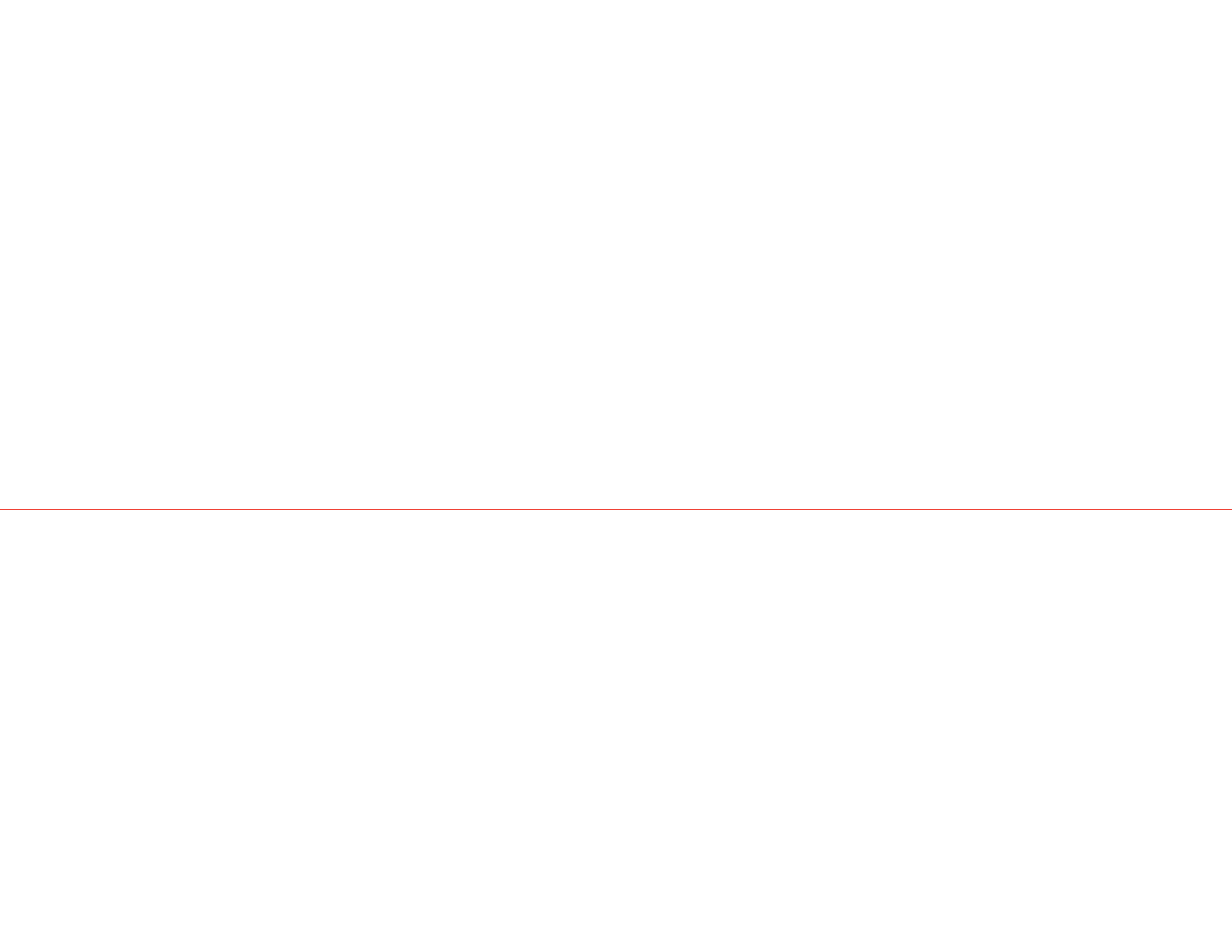




RAISING THE BAR

2018-2019 | ANNUAL REPORT



MISSION

The mission of the Melanoma Research Alliance (MRA) is 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 by melanoma survivor Debra Black and her husband, Leon, under the auspices of the Milken Institute, MRA has ushered in a dynamic new era of scientific progress. MRA has become the largest non-profit funder of melanoma research, funding \$110 million in cutting-edge studies and leveraging millions more from other sources during the last decade. Thanks to the generous support of our founders, 100% of all donations to MRA go directly to research.

