

ANNUAL REPORT 2022-2023



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Melanoma Research Alliance

As the largest non-profit global funder of melanoma research, MRA has dedicated over \$150 million to date in support of the fight against melanoma.

Learn more at curemelanoma.org



LETTER from the chair and CEO

The Melanoma Research Alliance is committed to ending suffering and death due to melanoma by collaborating with all stakeholders to accelerate research, advance cures, and prevent more melanomas.

MRA is a world leader in advancing transformational science that has caused paradigm shifts in what it means to be diagnosed with and treated for melanoma. We've directly invested over \$150 million towards our lifesaving grants program — and leveraged an additional \$415 million from outside partners — to advance our mission.

The innovative research we support isn't just changing science — it's giving patients more treatment options that translate to longer, fuller lives.

A person diagnosed with advanced melanoma today has access to 16 FDAapproved treatment options and hundreds of clinical trials that are enrolling patients to further improve our treatment arsenal. And while we still have many challenges ahead of us, the future of melanoma research - and the prognoses for patients facing this disease — have never been brighter.

This progress isn't just benefiting patients with melanoma, it's transforming the entire field of oncology. It's a testament to the innovation and commitment of melanoma researchers that therapies that were conceived of, tested in, and first approved for melanoma are now being used to treat dozens of other cancers.

While we are proud of what we have achieved together, we know that there is still much work to be done. Throughout this report, you'll find highlights of our most recent accomplishments, as well as stories of the researchers, clinicians, patients, and advocates who make this progress possible. You will also learn about our strategic priorities and goals for the future, as we continue to pursue our vision of a world where no one suffers or dies from melanoma.

We remain profoundly grateful for the patients who participate in research and for the support of our many advocates, donors, volunteers, partner organizations, government allies, and corporate colleagues who work with us to fund cutting-edge research, foster collaboration and innovation, and change the status quo surrounding melanoma prevention and sun safety.

Together, we can continue to accelerate the pace of discovery, translate research findings from the lab into the clinic, and improve the lives of millions of people affected by melanoma.

Sincerely,

Deba Rlock Mare Cultert

DEBRA BLACK Chair and Co-Founder

MARC HURLBERT, PHD Chief Executive Officer



DEBRA BLACK Chair and Co-Founder



MARC HURLBERT, PHD **Chief Executive Officer**

MRA By the Numbers

\$151

million in grants

funded investigators

research awards granted

million in leveraged and follow-on funding

6415+ 29,328+

donors

people have used MRA's clinical trial navigator to find personalized clinical trial results in their community



MRA

at 162 institutions supported research... and in 19 countries



23()+

different agents for treatment of melanoma studied

722 corporate partners who've raised

\$68 million to support melanoma research

of all donations go directly to research—no admin, development, or other fees





Albert Chiou, MD - Stanford University

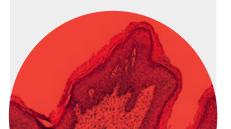
INTRODUCTION A New Era of Advancement

When MRA was launched 15 years ago, few could have imagined the catalytic effect it would have in both the melanoma and cancer research spaces. At that time, there was little by way of treatment options for patients with advanced melanoma, the field was all but stagnant, funding was difficult to come by, and most individuals with advanced disease died.

Despite the obvious obstacles, MRA boldly stated from day one its mission to cure melanoma. The organization knew that to make true innovations in the field, it must be willing to operate differently than organizations that came before it. It provides scientists and researchers the freedom and flexibility to take them where science, data, technology, and their intuition lead them. MRA fosters the next generation of melanoma researchers and clinicians with the tools and experiences they need to be the leaders of tomorrow. Similarly, MRA's Annual Scientific Retreat promotes networking and new collaborations across institutions, borders, and specialty areas. The result? Breakthroughs in treatment, including the support of 16 new FDA approvals, improvements in quality of life and survivorship, and a whole new landscape with which patients, clinicians, researchers, advocates, and others can collaborate to further move the needle.

"Transformative results require visionary philanthropy."

Stephanie Kauffman, President and Chief Operating Officer at MRA



Over these 15 years, MRA has proudly invested more than \$150 million directly into the world's most promising science and research. This includes more than 440 grant awards yielding some of the best return on investment (ROI) in clinical research; nearly half-a-billion dollars in follow-on funding. MRA funding often represents an early-career investigator's first major grant award, providing the resources they need to test their hypothesis and generate data, and ultimately yielding innovative discoveries providing the basis for future grant support for years to come. Similarly, MRA supports leading scientists from across the globe, giving them the funding and support they need to fully explore innovative ideas and paradigm shifting research. The result: measurable progress that makes a difference in the lives of patients every day.

"We know more about melanoma than we've ever known before—and in large part to the contributions of the MRA," says Dr. Marc Hurlbert, Chief Executive Officer at MRA. "We know more about the biology of melanoma, treatment resistance, tumor mutations, how melanoma spreads and metastasizes, and the genetic difference between rare melanoma subtypes and cutaneous melanoma. Because of all the progress the field has made, we're also able to identify the specific research gaps that exist."

The juxtaposition between the research advancements and the research gaps are stark. Answering these questions, however, has become MRA's North Star, directing the focus of what has become a new, bold, and ambitious plan. Efforts include MRA doubling its fundraising efforts — and capacity to fund innovative and lifesaving research — to an extraordinary \$100

million dollars over the next 5 years. MRA is determined to actively move science forward, help patients most in need, and to scale as quickly as possible.

The vision includes four primary goals. These include:

- Developing new treatments for patients that don't respond to existing therapies. Although half of all patients with advanced melanoma benefit from existing treatments, the remaining half do not. "Even with the stories of triumph, success, and cure," says Hurlbert, "we also have really devastating stories of lives cut too short — and it's magnified because of the progress we've seen." MRA is working hard to explore new treatments and novel immune therapies to address the gap where the current standard of care is not effective and to level the playing field for all patients. "We don't want any patients to feel left behind," says Hurlbert.
- 2. Improving treatment options and outcomes for patients with brain metastases. Melanoma has a high propensity to metastasize and spread to the brain and other central nervous system areas. Approximately 60% of patients with advanced melanoma develop brain metastases during the course of their disease.¹ "We really need to understand why melanoma spreads to the brain and is able to go dormant, evading immune system detection, and what triggers melanomas out of that dormancy to initiate growth," says Dr. Joan Levy, Chief Science Officer at MRA. Basically, why is the brain fertile soil for melanoma tumors to settle in and grow? MRA is working collaboratively across cancer types to better

¹Diaz MJ, Mark I, Rodriguez D, et al. Melanoma Brain Metastases: A Systematic Review of Opportunities for Earlier Detection, Diagnosis, and Treatment. Life; 2023, 13(3): 828. Available at: www.mdpi.com/2075-1729/13/3/828#:~:text=Metastasis%20to%20the%20central%20nervous.of%20their%20disease%20%5B7%5D.



