Challenge Accepted
Accelerating Research & Saving Lives
Our Mission: To end suffering and death due to melanoma by collaborating with all stakeholders to accelerate powerful research, advance cures for all patients, and prevent more melanomas.

Founded in 2007 with the generous support of Debra and Leon Black, MRA is the largest nonprofit funder of melanoma research. To date, MRA has awarded $131 million to 380 research programs. Thanks to the generous support of our founders, 100% of all donations to MRA go directly to research.
The Melanoma Research Alliance was founded in 2007 with an unwavering commitment to end suffering and death due to melanoma. At the time, this mission wasn’t just ambitious — it was a complete rejection of the status quo.

Since then, MRA has become a world leader in advancing transformational science and has contributed to unprecedented progress on behalf of patients. To date, we’ve directly invested more than $131 million in research — and leveraged an additional $415 million from outside sources — to advance our mission.

In the last decade alone, more than 13 new therapeutic approaches for melanoma have earned FDA approval. Today, patients have more treatment options than ever before and many are living longer, fuller lives as a result.

The melanoma community is leading the way for oncology as a beacon of innovation and scientific excellence. In fact, the 2021 Annual Report to the Nation on the Status of Cancer (ARN), found a greater decline in deaths due to melanoma than all other cancers in the last several years.

Despite this progress, it still isn’t enough, as half of patients facing advanced melanoma are still not benefiting from available treatments. Many challenges remain, including:
● Optimizing artificial intelligence to ensure all communities benefit from new detection tools;
● Overcoming primary and secondary resistance to existing melanoma treatments;
● Better understanding the unique features of rare melanoma subtypes to find more effective treatment options; and
● Modulating the array of factors that can impact treatment effectiveness and quality of life.

We are tackling these and future challenges yet to come. This report features a few examples of our work over the last year.

MRA, in partnership with government, industry, patients, other foundations, and of course researchers, is hard at work unraveling some of the biggest unanswered questions facing patients today. Together we will continue to push forward and to overcome challenges needed to achieve our mission.

As always, we greatly appreciate the many individuals, organizations, government leaders, and companies whose support has allowed us to remain steadfast in our approach. Together, we will overcome the many challenges needed to achieve our mission.

Debra Black
Chair and Co-founder

Michael Kaplan
President and CEO
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MRA by the Numbers
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<th>Statistic</th>
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<td>$131 million in grants</td>
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<td>500+ investigators</td>
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<td>380 research awards granted</td>
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<td>$415 million in leveraged and follow-on funding</td>
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<td>11,248 donors</td>
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<td>15,000+ people have used our clinical trial navigator to find personalized clinical trial results in their community</td>
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<td>158 institutions in 19 countries funded</td>
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<td>211 different agents for treatment of melanoma investigated</td>
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<td>610 corporate partners who’ve raised over $59 million to support melanoma research</td>
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<td>100% of all donations go directly to research — no admin, development, or other fees</td>
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Participation in MRA's virtual Scientific Retreat flourished in 2021, almost doubling to more than 500 people and growing the MRA community even more.
Challenge Accepted.

This was a year like no other.

We witnessed the importance of science, research, and human tenacity in rare but powerful ways. COVID-19 forced so many of us to adapt seemingly overnight. It pushed us in ways we never knew and persisted without an end in sight. Nevertheless, we persevered.

And, indeed, perseverance is at the core of what we do at MRA. We never stop challenging ourselves, no matter the odds or obstacles, in pursuit of conquering melanoma and saving lives.

Despite the tumultuous year, we continued to share lessons learned, collaborate with partners across industries, engage patients and advocates, and bring people together to discuss and advance scientific breakthroughs. We funded investigators who are tackling some of the most vexing issues facing patients with melanoma, such as rare subtypes and treatment-resistant disease; as well as innovations, including therapeutic vaccines and microbiome diversity in immunotherapy response.
Paving a Path for Cancer Vaccines

“It’s exciting that we can consider in the future what we haven’t been able to before. I think the field has advanced tremendously and I’m very hopeful.”

DR. NINA BHARDWAJ

One such innovator helping pave the way is Dr. Nina Bhardwaj, Director of Immunotherapy at The Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai and Professor of Hematology and Oncology.

Although vaccines to prevent COVID-19 have dominated conversations and the news cycle since the start of the pandemic — Bhardwaj and her team have been busy at work with a different type of vaccine altogether: one to support melanoma treatment and reduce risk of recurrence.

“There are two types of vaccines,” explains Bhardwaj. “There are prevention vaccines and therapeutic vaccines.” Prevention vaccines are designed to prevent people from becoming infected with or facing serious illness from a particular pathogen. As it relates to cancer, these exist for HPV and hepatitis B. Recent COVID-19 vaccines are another example of prevention vaccines. Therapeutic vaccines, however, are given when someone has already been diagnosed with cancer; the vaccine helps boosts the immune system in order to better attack cancer cells or to prevent the recurrence of cancer.

Cancer Vaccines to Prevent Melanoma Recurrence

Bhardwaj and other researchers are studying if therapeutic vaccines could be used to prevent relapse following surgery, in what is called adjuvant therapy. The vaccines could help the immune system eliminate any micro-metastatic disease that might be remaining, but otherwise not detectible via scans.

Researchers hope that this would also help prime the immune system so that should the cancer recur, the patient has some reasonable immunity to the cancer antigens.
Although cancer vaccines have shown some efficacy on their own, the latest research suggests that they become much more potent in their cancer-fighting abilities when combined with other, more established, immunotherapies. In a recent study that Bhardwaj and her team conducted, they found that adding immunotherapies to vaccines to mobilize antigen-presenting cells (key for initiating an immune response) made the vaccines twice as effective.¹

Simplistically, vaccines work by training the immune system to rapidly respond to a foreign invader. To do this, certain protein fragments — called antigens — must be introduced into the body to trigger an immune response.