A LETTER FROM THE CHAIR AND PRESIDENT



A conversation with someone who has recently been diagnosed with late stage melanoma is radically different than it was just a few years ago. Today, we have more treatment options than ever before—in fact 12 new options have earned FDA approval since MRA’s founding, and each year, progress continues to be made. This unprecedented progress serves as a testament to the tenacity and determination of patients, clinicians, researchers, and the generosity of countless donors.



Despite this incredible progress—and the prolific research pipeline that has made it possible—facing melanoma is still incredibly difficult. Because melanoma remains a very serious foe.

When talking with people starting—or in the thick of—their melanoma journey, we outline the incredible advancements that have been made and do what we can to offer as much hope as possible.

For the Melanoma Research Alliance (MRA), this hope is grounded in sound science and promising research—something we know well. That’s because no other nonprofit has funded more research in the fight against melanoma than MRA. Since our founding, we’ve directly invested more than \$110 million into innovative research and leveraged an additional \$200 million from outside sources.

While impressive, we know that this progress is not sufficient. This year alone over 7,600 people will die from late stage melanoma and over 96,000 will be diagnosed with invasive disease.

Some people’s melanoma is resistant to even our best treatment options. Other people develop melanomas that are so rare—or so stubborn—that successful treatment options have yet to be found. And regardless of treatment options available, far too many people are forced to have the difficult conversation—telling their loved ones that they have melanoma in the first place.



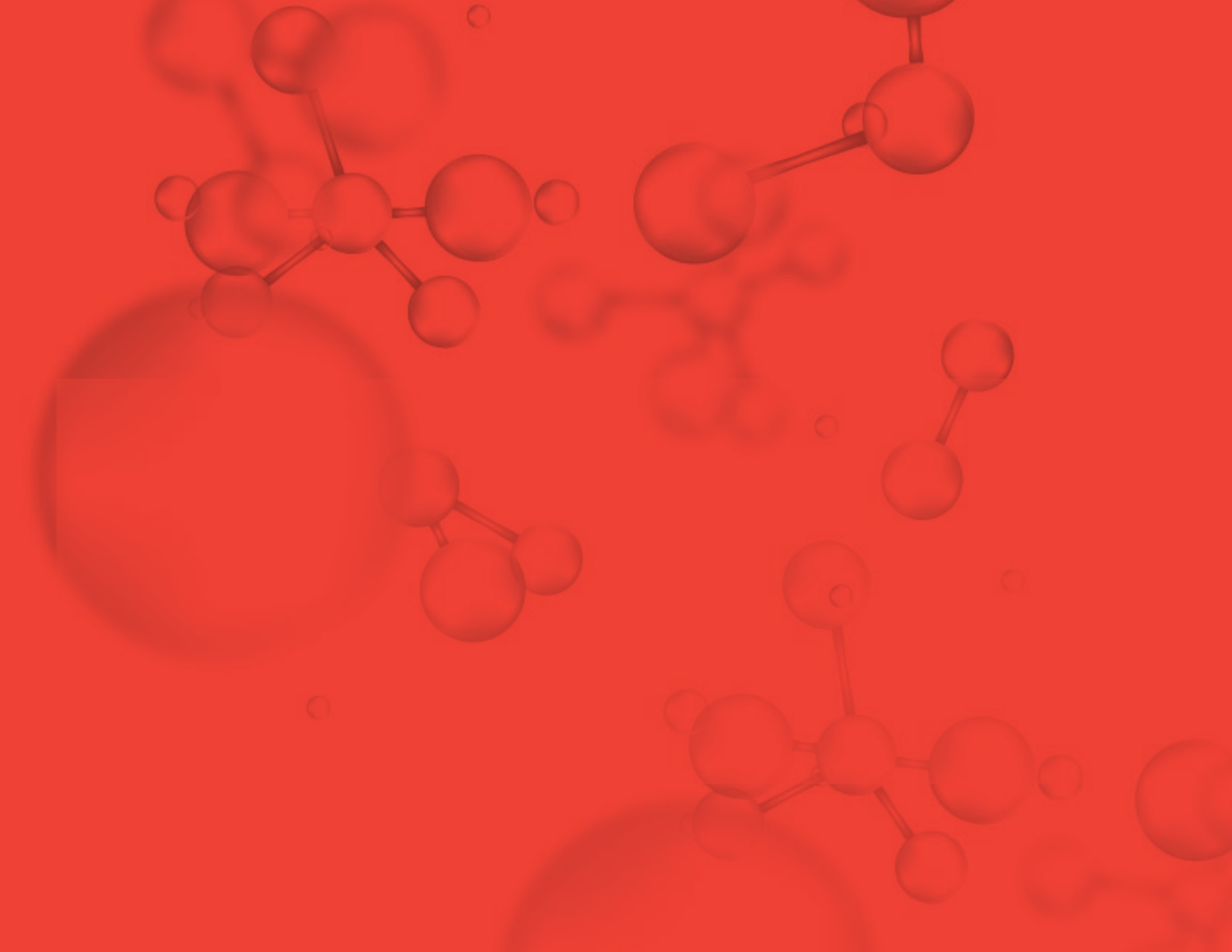
This report is for these people.