"At MRA, we unite around research, the only way we will achieve a future beyond melanoma. But that research relies on us all. Everyone has a critical role to ending melanoma."

Stephanie Kauffman, President and Chief Operating Officer at MRA

Stephanie Kauffman

Leveraged Finance Fights Melanoma (LFFM) 2023 event at the Museum of Modern Art

understand and develop treatments for brain metastases. We also have to ensure that when we find new treatments for brain metastases there will be clinical trials inclusive of these patients.

Translating new treatments for rare melanomas 3. — including acral, mucosal, uveal, and pediatric melanoma. Patients with rare melanomas face unique challenges ranging from later diagnoses, poorer prognoses, and a lack of treatment options designed specifically to address the unique features of their tumors. MRA research investments of over \$18 million have begun to advance the field's understanding around the biology of these rare melanomas and their molecular genomics. To help answer additional critical questions, MRA has launched the RARE Registry (raremelanoma.org), a web-based, bidirectional, and interactive registry for patients with acral or mucosal melanoma. "Through the registry, patients with these rare melanoma subtypes can partner with researchers to accelerate research by helping the field better understand their unique patient journeys," says Levy. "We're also able to return de-identified data insights back to participants in real time. This allows them to access customized data snapshots to see how they fit into the entire cohort something that can be really powerful for a rare cancer community. It's exciting that participants can see research as it emerges as well as get tailored educational materials, clinical trial alerts, and webinars that they might be interested in," says Levy. "The registry will be critical both in helping researchers get the data they need, but just as importantly helping them understand the patient's journey as they experience it."

Joan Levy, PhD — MRA Chief Science Officer

4. Improving prevention, risk prediction, and diagnosis. Despite incredible progress in advancing new treatment options, melanoma continues to be the deadliest form of skin cancer with an estimated 100,000 new cases diagnosed each year in the United States alone. "There is an urgent need for new tools and new technologies to help a patient be empowered at home to check their own moles and for primary care doctors and nurse practitioners to say, 'Aha, that is suspicious, let's refer you to a dermatologist," says Hurlbert. "Dermatologists also need more tools, such as artificial intelligence and machine learning algorithms, to help them answer questions like, 'Should I biopsy or not' and then to assist pathologists to make definitive diagnoses."

Just as MRA's operating model has been unique, so too has its approach to partnerships. MRA helps bring together scientists, physicians, researchers, industry partners, government and regulatory officials, patients, advocates, philanthropists, and other nonprofit groups. This has been done through its Team Science Awards, nurturing collaborations across departments and institutions while also training a young investigator and through its Scientific Retreat where the best and brightest from across the world convene to share information and advance progress.



Marc Hurlbert

"I think that's a real differentiator," says Hurlbert, "we're willing to partner with and collaborate with everyone. I think what we'll see five years from now is that it won't just be MRA working with other melanoma nonprofits, but we'll also be working across cancer communities — from breast, to lung, and pan-cancer organizations like the American Cancer Society. "We're also forging research partnerships with organizations beyond cancer," says Levy. For example, research shows that some specific cells and proteins may play a role both in the neurodegeneration seen in Parkinson's Disease and in the progression of melanoma. To explore this further, MRA partnered with the Michael J. Fox Foundation to co-fund two scientists. "It will take all of us working together to move the needle quickly."

Activating this vision also requires new tools and strategies to engage the community. MRA is doing this through its online patient community, the Melanoma Exchange available at **CureMelanoma.org/Community**, its own digital communications channels, as well as a newly launched in-person salon series. Each salon is an intimate event that pulls in luminaries in the field to facilitate discussion about the future of skin health. "We are working with board members and other interested donors to open up their homes, or a place of their choosing, to create a dialogue with people who may not know about us but are interested in their skin health, melanoma, immunology, and where things are headed in terms of cancer research," says Kauffman. To date, salons have been hosted in Los Angeles; Boston; Naples, Florida; Aspen; and New York.

MRA hopes that people leave with knowledge of all the interesting and groundbreaking work being conducted in cancer research. Moreover, investing in melanoma is

very much an investment in cancer research broadly. Melanoma has been at the forefront of immunology, targeted treatments, and other innovations that have gone on to inform the way many other types of cancer are treated. "What happens first in melanoma often is then applied to other cancer types," says Hurlbert. "It makes supporting melanoma research a very powerful way to advance oncology."

MRA is also embracing science; working with patients to design the next generation of clinical trials; uncovering new answers — and questions — through its RARE Registry; and leading big data science projects with the Department of Veterans Affairs, the VA Hospital System, and Massachusetts General Hospital. Other MRA funded investigators are looking at cutting-edge technologies, including single cell analysis to study the tumor in context of its microenvironment including its neighboring cells, as well as projects in aging and how that impacts response to therapies.

Imagining what might be possible in the next five years, Hurlbert says, "It won't be that MRA just funded it. It will be that we partnered and collaborated with everyone. We brought to bear tools to support patients, tools to improve diagnosis, and we'll have supported the discovery of much-needed new treatment options. We'll be the *funder* but also the *partner* and the *collaborator* in doing that research. We will be the leader moving the entire field forward. It's not about redoubling the budget; it's about recognizing the real sense of urgency that we feel a personal commitment to every day."



(L to R): Elizabeth Ottinger, PhD – National Center for Advancing Translational Sciences, Caroline Robert, MD, PhD – Gustave Roussy (France), & Antoni Ribas, MD, PhD – University of California Los Angeles

The Future of Immunotherapy & Cell-based Therapies

"Melanoma research helped lead the way to a lot of paradigm shifts in cancer treatment," says Dr. Antoni Ribas, Professor of Medicine, Surgery, and Molecular and Medical Pharmacology at the University of California Los Angeles (UCLA).

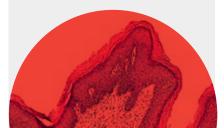
Today, Ribas is a world-renowned physician-scientist, an elected fellow of the American Association for Cancer Research (AACR) Academy, the American Society of Clinical Investigation, and the National Academy of Medicine, among others. However, early in his career, Ribas was discouraged from pursuing tumor immunology.

"For a while, people were not keen on anyone who wanted to do research in tumor immunology," he says.¹ But Ribas was intrigued. He wanted to learn more about the biology of tumors and bring this knowledge to his patients. Tumor immunology studies the relationship between immune function and tumor cells, including the cellular and molecular mechanisms that affect how a tumor interacts with immune system cells, the tumor environment, and how the immune system can be harnessed as a treatment for cancer.