When it comes to the flu, measles, shingles, or even COVID-19 the concept of a “foreign invader” makes sense. Vaccines introduce small molecular snippets from the virus. These snippets, completely harmless on their own, are enough to teach our immune system how to fight the full-fledged virus should you become exposed to it.

However, if instead you focus on cancer vaccines, this quickly becomes more complicated. That’s because cancer develops within our own cells — so not only do these vaccines need to work, they also need to be able to differentiate between healthy and cancerous cells. Despite the challenge, researchers including Dr. Bhardwaj are confident that vaccines have a place at the table in the fight against melanoma and other cancers.

Bhardwaj and her team are investigating “one-size-fits-all” melanoma vaccines that would introduce antigens found in all or most melanomas. They are also working on personalized vaccines based on antigens found in a specific patient’s tumor. She says she’s cautiously optimistic of what the cancer vaccine future looks like, particularly because researchers are able to stimulate the immune system in ways they never could before and in combinations with immunotherapy that make such approaches more effective than ever.

In addition to identifying the right antigens to include in a melanoma vaccine, researchers must also select the right delivery mechanism — what they call a “vaccine platform.” For example, the flu shot uses viral fragments or inactivated virus, the measles vaccine uses a weakened version of the virus, and the shingles vaccine uses part of the virus to train the immune system.

One platform that researchers have been studying for decades for the delivery of vaccines is Messenger RNA (mRNA). This technology made its mainstream debut in several of the COVID-19 vaccines, such as those by Pfizer-BioNTech and Moderna, who are now pursuing this platform in many cancers. Bhardwaj is planning the same delivery mechanism for her work to develop a melanoma vaccine.

“We want our vaccine to create a super immune response,” says Bhardwaj. “These RNA platforms are inducing high-quality immunity; so, we’ll have to see whether or not in combination with checkpoint inhibitors if they will give us the kind of impact that we want and further improve response rates. This is a very exciting area to study right now.”

Bhardwaj and her team have developed computer algorithms to help identify which antigens should be included in a vaccine candidate. They have also examined what model systems are best suited to study experimental vaccines before first-in-human clinical trials. A recent clinical study — led by Bhardwaj — compared formulations of a “one-size-fits-all” vaccine for melanoma to identify the formulation that elicits the best anti-tumor immune response. This research is not only advancing the field for patients facing melanoma, but those with other cancers.

“With a better understanding of the patient’s antigen repertoire and all the technology that has come out, plus the ability to monitor a response so carefully and individually is incredible,” says Bhardwaj. “For me, the Melanoma Research Alliance has been instrumental in supporting all of these initial studies and allowing us to progress them forward into vaccines in the clinic. It’s exciting that we can consider in the future what we haven’t been able to before. I think the field has advanced tremendously and I’m very hopeful.”

“...Melanoma Research Alliance has been instrumental in supporting all of these initial studies and allowing us to progress them forward into vaccines in the clinic.”

DR. NINA BHARDWAJ
Melanoma survivor and MRA Board Member Amanda Eilian.

CHALLENGE ACCEPTED
As recent history shows, when it comes to transformational melanoma research, innovation takes many forms. From treatment to detection — the field is evolving, and expanding rapidly to best meet the needs of people facing the disease. One researcher leading the way in melanoma detection is Dr. Roberto Novoa, a Clinical Associate Professor and Associate Program Director in the Division of Dermatopathology at Stanford University. Novoa is harnessing the power of artificial intelligence (AI) to more accurately detect and diagnose melanoma with a 2020 MRA Team Science Award supported by L’Oréal Dermatological Beauty Brands.

If you browse through your phone’s app store, you’ll find dozens of offerings related to melanoma. Several apps promise to help determine if a mole you’ve been staring at is cancerous or not based on the power of AI. While a great goal, none of these apps have earned approval from the Food and Drug Administration (FDA). However, to do so, apps — and the algorithms that they rely on — will need to be rigorously tested in the real world and across diverse populations. This is exactly where Dr. Novoa’s research is aimed.

Dr. Novoa, both a practicing dermatologist and dermatopathologist, has always been interested in recognizing patterns and making the right diagnosis. In fact, it’s what initially drew him into dermatology and to later subspecialize in dermatopathology. “While I liked many different aspects of medicine, I liked putting all the pieces together to find out what is going on … Visual diagnosis, it isn’t everything, but it is a big part of the practice of dermatology,” says Dr. Novoa. “Dermatopathology is an even further distillation of the same aspects that drew me to dermatology. You become a resource for all other dermatologists as you incorporate visual data with all available clinical data to get to an answer. I love it.”

Between splitting his time seeing patients and interpreting slides, Dr. Novoa also leads significant research efforts. “I’m interested in applying new technologies to the process of diagnosis. It all started for me seven years ago when I heard of some of the work being done in AI where they were using the..."
technology to classify dog breeds. If they can do that, this technology can diagnose skin cancers."

This is important because when melanoma is diagnosed at its earliest stage, it’s curable. However, significant disparities in the appropriate diagnosis of melanoma exist in the United States — especially for communities of color, economically disadvantage individuals, and those living in rural areas.

While many studies have demonstrated that AI and machine learning can work to diagnose melanoma — at least in retrospective studies — real world assessment and practical lessons learned are still critically needed. What we don’t know is how these new technologies work in the clinic, what the ideal use-cases might be, what refinements are needed, and if any unforeseen benefits or pitfalls might exist.

In his study, Dr. Novoa and his team will evaluate the impact of their algorithm as a telemedicine triage tool across the entire Stanford Medical Center referral system. The team will then measure the efficacy of human-plus-machine performance versus either one alone. “Too often, data sets that are collected don’t represent the true complexity of pigmented lesions we see in the real world. In our study, we are correcting for that by going beyond the classic textbook — because in the real world, these lesions don’t read the textbook.”