We are proud to showcase our many achievements from the last year, and also highlight examples of how MRA strives every day to push the field further and to raise the bar higher for patients who need it most. Our mission of ending death and suffering due to melanoma remains steadfast in all we do, and this report captures just a few of those efforts.

None of this would be possible without the many individuals, organizations, government officials, and corporations who have joined us in our mission. Our work would not be possible without you.


Debra Black
Chair and Co-Founder


Michael Kaplan
President and CEO



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Dr. A. Hunter Shain presents at the 2019 MRA Scientific Retreat

RAISING THE BAR

Over its 12 years, MRA has been a catalyzing force in mobilizing resources, talent, and energy towards its mission to end suffering and death due to melanoma worldwide.

As a funder, MRA has directly invested more than \$110 million – and leveraged an additional \$200 million from other sources – to become the largest non-profit funder of melanoma research worldwide. This flood of capital has helped to usher in a new paradigm in melanoma treatment – where patients have more options and hope than ever.

As a convener, MRA's Scientific Retreat brings partners together from across the globe to share best practices, emerging technologies, and promising treatments. The Scientific Retreat also serves as a reminder about the importance of this work, who it's for, and that no one individual or institution can go it alone. MRA's Melanoma > Exchange (available at www.curemelanoma.org/community) connects patients and loved ones to a vibrant online community that understands what it means to face melanoma, head on.

Inch by inch, year by year, and breakthrough by breakthrough, the melanoma field has made unprecedented progress that has transformed the way melanoma is diagnosed and treated. For many patients this progress is rewriting the book about what it means to face melanoma. However, there is still more to do.

That's because for about half of patients with late-stage melanoma, the road ahead is still fraught with uncertainty. Despite the paradigm-busting progress that has been made, too many people still aren't responding to any of the currently approved therapies.

MRA is moving full steam ahead by focusing on traditional areas of exploration such as drug development and predictive biomarkers, approaching stubborn challenges with new perspectives, and by leveraging new technology and science from all areas.