¹Cancer Research Institute. "Antoni Ribas, MD, PhD." Available at: www.cancerresearch.org/stories/scientists/antoni-ribas-md-phd

"Over the last 10 years, melanoma has been at the forefront of the development of immunotherapies and targeted therapies – informing research in many other cancers,"

Dr. Antoni Ribas



Reflecting on how the field has evolved, Ribas points to the number of therapies that were being studied just ten years ago in clinical trials that have now become standard of care for patients with melanoma. This has particularly been true for anti-PD-1 drugs, which Ribas knows firsthand.

That's because ten years ago, he was the principal investigator of a large phase 1 trial studying the anti-PD-1 drug and checkpoint inhibitor pembrolizumab, which enables the immune system to better attack cancer. This work demonstrated how the immune system could lead to durable responses in patients and helped pave the way for melanoma treatment as we know it today.

"Another step forward has been the testing of anti-PD-1 antibodies before surgeries," says Ribas. Currently anti-PD-1 immunotherapy has been approved to be given after surgery, what is called adjuvant therapy. However, what Ribas and others soon realized was that in doing so, they not only removed tumor tissue but also surrounding immune cells that could recognize the tumor. When immunotherapy was given following surgery, these potent anti-tumor immune cells would no longer be present to respond to anti-PD-1 antibodies.

To explore this area further, Ribas and his collaborator Dr. Sapna Patel (MD Anderson) conducted a study of patients who received three doses of immunotherapy first, underwent surgery, and then continued with immunotherapy. This approach, called *neoadjuvant therapy*, proved effective with a nearly 50% improvement of survival over adjuvant therapy.² "This is another place where melanoma's leading the way, because the paradigm should be the same for other cancers," says Ribas. "We hope that patients with other cancers can benefit from immunotherapy before surgery."

Ribas is exploring other innovative areas of treatment as well, including *cell-based immunotherapy*. Certain immune cells appear to recognize differences between melanoma and normal healthy cells. Ideally, these cells would be activated naturally by the body to attack cancerous cells. However, in situations where this does not work, scientists like Ribas are studying ways to take the immune system cells out of the body, grow them in a laboratory, and infuse them back into the patient. This is called *cellular therapy* for cancer and there are two main groups:



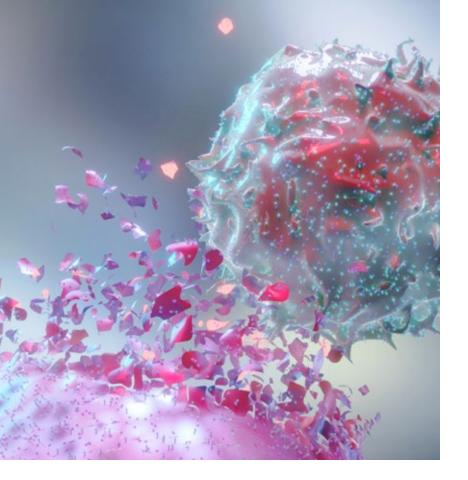
Sapna Patel, MD - The University of Texas, MD Anderson Cancer Center

- Immune cells purified from a surgically removed tumor or biopsy, called tumor-infiltrating lymphocytes or TILs, are expanded in the lab and reinfused back to the patient to elicit a stronger anti-tumor immune response.
- 2. Immune cells isolated from the patient's blood are genetically modified to recognize and attack melanoma, and then infused back into the body. This gives the immune system cells a kind of "GPS" to find the melanoma and destroy it.

TIL therapy, first pioneered by Dr. Steven A. Rosenberg at the National Cancer Institute, is a labor intensive process and involves isolating specific immune cells from a surgically removed tumor and then giving nutrients to help them grow to very large quantities. This creates a proverbial army of immune cells that are then infused back into the patient with the goal of supercharging the immune response against and ultimately killing all cancerous cells. The field is closely watching several companies who are working to streamline this process into a safe, effective, and commercially available product.

Genetically modified immune cells (as mentioned in the second example above), have acquired new receptors to recognize and attack melanoma. "The key question is, do we

²Patel SP et al. Neoadjuvant-Adjuvant or Adjuvant-Only Pembrolizumab in Advanced Melanoma. N Engl J Med 2023; 388:813-823. https://www.nejm.org/doi/full/10.1056/NEJMoa2211437





"Investments in science result in better treatments."

Dr. Antoni Ribas

have receptors that redirect the immune system to melanoma in a safe way, avoiding the immune system attacking normal cells?" says Ribas. "This has not been the easiest thing to tackle, but progress is being made."

Once the cell therapies are developed, patients still need to be conditioned with high doses of chemotherapy to deplete their existing immune systems. Once the immune system is wiped out, the new immune system — that has been carefully created for them in the lab — can be infused into the patient. This puts limitations on who can receive cell therapies because of the toll it takes on the body.

"Cell therapies have become the standard of care in patients with lymphomas, leukemias, and multiple myeloma," says Ribas. "We know that the same principles could work in melanoma, because of TIL therapy, but more work is still needed to better target those immune system cells."

Although there is still more work to be done, it's incredible to see just how far the field has come. A big contributor of this work has been MRA. "Since its founding, MRA has been the largest non-profit funder of melanoma research," says Ribas. "The grants chosen for funding by MRA are reviewed by a panel of experts that include the best in the field. MRA's early stage grants enable researchers to venture into new fields and are very important to opening up new areas of research," he says.

"As scientists we try to understand the problems that limit treatments and then we innovate from there, hoping that what we discover can have a beneficial impact on the patients we serve," says Ribas. "This approach is what leads to advances both in our scientific understanding but also in improved patient outcomes."

And it's working.

"If we look back 10 years ago, less than 1 in 20 patients had a chance to live long-term," says Ribas. "Now, close to half of the patients with advanced melanoma are living years beyond their diagnosis, and probably many of them have in fact been cured. That's why we as scientists continue to do what we do. This is the power of research — and I'm proud to be part of it." \bigcirc



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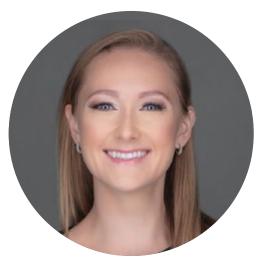
AT THE FOREFRONT OF CLINICAL CHALLENGES Tackling Melanoma Brain Metastases

Not many people can pinpoint the exact moment their lives changed forever, but for Dr. Inna Smalley, Assistant Member at Moffitt Cancer Center, that moment came after a health scare when she was young. "I had a growing tumor that affected me," she says. "It was a lymphatic malformation. I went from resection and relapse for years without anyone knowing what to do, what it was, or how to treat it."

But hope finally came. "One day I met a clinician who said, 'I know what this is, and I know of a clinical trial."

The clinical trial was a success in more ways than one. Smalley responded well to treatment — and she got her first glimpse into medical research. "I thought, 'Wow! There are people doing research and it affects how things are managed clinically," says Smalley. "That's when I knew I was interested in this work."

