the tumor. The cell therapy itself can be therapeutic, but could also catalyze a change in the equilibrium that’s been established between tumor and the patient’s immune system. We have the potential with cell therapies to break that cycle and have the patient’s immune system come back and be functional against the tumor. We call that antigen spreading. That is a Holy Grail in the field: to be able to trigger a really transformative event against the tumor and shift things so that the patient’s immune system can come back and start recognizing that tumor as something that shouldn’t be there.

Your background is not in immuno-oncology originally. What has surprised you about the field since stepping into it?

I’ve been surprised by the patient responses to these therapies, and the durability of those responses for some patients. Early in my career, I chose to work in the CAR-T field because the clinical data was so promising in hematologic malignancy patients who had no other therapeutic options.

Is there a piece of advice that you often come back to over the course of your career?

No one is going to be great at everything. The most important thing is to have self-awareness of your limitations. Reach for the sky in your areas of strength and empower your team to complement your weaknesses.

What would be your advice for young women entering STEM careers?

I would say that you have an opportunity to learn the incredible way that nature works and an opportunity to discover or make something new. The most important thing is to stay connected to your curiosity, keep asking questions, and be motivated by what you learn.

A challenge for women is that it can be difficult to find female role models. And so, you need to be able to keep your confidence in yourself, and go back to that fundamental drive of wanting to understand something.

I have two daughters. The thing I try to support them with in their STEM work in school is not the content itself, but helping them to get past their self doubt when they find the work difficult. There’s no question, this is difficult work, and it requires dedication. But what I want to teach them is to see the difference between hard work, versus them not being capable, and reinforce to them that they can do it. They just have to work their way through the challenges.

You’re on a panel discussion about synthetic biology and its role in cell therapy. What are you excited about in terms of either bringing to the table or learning from the other panelists?

Historically in cell therapy we’ve been quite constrained, based on the engineering approaches available. Synthetic biology is changing all of that. We can now arm cell therapies with biological switches and functionalities to allow them to address solid tumors. We have the tool kit to make sure we direct them into the right place, that they’re functioning in the immunosuppressive tumor microenvironment, and that they have long lives for durable therapeutic responses.

And then we’d like to catalyze changes in the tumor and start impacting other cells that are present, turning dysfunctional cells into functional cells, and tap into what the patient’s cells can actually do for them. Ultimately, our goal is to reactivate the host immune system.

The ability to change the tumor suppressive environment and reactivate the host system: those are the frontier areas for synthetic biology.

You touched upon two areas – creating stronger and more durable cells and catalyzing the immune system. Can both goals be achieved in one therapy?

Until now, scientists haven’t been able to do that because of the limitation of the available engineering approaches. But the field is at a turning point now. And that is what’s so exciting to me about working at Catamaran. With the transposon engineering technology and synthetic biology, we can figure out what to put in the cells for new switches and pathways and the large cargo carrying capacity of transposons enables that engineering – the two technologies go hand-in-hand – you can’t do one without the other. We also have another gene editing approach for changing the cell and what it does. So I think the synergy of these technologies represent a turning point in this field. Combined, they are allowing us to open up what we can do, far beyond what’s been done in the past.
Can you describe the work you’re leading at Johns Hopkins in your lab?

I’ve been involved in the development of immune checkpoint blockers for cancer therapy. I have been at Hopkins for the past 15 years and really started this work in earnest as soon as I arrived in 2006. 2006 was an important year because it was the year that the very first patient was treated with an anti-PD-1 drug, any of the anti-PD-1 drugs. And this happened to be nivolumab in a first-in-human trial. I was involved in that study, and things evolved from there. It’s been a very exciting trajectory.

We found out from our very earliest study that patients with advanced cancers could respond to anti-PD-1 as a single drug. These were patients who had not responded to other forms of therapy available at the time, and really had run out of other options. And so it was really remarkable to see that at least in a subset of these patients, their tumors did regress. And I think one of the earliest observations that was very exciting to us is that advanced lung cancer could respond to anti-PD-1.

This really opened the doors to many other opportunities for clinical testing and other common cancers, which before then had not responded to cancer immunotherapies of all kinds. And so it was really this observation in lung cancer that then catapulted this entire field, I think, into the mainstream of oncology.

How has your work with nivolumab evolved, in terms of applications and understanding, over the course of the last 15 years?