His team is also collecting expansive imagery for each lesion studied, including clinical pictures of the region of interest as well as dermoscopic images. This combination is not frequently found in existing datasets, and Dr. Novoa is hopeful that combining both will improve diagnostic accuracy.

“We are trying to collect a broad variety of skin types in our analysis. This includes a partnership with Dr. Brian Gastman at the Cleveland Clinic, and the diversity of the patient population that institution serves. There are certainly issues about representation in the literature and datasets currently in use,” says Dr. Novoa. “We want to see how well our algorithm performs across all skin types and to make sure that the tools that we develop are equitable and applicable to all people.”

For Novoa — and other AI researchers — representative datasets and imagery are only part of the puzzle. That’s because for AI to work, a complex series of algorithms also need to be created. Taken together, these systems form a “neural network” capable of identifying patterns, classifying data, and even learning over time. Unfortunately, the inner workings and decisions made by neural networks aren’t easy to understand; this is often referred to as the “black box” of AI. This lack of transparency reduces the utility of AI as a diagnostic companion for dermatopathologists and makes it harder to further improve the way the AI systems work. Novoa, and his team, are also taking steps to break this down — creating better insights and more opportunities to improve the technology over time.

“We wanted to see if we could move this technology beyond ‘the promise’ and see how it can help patients in day-to-day practice,” says Dr. Novoa. “We know there is potential, but now we want to know what are the best uses of artificial intelligence, and how can it help patients and doctors in real life?”

"We really wanted to see if we could move this technology beyond ‘the promise’ and ... help patients in day-to-day practice.”

DR. ROBERTO NOVOA
Every day, we hear from patients who want to know what, if anything, they can do to have the best health outcomes possible. For people facing melanoma, it’s common to feel overwhelmed and out of control with everything that a melanoma diagnosis and treatment entail. Yet, how one faces those challenges, can make a big difference. MRA-funded investigator Lorenzo Cohen, PhD is working hard to help patients understand the pivotal role of the microbiome, diet, stress — and their melanoma — on treatment outcomes.

Cohen, Distinguished Professor in Clinical Cancer Prevention and Director of the Integrative Medicine Program at the University of Texas MD Anderson Cancer Center, is interested in lifestyle factors that may be able to help improve treatment outcomes and the lives of patients.

“We are looking at different lifestyle habits,” says Cohen. “In addition to assessing diet, we’re also assessing stress, social support, physical activity, and with our colleague Takis Benos, PhD at the University of Pittsburgh, we are doing some complex modeling to see what are the factors that are the most predictive of treatment response.”

In his 2018 MRA Team Science Award, Cohen, alongside collaborators Drs. Jennifer Wargo and Jennifer McQuade, aims to build upon existing research to further explore how lifestyle factors, including diet, exercise, and stress and anxiety, as well as the trillions of microorganisms living within the gut microbiome, can be modified to improve outcomes for patients with melanoma.
Over the last few years, it has become well understood that the microbiome plays a critical role in our lives. Thanks to research breakthroughs, including those by MRA-funded investigator Drs. Jennifer Wargo (MD Anderson), Thomas Gajewski (University of Chicago), and Yardena Samuels (Weizmann Institute), we know more than ever about the correlation between the microbiome and the immune system—including the body’s response to immunotherapy.

Cohen and the research team have been able to show that melanoma patients with diets rich in fiber had an almost fivefold greater chance of responding to immunotherapy compared to patients with diets low in fiber.

“If the microbiome truly is the determiner of who responds to immunotherapy and who doesn’t, we potentially have it in our control to turn a non-responder into a responder and that could be through something as simple as modifying lifestyle factors," explains Cohen. “Currently we know that [microbiome] biodiversity is key.”

Biodiversity refers to the variety of microbiomes found in the gut rather than the total number of microbiome organisms. In this way, Cohen recommends plant-based foods rather than pill-based probiotics that can sometimes push out diverse organisms in the name of quantity rather than quality and have the reverse intended effect. In fact, the research team found that probiotic use by melanoma patients was associated with worse outcomes to immunotherapy.

The team is also looking at the role of stress and anxiety management on treatment response. That’s because while stress and anxiety are normal parts of life — and can be helpful in many situations — but left unchecked, they can also be detrimental to your health and wellbeing. Stress activates a host of nerve and hormonal signals that release a rush of hormones throughout the body, including adrenaline and cortisol.

We all know what a flood of adrenaline feels like, while boosting short-term energy levels it also elevates blood pressure and heart rate. Meanwhile, cortisol helps us better focus by upregulating the brain’s use of glucose and increasing the body’s ability to repair tissues. Unfortunately, these stress hormones also alter or down-regulate many body functions deemed unessential in a fight-or-flight situation, including our immune responses. It’s easy to see how this could become problematic for melanoma patients undergoing immunotherapy. There is also evidence that stress can alter the tumor microenvironment, making it more hospitable to cancer growth.

Fortunately, it’s possible to manage stress and anxiety through regular meditation, yoga or other exercise, prayer, other spiritual practices, or hobbies.

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Stress and stress management, along with food, sleep, exercise, and other lifestyle and behavior factors inform much of Cohen’s integrative medicine work. Integrative medicine incorporates elements of complementary and alternative medicine — such as yoga, acupuncture, or herbs — into a comprehensive treatment plan alongside conventional treatment. Through the Team Science Award, Cohen says that they are looking not only at the microbiome and the immune system but, indeed, the whole complex system which is the human being and the person’s interaction with the world.