Today, Smalley's research — supported in part by an MRA Young Investigator Award co-funded by the Tara Miller Melanoma Foundation — is focused on one of the biggest challenges facing patients with melanoma today: treating those who have brain metastases. This is an urgent area of unmet patient need, because despite dramatic advancements in melanoma research overall, the understanding and treatment of brain metastases has lagged behind.



"I want to do something that makes a difference for patients that don't have a lot of options right now. We wanted to take on a challenge that could alter the course of disease for these patients."

Dr. Inna Smalley



- Brain metastases represent one of the most difficult-to-treat complications of melanoma and are a significant cause of patient morbidity and mortality.
- Today, nearly 40% of patients with metastatic melanoma have brain metastases at diagnosis. This figure increases to 75% of patients at autopsy.
- While currently approved therapies do work in the brain in some patients, they are far less effective at treating tumors there than in other parts of the body.
- Among solid tumors, rates of brain metastases are higher in melanoma patients than many other cancers.

"Historically the brain has been an area that's difficult to study," says Smalley. "We haven't had a lot of access to brain metastatic tumors to even figure out what's going on. We really don't know why cells respond differently to therapy in the brain than they do at other sites."

What Smalley's research hopes to do is better understand how melanoma metabolism in the brain affects the pro-tumor, immune-suppressive functions of cells called astrocytes. Astrocytes play an incredibly important role of protecting brain tissue, supporting homeostasis of the central nervous system, and helping repair damage.

In many ways, astrocytes are like our body's police, emergency medical technicians (EMTs), and traffic safety unit all in one: They help keep orderly function, support healthy blood flow, and can protect and repair. However, when tumors spread to the brain, they adapt to their new environment by changing their metabolism which can affect the function of normal cells surrounding them such as astrocytes. As a result, astrocytes don't just ignore tumor cells, they treat them like never-healing wounds, ultimately promoting tumor survival in an otherwise harsh environment. Smalley is studying the metabolic programs in melanoma cells that have infiltrated the brain to identify vulnerabilities within the tumor-astrocyte interaction. Doing so could lead to the identification of new drugs that can increase the effectiveness of existing treatments, and ultimately weaken the tumor's hold on the brain.

> Smalley's award is co-funded by the Tara Miller Melanoma Foundation, which was founded by Tara Miller in 2014 following her diagnosis with melanoma. While Tara tragically passed away later that year at just 29 years old, her legacy continues. Over the last decade, the Tara Miller Melanoma Foundation has raised over \$7.5 million to support melanoma research at both University of Pennsylvania and in partnership with MRA.

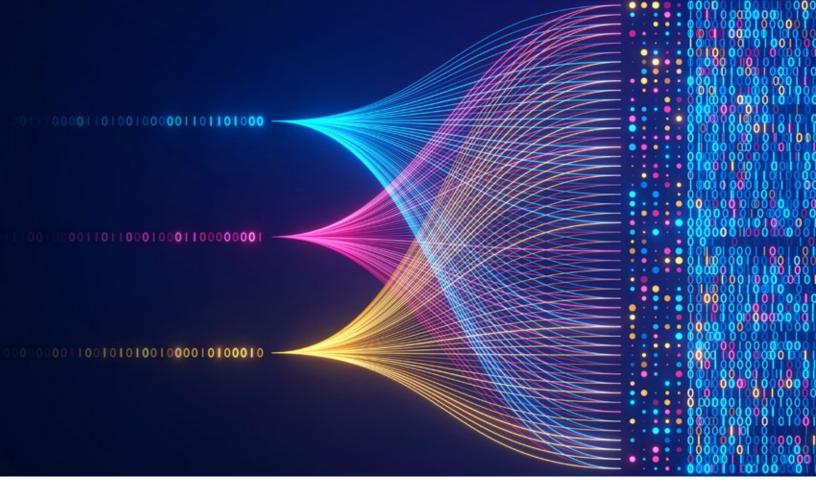
"I'm truly honored to have received the award from MRA and the Tara Miller Melanoma Foundation," says Smalley. "Tara's faith in research and vision of rendering cancer powerless by advancing science resonates with me."

Smalley says grant awards like the one she received are both humbling and incredibly impactful. "The funding environment can be brutal, especially for young investigators because we don't yet have a history of successful funding. These grants are like a bridge to begin our research and secure future funding. They allow us to take risks with good ideas, build up evidence, encourage more people to study it, and make an impact clinically."

Smalley says that the intent of her research is to be very translational. To do this, she tries to be as tuned into what's happening clinically as possible, so she regularly participates in tumor boards and discussions with clinicians. When possible, she even shadows clinicians to better understand patient perspectives and what is important to them. "I want to address questions that are directly relevant to patient care in the clinic," says Smalley.

And she is. Although it's still early in the research project, preliminary data suggests that Smalley's hypothesis may be right: Tumor cells affect astrocyte function; and astrocytes may be improving tumor cells' ability to grow and survive in the brain microenvironment.

"This work is possible because of advocacy and patient involvement. Without having access to tissues to study and samples to study, we wouldn't be able to do any of this. I want to tell patients and their families how valuable their contribution has been to our research in the field," says Smalley. "I want them to know that their willingness to participate makes a huge difference in advancing scientific knowledge and we are very grateful."



AI AND MELANOMA Innovation for the Future

"Artificial intelligence (AI) is going to transform how we diagnose, treat, and eventually overcome melanoma," says Dr. Veronica Rotemberg, Director, Dermatology Imaging Informatics Program at Memorial Sloan Kettering Cancer Center.

Rotemberg believes in the incredible role that AI can play in the detection and treatment of melanoma. Through the International Skin Imaging Collaboration (ISIC), there are more than 75,000 publicly available images of different skin conditions. In addition, ISIC has hosted five yearly challenges related to melanoma—with AI programs in the competition consistently demonstrating better and better performance at diagnosing the disease. It's an incredible collaboration that has yielded millions of image downloads, advanced published research, and had an extensive ripple effect on the reach and impact of melanoma research.

Rotemberg sees AI playing a number of different roles in melanoma, including:

- Reducing the number of benign biopsies,
- Improving prognosis and treatment selection,
- Identifying more melanomas, and
- · Helping to address research voids.



"When you want to identify something that could be a game changer, [AI] is the way to go."

Dr. Veronica Rotemberg

While AI has earned considerable media attention in recent years based on reports of its ability to outperform dermatologists in head-to-head competitions, these competitions have typically been based solely on images of lesions with little additional context. However, like many things the devil is often in the details. In clinical practice, dermatologists have the benefit of seeing patients — and their skin — in real life and up close. Dermatologists also have access to additional information, including patient and family medical history, that can help refine decision making.