Our first objective was to find out which cancer types might respond to anti-PD-1 and the list continues to grow. The activity spectrum turned out to be broader than we had originally imagined. Nevertheless, there are many patients whose tumors do not respond to this therapy. So the next objective was to figure out what we could use as markers of response or resistance to anti-PD-1. The first attempt we made to find a biomarker was to stain pretreatment tumor specimens for expression of the ligand PD-L1. We reported the first results in that area in 2012, showing that tumors that expressed PD-L1 were more likely to respond to anti-PD-1 therapy.

How did you first get involved in the field of immunotherapy?

I trained as a surgeon. And during my surgical residency, I wanted to take a year off to do research. And at the time, over 30 years ago, it actually wasn’t so popular for surgical residents to do research. Now, it’s built into every surgical residency program. My advisors said it was fine. I spent a year working at the Children’s Hospital in Philadelphia. I went into a laboratory there because, at the time, I thought I wanted to be a pediatric surgeon. It turned out that the laboratory I joined was a cancer immunology lab. That was my first exposure to cancer immunology, on a research basis, doing murine tumor model experiments. I became hooked on the idea that the immune system should be able to reject cancer, the same way that it rejects bacteria, viruses and transplanted organs, and that we just needed to know more about how cancer interacts with the immune system to be able to manipulate that to our advantage.
And after that, the field jumped in and did additional studies, which confirmed that in some cancer types – not across the board – PD-L1 expression as detected in pretreatment tumor biopsies may identify a group of patients who are more likely to respond than other patients.

Since then, we have continued to look for biomarkers. There are two other markers that are FDA approved for anti-PD-1 or PD-L1 drug use. One is microsatellite instability (MSI) and the other is tumor mutational burden.

And so, it turns out that tumors that have more complex arrays of DNA mutations are generally more likely to respond to anti-PD-1, probably because those mutations lead to the translation of proteins that are abnormal and are sensed by the immune system. But the work for biomarkers that are even more predictive and more sensitive continues. So this is a huge area of research today. It’s something that’s going on in my lab here at Hopkins.

You’ve cited melanoma as a good immunotherapy example because it’s responsive. What is the latest on your work with melanoma and what it means for immuno-oncology?

My clinical specialty is melanoma but I came to that through immunotherapy research.

After I finished my surgical residency, I did a fellowship at the National Cancer Institute and I was in Steve Rosenberg’s group. It was a very exciting time in the mid-to-late 1980s. We were discovering interactions between the immune system and cancer, and testing new treatments in the clinic.

It became obvious early on, even though we were enrolling patients with a variety of different kinds of cancers in these immunotherapy trials in the 1980s, that it was the patients with melanoma who were most likely to show some kind of response. Even though it was a very small proportion of those patients, this was what grabbed our attention.

Gradually immunotherapy research in the 1980s and 1990s came to focus mostly on melanoma, and also on kidney cancer, which it turns out is also very well-seen by the human immune system. That’s how I came to know a lot about melanoma and eventually specialized in that disease clinically.

Melanoma has always been a good model to test new immunotherapies. Where we are today is that melanomas have a high response rate to immunotherapy, to anti-PD-1 therapy and also to some of the new combination therapies that are being tested.

However, still about 50% of patients are not helped by this approach. There’s still a lot of work to do. But for studies looking into biomarkers, a disease like melanoma gives us a group of responders, which is fairly large, as well as a group of nonresponders, where we can do these comparisons.

The story now for melanoma is the development of combination therapies that are going to be more effective than anti-PD-1 alone. There was a lot of exciting work that was reported at the AACR and ASCO meetings this year about new treatment combinations that may actually be helping patients who have not seen a response to anti-PD-1 alone, but who may respond to a new drug combination.

What are the goals or targets on the horizon that are driving your work?

At the conference, I’m going to be talking about neoadjuvant therapy, which is pre-surgical immunotherapy. This is a huge area of focus for us now. The idea there is that we’ve learned a lot in the past 15 years about treating advanced cancers of many different kinds with anti-PD-1 or anti-PD-L1. We are learning about more effective treatment combinations. We’ve even learned about some biomarkers that are useful. We’ve also learned that these drugs are relatively safe. That supported the notion that maybe it would be safe to treat patients with earlier stages of cancer.

It’s all about risk and benefit. But once we had a pretty good idea about the risks and the potential benefits, we started to ask if we could move this treatment earlier in the course of cancer and would it prevent tumors from progressing to advanced Stage IV, which is difficult to treat?

Going back to melanoma was the first tumor type where adjuvant anti-PD-1 therapy became FDA-approved. And after that, we asked a question, “Could we even give this before surgery to patients who were candidates for surgery, but at high risk for relapse because of certain properties of their cancer?” That’s what we’ve done.