Patients diagnosed with melanoma today have more reasons than ever to be optimistic:

- Advancements in melanoma research and available treatments—including targeted therapies, immunotherapies, and novel combinations—are on the rise.
- In fact, 12 new treatment approaches have earned FDA approval since 2011.
- And because of these new treatment options, people are living longer and healthier lives with melanoma. We are making great headway.
- MRA continues to raise the bar by galvanizing unprecedented partnerships, support, and funding across academia, government, and industry to go even further, faster.



Dr. Ashani Weeraratna and MRA Chief Science Officer Dr. Marc Hurlbert at the 2019 MRA Scientific Retreat



Dr. Pan Zheng and Dr. Lynn Schuchter at the 2019 MRA Scientific Retreat

THE GOOD FIGHT: RESISTING RESISTANCE



“For a lot of people, the revolution isn’t here,” says Dr. Caroline Robert, Head, Dermatology Unit at the Institut Gustave Roussy, the largest cancer center in France and Co-Chair of the MRA Grant Review Committee.

“We know that some people will do less well than others,” says Robert, “but honestly, when we begin treatment, we can’t predict who will respond, so we need new biomarkers.” Dr. Robert’s work focuses on resistance, where treatment either stops working—a term called “acquired resistance” or where patients do not respond to any therapy at all—a term called “primary resistance.”

Dr. Robert is a recipient of a 2018 Team Science Award and is spearheading a three-year project funded by MRA seeking to learn why some cancer cells, instead of dying, adapt and modify their protein and messenger RNA production in response to treatment. Knowing this will help clinicians better identify when to provide treatment, when to stop, and better predict how a patient is likely to respond to treatment prior to starting it.

Hearing Dr. Robert talk about her work sounds akin to a general preparing for battle: “I want to kill melanoma cells. I don’t care what tool I use to do it,” she says. Robert tries to think like the enemy. “We need to put ourselves in the role of the cells: What would we do if we were trying to invade someone? We would hide, eat whatever is available—these cells eat what other cells don’t want—and we would wait. We know they hide because they appear years later and we’re trying to figure out where they’re hiding so we can stop their reappearance.”

MRA-funded research is particularly important in advancing this knowledge. Despite targeted therapies killing the majority of tumor cells, often a small population of drug-resistant “persister” cells remain by making large-scale changes to their protein expression patterns. “Cells are getting smarter and are modifying themselves so we need to focus on the nexus,” says Robert, referring to a

complex of proteins. Blocking a component of the protein complex that translates the genetic code has the potential to inhibit these evasion tactics.

For patients whose tumors are regressing, Dr. Robert and her team take samples and study the expression of the genes. They are looking closely at the tumor cells that persist in the face of targeted therapy, and are testing a new protein inhibitor designed to kill these cells. Lab results with mouse models are promising and suggest that when combined sequentially with already existing targeted therapies, this new inhibitor enhances tumor cell death.