Rotemberg's research, supported by a Michael and Jacqueline Ferro Family Foundation-MRA Young Investigator Award, is working to improve AI by determining what contextual information is most helpful to improve its performance in specific situations.

"There are certain types of information that might help the models perform better in specific situations, for instance in certain anatomic sites or with certain types of imaging features," says Rotemberg. "It really depends on the distribution of data that the models are trained on. Ours was one of the first quantitative evaluations of how model performance might change with different [contextual] inputs."

As a leader in this field, Rotemberg is also assessing and validating existing algorithms, which is a critical area of research, especially as AI becomes more integrated into doctors' decision making in the clinic. For example, current models were not sufficiently trained using images of diverse skin tones and as a result they aren't as accurate when applied to people with darker skin.

Rotemberg's work will help change this by ensuring that models are assessed for bias and that the underlying data is appropriately labeled, making it easier to understand potential benefits and harms of a particular model. This also streamlines the benchmarking and validation process that will be required for wider adoption.

"At some point in the future, AI-enhanced tools for melanoma detection will end up in the clinic," says Rotemberg. "As we usher in this new and exciting era, we need to do the work now to ensure these technologies are actually providing the benefit we intend."

According to Rotemberg, there are more than 500 AI algorithms approved by the FDA today; but none in melanoma. She wants to change this by helping to identify what outcomes are most important to patients and then ensure that there are



Kamran Avanaki, PhD - University of Chicago

appropriately validated and benchmarked models that result in marked improvements in those outcomes.

Also helping advance the field is funding, like that from the MRA and the Ferro Foundation. "I think the science was really advanced by the award," says Rotemberg. "We've received numerous subsequent awards building off that initial work and our findings have been published in several journal articles. The collaborative opportunities we've identified by being part of MRA's network have been incredible. I never want MRA's impact to just be measured by the papers and grants that came directly from a project, because there's so much more that comes out of being connected with them on a personal and professional level."

Although the AI field is advancing quickly, Rotemberg thinks more innovations are needed in the following areas:

- Data curation, acquisition, and quality control,
- Standards development, and
- Identifying the right patient outcomes.

"AI research is expensive but when you want to identify something that could be a game changer, this is the way to go," says Rotemberg.

A DEEPER LOOK

Dr. Kamran Avanaki, Associate Professor in the Biomedical Engineering and Dermatology Departments at the University of Illinois Chicago agrees. "I think AI in dermatology is a must. It's not a choice anymore because it really is the result of experts' accumulated experiences and there is power in that."

"[AI] really is the result of our accumulated experiences and there is power in that."

Dr. Kamran Avanaki

Like Rotemberg, Avanaki is trying to harness AI's abilities to advance melanoma research, improve diagnosis, and determine when or even whether a biopsy is actually needed.

Avanaki became interested in melanoma research during his PhD training, when he realized that non-invasive optical imaging could be used to explore and understand skin health with great accuracy. Avanaki also saw the incredible challenge faced by dermatologists in differentiating between melanoma and benign moles using the naked eye. Studies have shown that the ratio of benign lesions to melanoma biopsies can range from around 10 to 1 up to 50 to 1 depending on the experience of the dermatologist and patient medical record. This means that for every melanoma found, there may be anywhere from 10 to 50 or more benign lesions that were biopsied.

Surgical biopsy isn't a no-risk procedure for patients. It can result in pain, anxiety, and scarring — not to mention additional healthcare costs. Moreover, identifying malignant lesions in areas of the skin with many pigmented spots, such in the case of a person with many freckles, is difficult with visual inspection alone. "To overcome these challenges, we have developed a computational method that, using a sophisticated algorithm, analyzes the Optical Coherence Tomography (OCT) images of skin and differentiates melanomas from benign nevi," says Avanaki.

OCT is a non-invasive imaging technique that uses low energy safe infrared light to capture high-resolution, crosssectional images of body tissues in real-time at a microscopic level. Compared to photo-based AI models, OCT is much less sensitive to patient characteristics such as age, skin color, and gender which would eliminate lots of dataset diversity problems.

Currently, Avanaki's OCT-based algorithm can differentiate melanoma from benign nevi with 99% accuracy, demonstrating

a significant improvement in melanoma detection over other diagnostic technologies.

"We're now working to further optimize the algorithm to improve accuracy, consistency, and its implementation in the OCT software so we can then launch a preliminary clinical trial," explains Avanaki.

Avanaki's hope is that his technology can assist clinicians in accurately diagnosing melanoma while reducing the need for surgical biopsies.

To use this technology, a patient sits down, and the clinician places a probe — resembling what is used for an ultrasound — on the suspected lesion. The system generates a 3D image and Avanaki's algorithm examines the generated image to determine the probability of the lesion being melanoma (or not) and provides additional technical information that can help inform the clinician's decision making.

In the near future, dermatologists could use this tool as opposed to performing a biopsy and then waiting for results. "When dealing with patients," says Avanaki, "I see the huge hope in their eyes when we tell them that we're using this methodology and we don't need to do a [traditional] biopsy."

Avanaki says that the MRA and the Ferro Foundation funding used to support the development of this algorithm has been incredible in helping refine and validate the work as well as for training the next generation of AI researchers. In the future, Avanaki hopes to make this technology more available to dermatologists, develop a related process to help support clinicians in staging a melanoma lesion, and he wants to develop a low-cost, miniaturized version that patients can use at home on any suspected lesions. The latter would be a gamechanger for people with many moles, a history of melanoma, or those who live in low-resource areas or have limited dermatology access.

As Rotemberg and Avanaki have shown, when it comes to AI's application in melanoma and clinical cancer research, the future is bright and the possibilities are within reach.



Patient advocates at MRA's 2023 Scientific Retreat & Patient Forum (L to R): Eileen Walther, Patricia Janiak, Alfonso Waller, Julie Dewey, Jonathan Swingle, Mary Harper, and J.B. Ward

RARE REGISTRY

Providing Hope Through Innovation

Each year approximately 5,000 patients are diagnosed with acral or mucosal melanoma.¹ These rare melanoma subtypes arise in non-sun exposed areas and are not believed to be caused by UV damage. Due to the relative obscurity of these rare subtypes, patients face mounting challenges ranging from late diagnoses, lack of support, limited — and often dated — access to information, and overall poorer prognoses. Treatment options are also more limited and less effective for these rare melanoma subtypes than for the more common cutaneous melanoma that forms on sun-exposed skin.

To address this, MRA launched the RARE Registry — a first-of-its-kind, direct-to-patient registry focused on acral and mucosal melanoma — in 2022. The registry:

- Collects data directly from patients with acral or mucosal melanoma using a series of surveys available online.
- Returns real-time de-identified information collected from participants in the form of 'Insights', provides educational opportunities that highlight emerging science and ways to connect with researchers and other advocates, and notifications about pertinent clinical trials.