“The type of funding that we receive from MRA allows us to push the envelope in answering these types of questions and to do so in very multidisciplinary ways,” says Cohen. “This is important because in medicine and science sometimes we can be reductionist in nature and miss the forest from the trees.” Cohen and his colleagues are optimistic about their findings to date and in unlocking further clues to the microbiome and how that can inform science, advance research, and enhance patient lives.

For Cohen, this isn’t just an academic interest. That’s because he knows firsthand what it’s like to experience the challenge patients face as they sit at the other side of the exam table. In 2018, after finishing his book Anticancer Living: Transform Your Life and Health With the Mix of Six, Cohen was diagnosed with stage III melanoma. “It’s never too late in your life or cancer journey to start making changes to improve your life. You can’t always guarantee an individual’s length of life, but you can definitely improve quality by modifying key lifestyle factors and improving your microbiome.”

**Gut-Brain Axis**

Gut-brain axis, otherwise known as GBA, refers to the bidirectional link between the central nervous system and the enteric nervous system. Recent research suggests that the microbiome plays an important role in how the gut and brain “talk” to each other. To date, most research on GBA has been in animals but suggests that the microbiome plays an important role in mental health and mood and plays a significant role in both health and prevention.

CHALLENGE ACCEPTED
Melanoma survivor and clinical trial participant Brandon Barriea and family.
Targeted and immune-based therapies have transformed the melanoma field and have led to substantial improvement in overall patient survival. However, too many people still don’t respond to existing treatments, termed primary resistance, and significant portions of patients who do respond initially develop acquired resistance, meaning a therapy works initially but later fails.

The challenges posed by treatment resistance, are being tackled by many melanoma researchers across the globe, including four-time MRA-funded investigator Roger Lo, MD, PhD. Lo currently serves as Professor of Medicine, Professor Molecular & Medical Pharmacology, Associate Chief of Dermatology, and Director of the Melanoma Clinic in Dermatology at UCLA. He and his lab are currently working to understand how treatment resistance develops at a molecular level and if the location of the metastatic tumor in the body influences this process.

This is important because Lo hopes that by understanding the mechanisms at work during treatment resistance, he and his team can design treatment regimens that can breakthrough and overcome these molecular adaptations. Currently, patients who develop resistance to both CTLA-4 + PD-1 combination immunotherapy and/or BRAF/MEK targeted therapy represent an urgent area of unmet medical need.

However, doing this will require:

• A better understanding of how tumors become resistant to existing therapies,
• Identifying patients who will and those who will not respond to treatment, and
• Developing new and improved treatments to defeat melanoma resistance.

“"This is such rewarding and important work and MRA helps make that possible.”

DR. ROGER LO
To address this, Lo and his team are looking at how resistance occurs in different parts of the body, in different organs, and how this process adapts in various organ systems — with a special focus on the brain. These are important research aims because right now, we don’t fully understand why, for example, a patient may develop treatment resistant tumors in a specific organ, but nowhere else. Understanding the factors at play, could give important insight into developing future treatments.

This is critically important for patients facing brain metastasis, otherwise known as “brain mets.” These are an all-too common and difficult-to-treat problem in patients with advanced melanoma. Lo explains that therapies that work elsewhere are often not as effective in the brain and that tumor resistance, especially in the brain, ultimately proves fatal for many patients. Through this work, Lo and his team are trying to uncover novel combinations and sequences of therapies that will work even better for patients facing brain mets and, to ultimately, extend patient survival.

“There is a vast amount of biology to be understood with regard to this disease,” explains Lo. “But I think the most practical and translatable approach is to study how the cancer adapts to the therapies. We can let the biology of resistance in the clinic teach us about the most critical aspects of melanoma biology. We want to find additional targets in order to develop combinations, sequencing regimens, and different strategies that involve well-established, FDA-approved therapies, plus more, in order for us to deliver the most realistic near-term cures.”

In a manuscript published in August 2021 by the journal *Cancer Cell*, Lo reports in his preclinical studies on mice, that starting with two-doses of PD-1/L1 based immunotherapy (with or without ipilimumab) followed by combining BRAF/MEK inhibition leads to a superior approach — more effective than either approach on its own or the use of both simultaneously.1

In his mouse models, this combination maximizes antitumor immunity and efficacy, including for controlling brain mets. Based on his findings, Lo urges clinical trials be designed to see if his findings bear out among people.

“What we did was test in animal and other models of metastases different ways of combining and sequencing therapies to find the regimen that works best. On top of that, we found the mechanism of why the optimal regimen works in contrast to the traditional way of doing one treatment until it fails and then moving on to another,” says Lo.

“In melanoma in particular, we were surprised by how well this regimen suppresses treatment resistance,” Lo said. “In a metastatic model where the majority of animals die within a couple of weeks with brain metastases, the regimen we proposed afforded survival with complete responses that extend routinely to 10 months, which is currently our longest follow-up.”

At the molecular level, Lo and his team found that the optimal treatment regimen involves targeting specific immune cell types—activating certain cells and decreasing the effects of others. “By knowing these immune mechanisms, we now have discrete targets to go after on top of the therapies that we already have,” says Lo. The hope is this research will facilitate enhanced immune-targeting regimens and, ultimately, improve the lives of patients with treatment resistant melanoma.

“MRA has a model of funding that’s very fast, very quick turnaround, and funds really exciting, innovative research. The Team Science approach is also very important by enabling large groups of investigators to come together to help advance the field,” says Lo.

Lo, who works in the clinic and the research lab, says it’s the excitement of discovery that keeps him going without any loss of enthusiasm. “I enjoy working at the intersection of knowledge and translatability and then taking that knowledge and making it practical. This is such rewarding and important work and MRA helps make that possible.”

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Creating Community & Driving Rare Melanoma Research Forward: The Launch of the RARE Registry

“...There’s real power and strength in each individual sharing their story.”