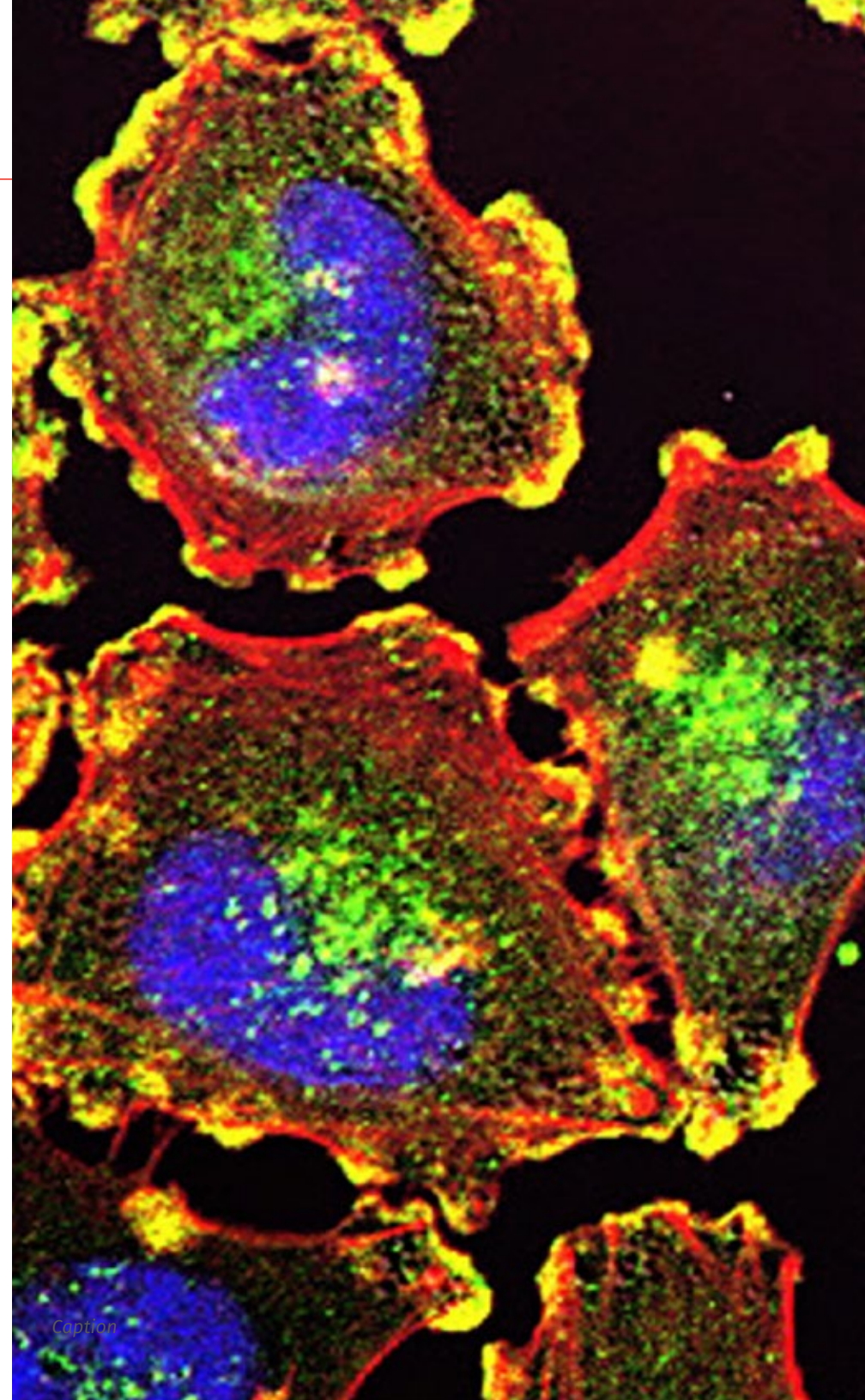
In time, Dr. Robert hopes to begin testing this work in the clinic with patients. If successful, it could represent a new chapter in the melanoma playbook—one that prolongs the length of time that treatment is effective and addresses resistance head on.