¹Melanoma Research Alliance (MRA). RARE Registry. Available at: www.curemelanoma.org/research/rare-registry

The RARE Registry is an example of MRA's unique ability to listen and respond to community needs while also addressing research gaps.



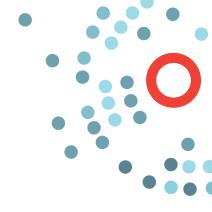
- Provides researchers and clinicians with an unprecedented look into the disease journey of patients with these rare melanoma subtypes, giving them the information they need to develop more effective treatment strategies.
- Includes an Oversight Committee comprised of patients, caregivers, and a multidisciplinary group of medical advisors to help further guide the registry over time.

The RARE Registry is an example of MRA's unique ability to listen and respond to community needs while also addressing research gaps. "MRA answered the call on every level," says patient advocate and registry advisor Julie Dewey. "They were the only group who could do it all. They could find the funding to support it; they had the team in place to create the surveys needed to collect the most pertinent information; and they were familiar with other cancer registries. They also had the ambition and the compassion to make it happen with the patient community. Finally, they understood the immediate need — lives were on the line."

The idea for the registry began years earlier in a Facebook support group called the Mucosal Melanoma Warriors, where a few hundred patients and family advocates shared information about their healthcare journeys as well as providing one another with much-needed support. Through this group, Dewey met Dr. Alfonso Waller. The two bonded, sharing information about their spouses who were diagnosed with mucosal melanoma: Dewey's husband Chris was diagnosed at age 48 and Waller's wife Lisa was diagnosed at age 39, 6 weeks after their second daughter was born. Everywhere they looked, the information available about the disease was based on a small sample of patients and did not line up with the journeys they were on.

As they explored this further, they discovered that many individuals in the Facebook group had experienced delays in getting a correct diagnosis. Moreover, even when properly diagnosed, there was no clear standard treatment protocol; and trends seemed impossible to identify across demographics, age, gender, and area of diagnosis — especially when any one medical center saw only a handful of patients with rare melanomas each year. "The more Alfonso and I talked, the more we wanted to find a way to bring patients together to accelerate research alongside the doctors and researchers. We wanted tumor DNA to be studied. And we wanted all of this in one place," says Dewey.

As they spoke to their extended network, the idea continued to blossom. Together, they dreamed of a community where



"We wanted answers for our community, and we wanted our community to be part of finding those answers."

Julie Dewey, Patient Advocate

patients and caregivers could help accelerate research by providing information and by helping set research priorities; a place where they could ask questions, seek support, and get updates on the latest advances; and a place where rare melanomas would always be front and center.

"We wanted answers for our community, and we wanted our community to be part of finding those answers," says Dewey.

Thanks to a mutual friend, Waller was able to get in touch with MRA's CEO Dr. Marc Hurlbert and he pitched just that. "I suggested we bring together a community of patients, caregivers, and advocates who've been impacted by rare melanomas to create a registry," says Waller. "Marc was very excited, and he told me about his experience with a similartype of registry he led in the breast cancer space."

As the MRA team looked further into direct-to-patient registries, it became clear that patients with mucosal melanoma weren't the only ones who could benefit from such a project. While patients with uveal melanoma — which affects the eye — had several registries open to them, those with acral melanoma had no such options.

The MRA team quickly set up conversations with advocates from the acral melanoma community. Call after call, similar frustrations about delays in diagnosis, lack of standard treatment plans, and feelings of isolation kept coming up. "The challenges experienced by these two communities while distinct on the surface — are quite similar," says Dr. Hurlbert. "More important than similar challenges, it was clear that advocates from both communities were eager to work together to change this status quo. That's when we knew that this project needed to move forward."

The RARE Registry was not only an idea by advocates, caregivers, and patients — they have quite literally been at the helm of designing it at every juncture, from its name, branding, web and mobile capabilities, survey questions, and even the request for a longitudinal study and tumor data.

The registry is creating a different journey for the betterment of patients with acral and mucosal melanoma. What was a once terrifying diagnosis riddled with outdated statistics and fear is now met with accurate information, community, and hope. It is nothing short of empowering. For example, the RARE Registry is focused on better understanding the quality of life throughout the treatment journey, from diagnosis to survivorship — something often overlooked by researchers but critical to patients.

It also allows participants to see how they fit into the larger picture by comparing their responses to others who have also answered specific survey questions. It's a lifeline during an otherwise scary and far too often isolating journey.

As she reflects on this registry journey, Dewey says, "Chris' life was not in vain. When he was diagnosed, he already had Stage 4 disease. We knew this registry wouldn't come in time to benefit him but, rather, for future patients diagnosed with mucosal melanoma. It feels remarkable to have created this registry. In that way, Chris was a pioneer. He had a purpose in his life, and I strongly believe the registry was it."

Be Seen. Be Heard. BE EMPOWERED

JOIN THE RARE" REGISTRY

RARE



Above, Julie Dewey holds photo of her husband Chris. Below, Dr. Alfonso Waller, Alfonso's late wife Lisa, and their two daughters.



LEARN MORE ABOUT THE RARE REGISTRY AT RAREMelanoma.org

2023 MRA AWARDS

A searchable database of all MRA grants is available at **CureMelanoma.org/Grants**

2023 AWARDS







David Lombard, MD, PhD — University of Miami

Melanoma Research Alliance Grant Awards

ESTABLISHED INVESTIGATOR AWARDEES

Memory T cell responses in primary melanoma

MRA Established Investigator Award, collaboratively funded by University of Michigan Christina Angeles MD, The University of Michigan

Armoring CD8+ T cells against energetic deficiency in melanoma

Leveraged Finance Fights Melanoma — MRA Established Investigator Award Timothy Bullock PhD, University of Virginia

Therapeutic targeting of Hdm2/HdmX E3 ligase in melanoma

MRA Established Investigator Award Julio Camarero PhD, University of Southern California

Genetic mechanisms early melanoma progression

Anna-Maria and Stephen Kellen Foundation — MRA Established Investigator Award Adam Dupuy PhD, The University of Iowa

Mechanisms underlying the oncogenic role of ORAI2 in melanoma

MRA Established Investigator Award Stefan Feske MD, New York University Grossman School of Medicine

Dissecting the mechanisms of melanoma cell adaptation to the brain

MRA Established Investigator Award Eva Hernando PhD, New York University Grossman School of Medicine

Precision, plasma-only, melanoma ctDNA residual disease monitoring

Ellen and Gary Davis — MRA Established Investigator Award Dan Landau MD, PhD, Weill Medical College of Cornell University