- DR. MARC HURLBERT

For patients facing rare melanomas, or any rare disease for that matter, getting the right diagnosis and effective treatment can be a real challenge. That’s because, while significant progress has been made in treating melanoma broadly, this progress doesn’t always extend to rare subtypes due to the limited number of patients and samples available for study. In melanoma, while patient-reported clinical registries have been launched for uveal melanoma to address this unmet need; no such registry existed to support research into acral and mucosal melanoma. MRA stepped up to this challenge.

Patients with these rare melanomas are often the only—or one of very few—patients at their clinic with this diagnosis. To date, it has been difficult for patients to connect and share information as well as for researchers to access the clinical information, tissue, and genomic profiles that they urgently needed to better understand the causes and possible treatment options for these melanomas.

And yet, while patients are willing to share information and researchers want to study it, the challenge is connecting the dots so that patients and researchers can move the needle, together.
NOT ALL MELANOMAS ARE THE SAME

While roughly 90% of melanomas form on sun-exposed skin, rare melanoma subtypes — such as acral and mucosal — form in or on parts of the body that are shielded from the sun (such as palms of hands, soles of feet, under fingernails, or nasal cavities). Each year, about 5,000 patients are diagnosed with these subtypes. Due to their relative obscurity, patients facing these rare subtypes are often diagnosed later and have poorer prognoses.

To bridge this divide, MRA began work in 2020 to launch RARE, a mobile app-based, bidirectional, and interactive registry for patients facing acral or mucosal melanoma with an anticipated launch in 4th Quarter of 2021. Through RARE, researchers will gain critical insight into the risk factors, treatment histories, and unique experiences of patients facing these subtypes in order to drive research forward.

“The RARE registry was the idea of patients and has been co-created with a group of patients, caregivers, physicians, and researchers. RARE is an opportunity for patients with acral and mucosal melanoma to share data about their diagnosis journey, treatments they were offered, and information on their quality of life. It’s a way for people to be actively involved and engaged in research,” says Dr. Marc Hurlbert, Chief Science Officer, MRA, and Co-PI of RARE. “There’s real power and strength in each individual facing a rare melanoma sharing their story.”

Unlike other registries that typically focus on a singular point in time (e.g., baseline survey), RARE will ask patients to provide data over time and will ask important, but often neglected, questions about their quality-of-life. This is important because preserving — and even advancing — quality-of-life is critical to patients and is often overlooked in medical research. In addition, RARE will enable patients to engage with one another as well as the research community in new ways. Doing so will provide a more comprehensive picture of patients facing these rare melanoma subtypes as well as what many patients crave most: community connection.

“One of the things that the RARE registry can do is to tie clinicians and patients together in a community,” explains Dr. Maryam Asgari, Professor of Dermatology at Massachusetts General Hospital, Harvard Medical School, and Co-PI of RARE. “I think there’s a lot of value in understanding what patients want to learn about their disease. It can help the researchers and clinicians focus on gap areas so that we can better deliver care.”

The RARE planning process began in earnest shortly after the COVID-19 pandemic took off, and from day one took a patient-first approach, including how the registry should work as well as its name and branding. MRA staff met virtually with patients every other week for three months, launching a patient advisory committee made up of 12 patients: six with acral melanoma and six with mucosal melanoma to guide and inform all aspects of the project.

“I think this is the first time that I’ve been really engaged in a project where patients were absolutely partners in developing the registry,” says Asgari. “They had just as strong of a voice, if not stronger, than the clinicians and researchers, and I think that struck a chord within me about the value of engaging patients from the get-go.”

Following the creation of the patient advisory committee, MRA staff set out to engage a diverse medical advisory committee. This includes surgeons, dermatologists, oncologists, epidemiologists, data scientists, and more across various institutions and agencies.
This type of convening and leadership has been a hallmark of MRA’s approach, and the patient and medical communities alike are excited. In fact, experts in Mexico City, Mexico and São Paulo, Brazil have already been in talks with the MRA staff and are eager to help translate the information so that the registry can be available in culturally relevant languages for their patients as well.

“Once it’s launched, we’d love to see people really stepping up to engage communities,” says Asgari. “The pivotal next step is to acquire tissue from our participants because that will give us so much more information about the genomics of the tumor, the genomics of the individual, and perhaps how they’re responding to therapy, and how the tumor is changing over time. This can really help us build the armamentarium of novel therapeutics which is, I think, what patients are really craving.”

“Patients with mucosal and acral melanoma, and their caregivers, called for an international effort to pool data about the experiences faced by this community. MRA answered that call and assembled a group of patients, advocates, leading scientists, and clinicians to co-design RARE to meet the needs of patients and researchers.”

JULIE DEWEY, MUCOSAL MELANOMA PATIENT ADVOCATE
Since its founding in 2007, the Melanoma Research Alliance has become the largest non-profit funder of melanoma research worldwide. Through 380 awards, MRA has directly invested more than $131 million, and leveraged an additional $415 million in collaborative and follow-on funding towards its mission. MRA is catalyzing strategic, collaborative, and accountable research efforts that have moved the field forward and given patients and their loved ones better treatment options and renewed hope.

MRA Snapshot
2021 MRA Research Awards

A complete listing of all MRA grant awards, along with abstracts, can be accessed online at CureMelanoma.org/Grants
Young Investigator Awards

MRA Young Investigator Awards aim to attract early career scientists with novel ideas into melanoma research, thereby recruiting and supporting the next generation of melanoma researchers. Young Investigators are scientists within four years of their first academic faculty appointment. A mentorship commitment from a senior investigator is required.