Caption

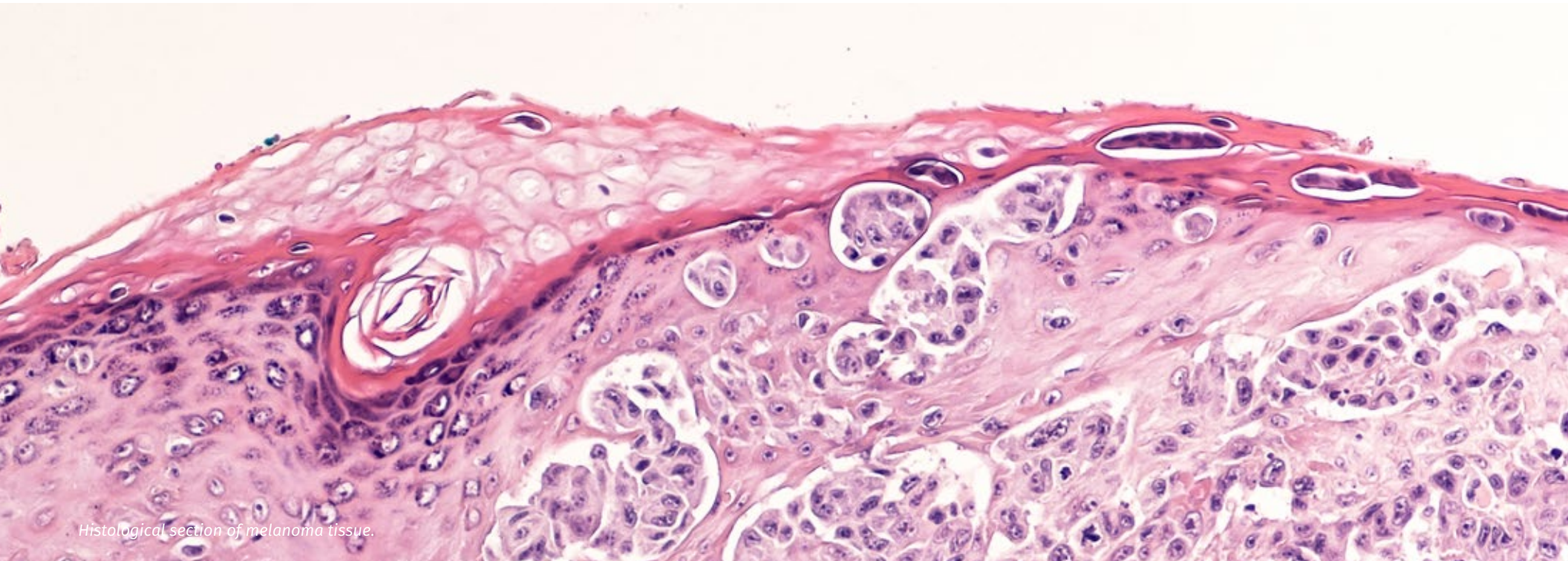
Dr. Caroline Robert presenting at the 2019 MRA Scientific Retreat

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Caption

DETECTING MELANOMA EARLIER WITH ARTIFICIAL INTELLIGENCE



Histological section of melanoma tissue.

As an internist, Dr. Joann Elmore was taught to ask questions. Those questions led her to spend much of her career in breast cancer research where she found extensive variability among radiologists' interpretation of mammograms. "Radiology data is subjective, just like art. You're being asked to classify visual data," Elmore says.

It wasn't until she was on the receiving end of a Friday night phone call alerting her to a "suspicious" skin biopsy, however, did Elmore's interest in melanoma peak. Elmore's biopsy specimens were sent to two pathologists. "As a physician, I had always assumed a pathologist's diagnosis was the 'gold standard,'" she says, "however, I received two very different diagnoses on the opposite ends of the spectrum on my own skin biopsy: one said it was invasive melanoma and the other said it was benign." As such, Elmore sent the specimen for yet another opinion, this one to a pathologist who had written textbooks on the topic and had decades of experience. His diagnosis

landed somewhere in the middle and acknowledged that it was atypical but not in the classification of invasive melanoma. Now, more than a decade later, Dr. Elmore has had no recurrences.

Based on this experience, Dr. Elmore expanded her research from radiology to pathology. "Pathologists, like radiologists, are also looking at image data and I realized there was way too much variability, and I wanted to better understand why—and what we could do about it."

Dr. Elmore received a National Institutes of Health (NIH) grant to study the accuracy of diagnostic screening and biopsy interpretation. The study looked at all melanoma-type biopsies and was able to capture how often there was variability in interpretation among providers. Slides were presented in random order to 187 pathologists who provided their diagnoses using an online histology data collection form. Months later, the same exact



Dr. Joann Elmore

“We want to give patients the right treatment—and all of patient care relies on an accurate pathologist diagnosis.”