Sustaining metabolic fitness of antitumor CD8+ T cells

MRA Established Investigator Award Bin Zhang MD, PhD, Northwestern University

YOUNG INVESTIGATOR AWARDS

Harnessing the immunomodulatory effects of NK cells in melanoma

Bristol Myers Squibb — MRA Young Investigator Award Kevin Barry PhD, Fred Hutchinson Cancer Center

Dissecting the dynamic immune ecosystem during melanoma evolution

Leveraged Finance Fights Melanoma — MRA Young Investigator Award Diego Chowell PhD, Icahn School of Medicine at Mount Sinai

Vaccine-tunable TME-restricted CAR T therapy for long-term melanoma control

Bristol Myers Squibb — MRA Young Investigator Award Leyuan Ma PhD, The Children's Hospital of Philadelphia

Dissecting melanoma brain metastasis and response to immunotherapy

MRA Young Investigator Award Eva Perez-Guijarro PhD, Universidad Autónoma de Madrid

Catabolic plasticity in acral melanoma metastases and drug tolerance

The Black Family — MRA Young Investigator Award Vito Rebecca PhD, Johns Hopkins University

Bioengineering approaches for advancing targetedimmunotherapy in melanoma

MRA Young Investigator Award Tanmoy Saha PhD, Brigham and Women's Hospital

Multi-modal machine learning for early-stage melanoma recurrence prediction

L'Oréal Dermatological Beauty — MRA Young Investigator Award Yevgeniy Semenov MD, Massachusetts General Hospital

Image-based three-dimensional radiation dosimetry for Ac-225-MTI-201

ASTRO — MRA Young Investigator Award Chris Tichacek PhD, H. Lee Moffitt Cancer Center & Research Institute

Resolving the spatial clonal architecture of acral lentiginous melanoma

L'Oréal Dermatological Beauty — MRA Young Investigator Award Meng Wang PhD, The University of California, San Francisco

Monitoring early response to immunotherapy with ultrasensitive plasma WGS

The Black Family — MRA Young Investigator Award Adam Widman MD, Sloan Kettering Institute for Cancer Research



Marisol Soengas, PhD – Spanish National Cancer Research Centre (Spain) and Ze'ev Ronai, PhD – Sanford Burnham Prebys Medical Discovery Institute

Tumor immune evasion through STING-mediated T cell death in melanoma

MRA Young Investigator Award Jianjun Wu PhD, Cleveland Clinic Foundation

PILOT AWARDS

The CoREST repressor complex as a mediator of RNA splicing and tumor growth

Leveraged Finance Fights Melanoma — MRA Pilot Award Rhoda Alani MD, Boston University

Epigenetic determinants of melanoma progression and immunotherapy response

The Denise and Michael Kellen Foundation — MRA Pilot Award Alfonso Bellacosa MD, PhD, The Research Institute of Fox Chase Cancer Center

Identifying genetic sex biasing factors in melanoma progression

The Denise and Michael Kellen Foundation — MRA Pilot Award Nora Engel PhD, Temple University



Marcus Bosenberg, MD, PhD, Yale University; Andrew Aplin, PhD - Thomas Jefferson University; & Elizabeth Patton, PhD — University of Edinburgh

Targeting ASAP1-induced transcription factors in metastatic uveal melanoma

ACIS — MRA Pilot Award in Metastatic Uveal Melanoma Shannon Odelberg PhD, The University of Utah

A drug-binding assay platform to optimize therapies for RAS-mut melanomas

MRA Pilot Award Poulikos Poulikakos PhD, Icahn School of Medicine at Mount Sinai

Micronuclear Rupture and DNA Damage in Primary Cutaneous Melanoma Prognosis

MRA Dermatology Fellows Award Xiao Zhang PhD, The University of California, Los Angeles

Dermatology Fellows Awards

Two Homeodomain-Dependent Gene Regulatory Networks Rewiring Melanoma Heterogeneity and Enhancing Tumorigenesis

MRA Dermatology Fellows Award Pietro Berico PhD, New York University Grossman School of Medicine

The Role of APOE Isoforms in the Hereditary Basis of Rare Melanomas

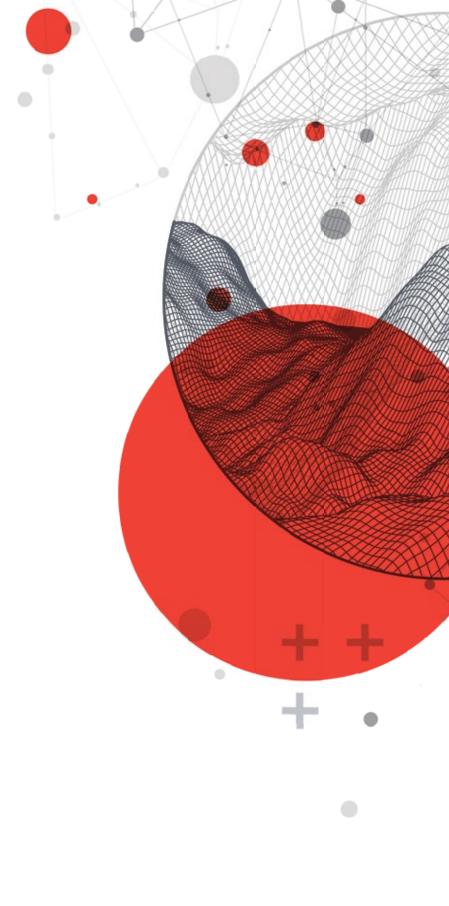
MRA Dermatology Fellows Award Neil Neumann MD, PhD, The Rockefeller University

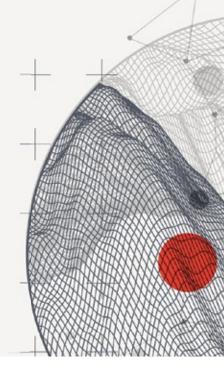
Epigenetics and Acral Melanoma Prognostic Model for Skin of Color Patients

MRA Dermatology Fellows Award Simon F. Roy MD, Yale University



Lorenzo Cohen, PhD - MD Anderson Cancer Center





TRIBUTE & MEMORIALS

In 2022, gifts were made in tribute to the following individuals.