Enhancing an Abscopal Response by Elucidating the Role of Stem-Like T-Cells
ASTRO-MRA Young Investigator Award in Radiation Oncology
Zachary Buchwald MD, PhD, Emory University

Targeting Liver Metastases to Enhance Immunotherapy Efficacy in Melanoma
MRA Young Investigator Award, collaboratively funded by The University of Michigan
Michael Green MD, The University of Michigan

Dissecting the role of CD58 in Cancer Immune Evasion and T Cell Exclusion
Tara Miller Melanoma Foundation — MRA Young Investigator Award
Benjamin Izar MD, PhD, Columbia University Medical Center

Dissecting Tumor and Immune Evolution in Unresectable In-Transit Melanoma
Amanda and Jonathan Eilian — MRA Young Investigator Award
David Liu MD, Dana-Farber Cancer Institute

Targeting SPP to Activate Antigen Presentation in Melanoma via HLA-E
MRA Young Investigator Award, collaboratively funded by the Broad Institute
Robert Manguso PhD, The Broad Institute

Tumor Microbiome Potentiates Cancer Immunotherapy in Melanoma
Bristol Myers Squibb — MRA Young Investigator Award
Marlies Meisel PhD, University of Pittsburgh

Uncoupling MEK and ERK To Treat Melanoma
MRA Young Investigator Award
Gatien Moriceau PhD, The University of California, Los Angeles

Delineating Novel Mechanism of Immune Evasion in Melanoma Brain Metastases
Inan Olmez MD, Pennsylvania State University

Mitochondrial Uncoupling: A New Therapeutic Approach for Melanoma
Merck — MRA Young Investigator Award
Rachel Perry PhD, Yale University School of Medicine

Understanding and Improving Neoepitope-Specific T Cell Response to Melanoma
Leveraged Finance Fights Melanoma-MRA Young Investigator Award
Cristina Puig Saus PhD, The University of California, Los Angeles

Immunotherapeutic Cytokine/Antibody Fusion Proteins to Treat Melanoma
MRA Young Investigator Award
Jamie Spangler PhD, Johns Hopkins University-School of Medicine

Improving Immunotherapy Outcomes Through Solving irAEs
Bristol Myers Squibb — MRA Young Investigator Award
Alexandra-Chloe Villani PhD, Massachusetts General Hospital

Adipocyte Remodelling in Melanoma Progression and Immunotherapy Response
MRA Young Investigator Award
Amaya Viros MD, PhD, The University of Manchester

Targeting CDK6 in T Cells for Melanoma Therapy
Bristol Myers Squibb — MRA Young Investigator Award
Haizhen Wang PhD, Medical University of South Carolina
Pilot Awards

MRA Pilot Awards test potentially transformative ideas that do not have extensive preliminary data but articulate a clear hypothesis and translational goals. Resources for such “high-risk, high-reward” projects are important to establish proof-of-concept, which may then leverage additional funding through more traditional avenues.

Overcoming Immunotherapy Resistance by Selective Inhibition of Notch1
MRA Pilot Award
Barbara Bedogni PhD, University of Miami, Miller School of Medicine

Imaging Biomarkers for Immunotherapy Resistance in Melanoma In Vivo
MRA Pilot Award
Pratip Bhattacharya PhD, University of Texas MD Anderson Cancer Center

Harnessing Proteasome Heterogeneity for Sensitization to Immunotherapy
MRA Pilot Award
Yifat Merbl PhD, Weizmann Institute of Science

Defining Mediators of Metastatic Spread in Acral Melanoma
MRA Pilot Award
Carla Daniela Robles-Espinoza PhD, Universidad Nacional Autónoma de México

Dissecting the Impact of Noncoding Structural Variation in Melanoma Genomes
Leveraged Finance Fights Melanoma-MRA Pilot Award
Eliezer Van Allen MD, Dana-Farber Cancer Institute

Identifying and Targeting Melanoma Resident Macrophages
MRA Pilot Award
Andrew White PhD, Cornell University

Established Investigator Awards

Established Investigator Awards support senior investigators with an established record of scientific productivity and accomplishment and who are past the initial four years of their first academic faculty appointment.

Role of Opioid Signaling in Disabling Immunity During Melanoma Progression
MRA Established Investigator Award
Ana Anderson PhD, Brigham and Women’s Hospital

Formation and Function of Tertiary Lymphoid Structures in Melanoma
MRA Established Investigator Award
Victor Engelhard PhD, The University of Virginia

Targeting Neuroinflammation for Inhibition of Melanoma Brain Metastasis
MRA Established Investigator Award
Neta Erez PhD, Tel Aviv University

CSDE1 Proteoforms as Novel Targets for Melanoma Treatment and Prognosis
MRA Established Investigator Award
Fatima Gebauer PhD, Fundacio Centre De Regulacio Genomica

Targeted Therapy of Melanoma with LZTR1 and CRKL Inhibitors
MRA Established Investigator Award
Ruth Halaban PhD, Yale University

Identifying Defects in Nucleic Acid Sensing that Drive anti-PD-1 Resistance
MRA Established Investigator Award
Rizwan Haq MD, PhD, Dana-Farber Cancer Institute

Tailoring T cell Anti-Tumor Response with Mitochondria-Mediated Regulations
MRA Established Investigator Award
Ping-Chih Ho PhD, University of Lausanne
**Established Investigator Academic-Industry Partnership Awards**

Established Investigator Academic-Industry Partnership Awards support senior investigators with an established record of scientific productivity and accomplishment through cross-sector collaboration. Each award is co-funded by MRA and an industry partner whose involvement is essential to the project.