A group of investigators here at Hopkins that I work with published the very first report of anti-PD-1 neoadjuvant therapy in lung cancer. This was a paper written by Patrick Ford and colleagues in the New England Journal of Medicine in 2018. The same approach is being used in melanoma by Christian Blank and colleagues, who have widely published on this and now in many other cancer types.

We published another portion of the CheckMate 358 trial that was done in Merkel cell carcinoma that was published in the Journal of Clinical Oncology in 2020. Those two studies – the head and neck, and the Merkel cell – are a good contrast to each other, because the neoadjuvant anti-PD-1 worked very well in Merkel cell carcinoma. Almost 50% of the patients had a complete microscopic disappearance of tumor in pathology specimens after only four weeks of anti-PD-1.

That was very exciting. But then with head and neck cancer, that cancer type is relatively resistant to this approach. There, we need to find something that’s going to be more effective, and very likely, it’s going to require a combination treatment approach before surgery.
Can you tell us about the work you’re currently leading?

My current role is Associate Director of Immune and Inflammatory Disease Group at Regeneron, where I am leading a team developing new immunotherapy strategies for oncology and autoimmune disorders.

What made you passionate about entering the field?

My grandfather passed away from lung cancer when I was very young, but he had a very big personality. His memory was a big influence on my family growing up, so I wanted to be a doctor and work in oncology. My interest, my motivation, has always been to help cancer patients.

After medical school, I did an internship at the Shanghai Cancer Center, one of the biggest in China, and saw up close how there aren’t any real treatment options for late-stage patients. Patients suffer under radiation and chemotherapy, often with poor results. That experience confirmed to me that the real work is in the lab and that is what makes me passionate in developing novel treatment strategies for cancer patients.

What has surprised you about working in immuno-oncology?

While I am amazed by the progress of the IO field on a daily basis, I am often surprised by how little we actually know about how the immune system works. This motivates me to understand more about the immune system in different states and leads me to study areas beyond immuno-oncology, such as autoimmune diseases, COVID-19 and etc. Learning from different fields deepens my understanding of the immune system. I hope it will help develop breakthrough therapies for patients, not only cancer patients but also other immune disorders.

What are your thoughts on how to encourage young women to enter STEM?

I think we need to create a nurturing environment that promotes science starting at a young age to promote the idea that science careers are within their reach. We also need to introduce young girls to diverse and reliable examples of women in STEM and highlight how they became scientists. It is important for young women to be able to envision themselves being a scientist following a path of success.

Is there anything else you would like to share with our readers?

As a working mom with young kids, I would like to shout out to all the working mom scientists there. I have learned that every working mom is Superwoman. You can be a mom and pursue your dream simultaneously. I would like to use a quote from Tina Fey: “I think every working mom probably feels the same thing. You go through big chunks of time where you’re just thinking, ‘This is impossible — oh, this is impossible.’ And then you just keep going and keep going, and you sort of do the impossible.”
Christine Ward, PhD
Vice President, Head of Oncology and Cell Therapy Precision & Translational Medicine at Takeda

What is the work you’re leading at Takeda?

Right now, we’re in the middle of building a precision and translational medicine organization for both oncology and cell therapy. I joined Takeda about a year ago; before that, the translational capabilities were very dispersed across the organization. And given the importance of precision and translational medicine to oncology, we needed to build a function to do this.

It’s basically a one-stop shop for everything translational in my organization, from the people that come up with the early translational strategies; to the colleagues that make and work in our clinical trials to implement the translational strategies, to really understand which patients are responding and how our drugs are working; to the group that does companion diagnostics. We’re building a team to do a lot of the assays and to help with the outsourcing of the assays. It’s a new model for Takeda. It existed in different parts around Takeda. But given the speed that oncology moves, we felt it was important to pull it all together in one organization.

What is the focus of Takeda in regards to oncology and immunotherapy?

Our North Star for oncology is that we aspire to cure cancer. So it’s a vision; obviously we have a ways to go to get there. But it trickles down into our mission to bring our treatments to patients as quickly as possible, and with as much data as possible, so that physicians can make informed treatment decisions for our patients.

The team that I’m building here at Takeda is really going to be central to that, because cancer drug development moves very quickly. You’re able to pivot and accelerate development programs based on understanding response in certain populations. So it’s really an important and integral part of what we do.