Memorial Gifts

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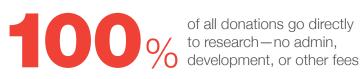
FINANCES

Financial presentation based on MRA's 2021 externally audited financials. Full audit and IRS 990 are available online at **CureMelanoma.org/Financials**

Statement of Financial Position

ASSETS	TOTAL 2022	TOTAL 2021
Cash and Cash Equivalents	\$10,912,733	\$12,982,423
Investments	\$10,877,034	\$11,630,333
Contributions Receivable (Net)	\$5,454,387	\$7,549,216
Prepaid Expenses		
and Other Assets	\$89,192	\$105,490
TOTAL ASSETS	\$27,333,346	\$32,267,462
LIABILITIES	TOTAL 2022	TOTAL 2021
Accounts Payable	\$133,430	\$152,043
Grants Payable (Net)	\$13,069,601	\$12,382,532
Deferred Revenue	\$277,500	\$609,500
TOTAL LIABILITIES	\$13,480,531	\$13,144,075
NET ASSETS	TOTAL 2022	TOTAL 2021
Unrestricted	\$12,027,815	\$16,300,897
Temporarily Restricted	\$1,825,000	\$2,822,490
TOTAL NET ASSETS	\$13,852,815	\$19,123,387
TOTAL LIABILITIES &		
NET ASSETS	\$27,333,346	\$32,267,462

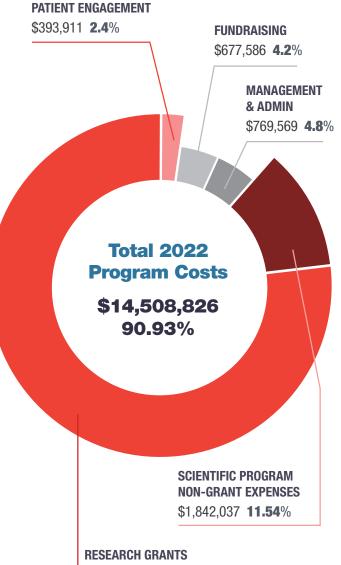




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Statement of Activities

T0TAL 2022	TOTAL 0004
	T0TAL 2021
\$7,877,755	\$4,786,386
\$2,651,407	\$2,046,963
\$744,500	\$459,555
\$(653,695)	\$236,854
\$105,762	\$82,524
\$(2,720)	\$54,518
610,685,409	\$7,565,800
T0TAL 2022	T0TAL 2021
\$12,272,878	\$8,761,340
\$12,272,878 \$2,065,037	
	\$8,761,340
\$2,065,037	\$8,761,340 \$1,837,282
\$2,065,037 \$399,336	\$8,761,340 \$1,837,282 \$49,006
\$2,065,037 \$399,336 \$518,951	\$8,761,340 \$1,837,282 \$49,006 \$540,770
\$2,065,037 \$399,336 \$518,951 \$251,723	\$8,761,340 \$1,837,282 \$49,006 \$540,770 \$31,261
	\$744,500 \$(653,695) \$105,762 \$(2,720) \$10,685,409



\$12,272,878 76.91%

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Bank of America Private Bank Goldman Sachs & Co. Kirkland & Ellis LLP Jonathan and Sheryl Sokoloff

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2023 LFFM Co-Chairs: (Back Row Left to Right): Lee Grinberg – Elliott Management, George Mueller – KKR, Kevin Pluff – HPS Investment Partners, Marc Hurlbert, PhD – Melanoma Research Alliance, Clare Bailhé – MidCap Financial, Ian Schuman – MRA Board of Directors & Latham & Watkins, Eric Wedel - Kirkland & Ellis, Kerry Dolan – Brinley Partners, and Matt Manin – Apollo. (Front Row Left to Right): Geoff Oltmans – Silver Lake, Trevor Watt – Hellman & Friedman, Jeff Rowbottom – MRA Board of Directors & General Atlantic Credit, and Cade Thompson – KKR. Not pictured: Brendan Dillon – Veritas Capital and Erwin Mock – Thoma Bravo.

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2023 GLOBAL

Milken Global Conference panel discussion: "Trust Your Gut - Is the Microbiome the New Disruptor in Healthcare" (L to R): Marc Hurlbert, PhD – Melanoma Research Alliance, Amanda Eilian – MRA Board of Directors & Able Partners, Manuel Fankhauser, PhD – Searave Foundation, Jack A. Gilbert, PhD – University of California San Diego, Sandrine Miller-Montgomery, PharmD, PhD – Micronoma, and Chidozie Ugwumba – SymBiosis Capital Management

Sir Paul Ruddock and Lady Jill Shaw Ruddock Secura Bio, Inc. Seix Investment Advisors LLC Shenkman Capital Management, Inc. Siris Capital Group, LLC James Skelton Sony Music Entertainment Beatrice Stern Stonepeak Sumitomo Mitsui Banking Corporation Stephanie Teicher Todd Goodwin Charitable Trust Z Capital Group

\$1,000-\$4,999

The 77 Foundation, Inc. Christopher Abbate Dina Acciai and Frank Basile Andrew Adams Jeffrey Aleshire Joanne Ally Amazon Anonymous Apple Rome and Lisa Arnold James Austin Shant Babikian Brandon and Lida Barniea Margaret Betzel Andrew Black Thomas Bolas Jamie Brodsky Vanessa Brown

Kellie Burdick John and Wendy Burnett Terri Butler Todd Carriker CBRE Group, Inc. Alan Cheng Brady Cherneski Jay and Gretchen Clayton Maurice and Gayle Cohen Linda Conely James Connolly Conscious Alliance Scott Cullerton Jerold Danis Jennifer Davidson Brian and Yvonne Day The Geaton & Joann Decesaris Family Foundation Inc. Kerry Dolan and Alexander Byers Max Dow Craig and Janet Duchossois Kelly Dybala Paula Ehrlich Jacob Elhganayan Dimitri Evanoff Susan and Peter Evensen John Eydenberg Erik Fiebert Fidelity Charitable Gift Fund Craig Fitt Margaret Flynn Angela Fontana Shelley Franco

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Bill Evans — Melanoma Patient Advocate

> Rachel Fischer, PhD — MRA Associate Director, Scientific Program & Registry

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Mara Eva Cline, Miss GA Teen 2021 titleholder, presents check to MRA

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Jeff Rowbottom (L) speaks at the 2022 Leveraged Finance Fights Melanoma event with (L to R): Charlotte Ariyan, MD, PhD — Memorial Sloan Kettering Cancer Center, Jedd Wolchok, MD, PhD — Weill Cornell Medical College, Michael Milken — MRA Board of Directors, and Stephanie Kauffman — MRA President & COO

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Mary Jo Rogers - MRA Board of Directors, Stephanie Kauffman at MRA Live: Naples, Florida Salon



The MRA team at the 2023 Leveraged Finance Fights Melanoma event

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Joan Levy, PhD Chief Science Officer

Tanisha Jackson, PhD Scientific Program Director

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Melanoma > Exchange

COMMUNITY LEADERS

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.

(Pictured below, left to right)

Cheryl Adams Jamie Troil Goldfarb Keith Tolley T.J. Sharpe Tracy Callahan



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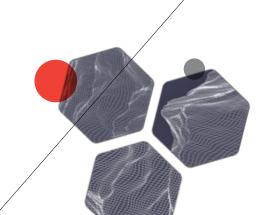
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