**Multimodal GNAQ signaling-targeted precision therapy approach for MUM**
MRA Established Investigator Academic-Industry Partnership Award  
J. Silvio Gutkind PhD, The University of California, San Diego  
Industry Partner: Verastem Oncology

**CD8+ Cell Imaging during Neoadjuvant ImmunoTherapy (The C-IT Neo Trial)**
MRA Established Investigator Academic-Industry Partnership Award  
Michael Postow MD, Memorial Sloan-Kettering Cancer Center  
Industry Partner: ImaginAb

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**Dermatology Fellowship Awards**

MRA Dermatology Fellowship Awards are designed to drive greater interest in the prevention, detection, diagnosis and early intervention of melanoma among dermatologists by investing in post-docs and medical residents focused on dermatology.

**Germline Genetic Mutations in Patients with Multiple Primary Melanoma**
Polka Dot Mama Melanoma Foundation — MRA Dermatology Fellows Award  
Audris Chiang MD, Stanford University

**Targeting Lipids for Melanoma Detection and Prevention**
Grace Wenzel MRA Dermatology Fellows Award for Women in Melanoma Research  
Marianne Collard PhD, Boston University School of Medicine

**Leveraging Social Media to Augment Education on Melanoma in Hispanics**
MRA Dermatology Fellows Award  
Collin Costello MD, Mayo Clinic Arizona

**Novel Biomarkers and Treatment Strategies for Acral Lentiginous Melanomas**
MRA Dermatology Fellows Award  
Dekker Deacon MD, PhD, The University of Utah

**Targeted Advertising to Promote Melanoma Awareness Among Black Americans**
MRA Dermatology Fellows Award  
Isabella de Vere Hunt MD, Stanford University

**Multimedia Learning for Melanoma Prevention and Early Detection Education**
MRA Dermatology Fellows Award  
Carter Haag MD, Oregon Health & Science University

---

**PARP14 Mediates Adaptive Resistance to Immune Checkpoint Inhibitors**
MRA Established Investigator Award  
Adam Hurlstone PhD, University of Manchester

**Balancing Stem-Like and Effector T Cells for Maximal Anti-Tumor Activity**
MRA Established Investigator Award, collaboratively funded by Massachusetts General Hospital  
Thorsten Mempel MD, PhD, Massachusetts General Hospital

**Targeting Acral/Mucosal Melanomas Using a Novel KIT-driven Murine Avatar**
Leveraged Finance Fights Melanoma-MRA Established Investigator Award  
Hensin Tsao MD, PhD, Massachusetts General Hospital

**Protein Kinase C Fusion — Rare Targetable Initiating Mutation in Melanoma**
Leveraged Finance Fights Melanoma-MRA Established Investigator Award  
Iwei Yeh MD, PhD, The University of California, San Francisco
Diagnosis of Melanoma Using Machine Learning and Confocal Microscopy
MRA Dermatology Fellows Award
Jonathan Kentley MBBS, Memorial Sloan Kettering Cancer Center

Evaluating Acral Pigmented Lesions via AI Algorithms in Black Patients
MRA Dermatology Fellows Award on Skin of Color
Mariela Mitre MD, PhD, Joan & Sanford I. Weill Medical College of Cornell University

Preventing Melanomagenesis Through Modulating HMGB1 Palmitoylation
MRA Dermatology Fellows Award
Zhipeng Tao PhD, Massachusetts General Hospital

Characterizing the Genomic Evolution of Acral Lentiginous Melanoma
MRA Dermatology Fellows Award
Meng Wang PhD, The University of California, San Francisco

Genomic Features of Primary Melanoma Predictive of Brain Metastasis
MRA Dermatology Fellows Award
Yujue Wang MD, PhD, The University of California, Los Angeles

Molecular Alterations and Immunotherapy Responses in Acral Melanomas
MRA Dermatology Fellows Award
Jennifer Wiggins-Crosby PhD, New York University School of Medicine

Distant Metastasis by Early ALM in Patients with Skin of Color
MRA Dermatology Fellows Award
Zhentao Yang PhD, The University of California, Los Angeles

As the largest non-profit funder of melanoma research, MRA has dedicated $131 million to date for life saving research in the fight against melanoma.
In 2020, gifts were made in tribute to the following individuals.

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Charlie Baird
Dean Barker
Margaret Barniea
John Beer
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Mark Brast
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Gary Brown
Thomas Brown
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Kimball Diamond
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Parents and brothers of Susan Everdell
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Danny Federici
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Mark Foley
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Matthew Loyd
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Kimberly Rosen
Jeff Rowbottom
Susan Schildt
Ian Schuman
Kent and Aynah Snyder
John Sullivan III
Laura B. Wells
Patricia Wexler
Jamie White

**Tribute Gifts**
Mary and Brian Barrett
Debra Ressler Black
Sara Breynogle
John Brown
Brendan Dillon
Will Flewelling
Gary Fries
Jamie Goldfarb
Steve Goldfarb
Stephen Greenawalt
Lee Grinberg and Jennifer Corwin and children
2020 Financials
# Statement of Financial Position

<table>
<thead>
<tr>
<th>Category</th>
<th>Total 2020</th>
<th>Total 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash and Cash Equivalents</td>
<td>$12,346,871</td>
<td>$12,481,416</td>
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<tr>
<td>Investments</td>
<td>$11,413,876</td>
<td>$10,857,778</td>
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<tr>
<td>Contributions Receivable (Net)</td>
<td>$13,225,054</td>
<td>$19,744,931</td>
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<tr>
<td>Prepaid Expenses and Other Assets</td>
<td>$69,028</td>
<td>$108,594</td>
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<tr>
<td><strong>TOTAL ASSETS</strong></td>
<td>$37,054,829</td>
<td>$43,192,719</td>
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<tr>
<td><strong>Liabilities</strong></td>
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<tr>
<td>Accounts Payable</td>
<td>$88,858</td>
<td>$139,414</td>
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<tr>
<td>Grants Payable (Net)</td>
<td>$13,640,454</td>
<td>$12,248,645</td>
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<tr>
<td>Deferred Revenue</td>
<td>$202,000</td>
<td>$285,000</td>
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<tr>
<td>Due to Affiliate</td>
<td>$12,976</td>
<td>$137,174</td>
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<tr>
<td><strong>TOTAL LIABILITIES</strong></td>
<td>$13,944,288</td>
<td>$12,810,233</td>
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<tr>
<td><strong>Net Assets</strong></td>
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</tr>
<tr>
<td>Unrestricted</td>
<td>$16,890,540</td>
<td>$17,045,668</td>
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<tr>
<td>Temporarily Restricted</td>
<td>$6,220,001</td>
<td>$13,336,818</td>
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<tr>
<td><strong>TOTAL NET ASSETS</strong></td>
<td>$23,110,541</td>
<td>$30,382,486</td>
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<tr>
<td><strong>TOTAL LIABILITIES AND NET ASSETS</strong></td>
<td>$37,054,829</td>
<td>$43,192,719</td>
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</table>
Statement of Activities