We have molecules in the proteasome inhibitor space; we have molecules that target specific mutations in lung cancer, so mobocertinib and brigatinib. Brigatinib targets ALK. And then over the past couple of years, we’ve really made a conscious effort to go down that immuno-oncology space. We have a number of programs that target the interferon pathway, as well as cell therapy now. We have an exciting collaboration with MD Anderson around CAR NKs that we’re very, very excited about.

From the Precision and Translational Medicine hub, how do you prioritize such a broad pipeline and develop a working team?

The good news is, the organization recognizes that this is a core area that needs to be resourced. So we’re
building the right team now. And secondly, we prioritize our pipeline very, very efficiently. Obviously, we have programs that are very exciting. They’re prioritized for various reasons, based on where they are in the potential launch map, as well as the data that’s been generated. Our team is very, very keenly aware of what the priorities are.

Can you describe Takeda’s approaches to immunotherapy, turning tumors cold-to-hot and redirected immunity, in its pipeline?

With redirected immunity, we consider cell therapy and T cell engagers as parts of that bucket. That’s really our cell therapy/T cell engagers pipeline. It’s a little bit earlier, so we still need to see what the potential is in the clinic. And then for what we call cold/hot, it’s about turning cold tumors warm. That’s where we have a lot of the interferon programs; we have a program called TAK-573, which is an exciting attenukine that delivers interferon into CD38-positive cells. That is very exciting. We have a STING agonist, also in this interferon space, as well as other programs. We think about it very mechanistically. But the two development paths are intertwined in terms of moving as quickly as possible, but the redirected immunity is a little earlier in the pipeline.

Why is it crucial to have an in-house translational capability?

Translational is an indispensable part of oncology drug development. There are numerous examples of many companies taking the quick all-comers approach, where you just move your molecule as fast as possible. You dose the highest dose you can get in your Phase I study, see where it works, and then all of a sudden, go fast and do a Phase III and then sometimes it doesn’t work.

The new way of doing this, the new model that most companies have embraced, is really taking a translational mindset. And to me, that is taking data from patients, very early on, to inform decisions.

That means you’re studying your target pathway in patients to understand which disease indications your drug might work best in. That means the way you run your Phase I one studies that you’re not just making decisions about your drug just based on safety, and early efficacy, but you’re looking at that pharmacodynamic relationship and the PK/PD relationship. It takes an incredibly strong partnership with clinical development. And in my experience, the best partnerships internally at a drug company are where the translational scientists and the clinical development/clinical science team are partnering, integrated in this same mindset, to bring the drugs as quickly as possible, but to study it very robustly while in the clinic.

It’s like a dance, and we have to make tradeoffs all the time. And sometimes you can’t do the things that you want to do, because they’re just not feasible and you’d never be able to recruit a study. And so we make those decisions together, between the translational and clinical team. And we’re also pushing innovation, because we are embracing those new technologies that may not be officially approved as a diagnostic yet, but have a lot of promise. We do work with the best partners to put the highest quality assays into our clinical trials.

What do you see as the biggest hurdle in getting a stronger response to immunotherapy and precision medicine?

There are a couple of barriers. When I was discussing our pipeline: we have molecules that target EGFR Exon 20. It’s a very specific mutation. And either you have it or you don’t. There are different flavors of it, but we know how to look for them, especially now that we can do sequencing and see different levels of mutations.

You can see different levels of the mutations, and not just the one point mutation. You can look at the whole gene and sequence it. The challenge with IO is that some of these biomarkers are what we call “continuous variables.” Rather than, “I have the mutation, I’m going to respond,” and “If I don’t have the mutation, I won’t respond,” it’s a continuum. As the marker of interest increases, you tend to see this increase in response. But how do you define that cutoff, because it’s not a binary readout?

That’s a challenge, particularly with immuno oncology. And if you look to the PD-1 space, you’ll see this with the PD-L1 story. You see it with tumor mutational burden as a biomarker. That was studied for a while and seemed to have some promise. It was the same thing: how do you define the cutoff to balance those that are responding and not responding? That’s a challenge.
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Director, Clinical Trial Patient Diversity, Global Clinical Trial Operations
Merck Research Labs

Sarah Anderson
Executive Director, Oncology, Therapeutic Strategy Lead, Business Development
Worldwide Clinical Trials

Vikki Cerniglia
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Angela Qu, MD, PhD
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Head of Site Strategy and Operations
BMS

Bei Wang, MD, PhD
Associate Director
Regeneron

Christine Ward, PhD
VP, Head of Oncology and Cell Therapy Precision & Translational Medicine
Takeda