Revenue & Expense Statement

<table>
<thead>
<tr>
<th>Revenue</th>
<th>Total 2020</th>
<th>Total 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contributions (Collectible Net)</td>
<td>$5,963,431</td>
<td>$2,562,352</td>
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<tr>
<td>Special Events (Net)</td>
<td>$1,382,366</td>
<td>$18,753,320</td>
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<tr>
<td>Sponsorship</td>
<td>$413,256</td>
<td>$490,000</td>
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<tr>
<td>Interest/Investment</td>
<td>$586,718</td>
<td>$820,089</td>
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<tr>
<td>In Kind Contributions</td>
<td>$76,859</td>
<td>$399,679</td>
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<tr>
<td>Other Income</td>
<td>($1,094)</td>
<td>$32,061</td>
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<tr>
<td>TOTAL REVENUES</td>
<td>$8,421,536</td>
<td>$23,057,501</td>
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</table>

<table>
<thead>
<tr>
<th>Expenses</th>
<th>Total 2020</th>
<th>Total 2019</th>
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</thead>
<tbody>
<tr>
<td>Research Grants</td>
<td>$12,549,005</td>
<td>$9,265,006</td>
</tr>
<tr>
<td>Personnel Costs</td>
<td>$1,734,967</td>
<td>$1,592,119</td>
</tr>
<tr>
<td>Travel &amp; Entertainment</td>
<td>$288,349</td>
<td>$384,245</td>
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<tr>
<td>Other Expenses</td>
<td>$484,052</td>
<td>$364,228</td>
</tr>
<tr>
<td>Meetings &amp; Conferences</td>
<td>$254,294</td>
<td>$253,609</td>
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<tr>
<td>Professional Fees</td>
<td>$219,379</td>
<td>$171,928</td>
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<tr>
<td>Occupancy</td>
<td>$163,426</td>
<td>$167,995</td>
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<tr>
<td>TOTAL EXPENSES</td>
<td>$15,693,481</td>
<td>$12,199,130</td>
</tr>
<tr>
<td>NET INCOME/(LOSS)</td>
<td>($7,271,945)</td>
<td>$10,858,371</td>
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</tbody>
</table>

Total 2020 Program Costs: $14,547,527 (92.7%)

MRA Functional Expenses

- **Scientific Program**: 10.0% ($1,575,441)
- **Fundraising**: 3.7% ($572,845)
- **Patient Engagement**: 2.7% ($423,08)
- **Management & Admin**: 3.7% ($573,109)
- **Research Grants**: 80.0% ($12,549,005)

Financial presentation based on MRA's 2020 externally audited financials. Full audit and IRS 990 are available online at curemelanoma.org/about-mra/financials/
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Leon Black
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Renee Orcione
Development Associate

The Melanoma > Exchange, available at CureMelanoma.org/Community is a vibrant online community led by patients and caregivers with firsthand understanding of melanoma and clinical trials and experts from the MRA staff.

Community Leaders

Tracy Callahan
T.J. Sharpe
Jamie Troil Goldfarb
Cheryl Trocke

Susan Hess
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Director, Melanoma Program
Associate Director, Bloomberg-Kimmel Institute for Cancer Immunotherapy
Johns Hopkins Medicine

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Olga Keith Wiess Distinguished University Chair for Cancer Research
Director, Parker Institute for Cancer Immunotherapy
Executive Director, Immunotherapy Platform
Deputy Director, David H. Koch Center for Applied Research of Genitourinary Cancers
The University of Texas, MD Anderson Cancer Center

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Memorial Sloan Kettering Cancer Center

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Senior Consultant Medical Oncologist, Cancer Medicine, Peter MacCallum Cancer Centre

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Vice President, Cancer Immunology
Genentech

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Co-Director, Melanoma Research Unit
Professor, Dermatology
Institute Gustave Roussy

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Deputy Director, Georgetown-Lombardi Comprehensive Cancer Center
Professor, Oncology and Medicine (Hematology/Oncology), Georgetown University Medical Center
Acting Chief, Division of Hematology/Oncology
MedStar Georgetown University Hospital

Paul Chapman, MD
Attending Physician, Melanoma and Immunotherapeutics Service
Professor of Medicine, Weill Cornell Medical College
Memorial Sloan Kettering Cancer Center

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Professor, Medicine
Harvard Medical School
Director, Henri and Belinda Termeer Center for Targeted Therapies, Cancer Center
Director, Clinical Research, Cancer Center
Massachusetts General Hospital

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Director, Solid Tumor Immunotherapy
Assistant Professor, Medicine
University of Utah, Huntsman Cancer Institute

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University of Washington, Fred Hutchinson Cancer Research Center

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Professor, Surgery
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From left: Drs. Marisol Soengas, Richard Carvajal, and Susan Swetter

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