— Dr. Elmore.

slides were sent to the same pathologists but in a different order. “There was less than 50% consistency among most of the pathologists and often they weren’t even consistent with their own initial diagnosis,” says Elmore. “This really showed me that there is an art to medicine and diagnosis is so critical.” Elmore emphasizes that this experience did not decrease her appreciation for pathologists but, rather, highlighted how difficult pathology is, particularly in melanoma and precursor lesions, and underscores the need for better diagnostic tools.

Thanks to the generous support of the Michael & Jacqueline Ferro Family Foundation, MRA issued three grant awards focused specifically on using artificial intelligence to better detect melanoma. Through one of these awards,

Elmore is partnering with a world renowned computer scientist Dr. Linda Shapiro at the University of Washington who specializes in computer visualization of complex information, as well as leading pathologists around the globe to develop an artificial intelligence (AI)-based diagnostic system.

Elmore and her team are evaluating whether computers can assess cell size, shape, and other details from images of skin biopsies in order to help improve the accuracy – and consistency – of melanoma diagnoses. “For each skin biopsy, there can be hundreds of thousands of cells,” explains Elmore. This also sheds light on why melanoma biopsies are so complicated and challenging for pathologists and why AI, which can scan thousands of cells and readily cross-reference information, may improve the future of melanoma medicine.

“Although we are still in the early phases, this is critical work,” says Elmore. According to a report by the National Academies of Sciences, Engineering, and Medicine, improvements in the diagnostic process are a “moral, professional, and public health imperative.”

Indeed, a diagnosis is the building block on which all other medical treatment is based. On the other end of these biopsies are real patients: patients answering the late-night, anxiety-inducing phone calls; patients undergoing invasive surgeries; patients weighing their next clinical steps. Not all of these patients will seek out three opinions like Elmore did, but all of them deserve an accurate diagnosis.

Elmore’s research also showcases MRA’s commitment to working across fields to fund the most promising research and to recruit innovative researchers. Doing so injects fresh ideas that are needed to move the field forward and to raise the bar ever higher, so that today’s challenges can be tomorrow’s success stories.

“MRA creates and supports multidisciplinary collaborations,” says Elmore. “They get it. Science is better as a team approach and I’m looking forward to seeing what’s next.”

¹ Balogh EP, Miller BT, Ball JR (Eds.). National Academies of Sciences, Engineering, and Medicine. *Improving Diagnosis in Health Care*. The National Academies Press, 2015.

A BRAVE NEW WORLD: APPLYING AI TO MELANOMA



Dermscopes are helpful tools that allow clinicians to more closely inspect lesions on skin

“AI will change everything in the world—and melanoma is no exception,” says Dr. Allan C. Halpern, Chief of Dermatology at Memorial Sloan Kettering Cancer Center.

Halpern is a board-certified internist and dermatologist with a specialization in skin cancer, especially melanoma. Much of his clinical career has focused on early detection and management of melanoma, and he has pushed the field to adopt and leverage technology to better image and track peoples’ skin over time.

Halpern pioneered the use of a whole-body, 3-D imaging system to assist in the detection of changing moles and other skin lesions. The computerized system creates a baseline digital photographic record of the patient’s moles, searchable by size, color, and other factors; which can then assist the dermatologist in monitoring and assessing subsequent changes over time. This includes subtle changes that can be more difficult for

dermatologists to catch but which are critical for identifying melanoma at the earliest stage possible. “This can help you identify the outliers,” explains Halpern. “In clinical practice, this technology isn’t being widely used yet, but we expect that this is where it’s going.” This work was first supported by an MRA-Industry Partnership Award, and has since been successfully commercialized.

According to the U.S. Preventive Services Task Force, limitations in clinician visual skin examinations can lead to both over treatment and over-diagnosis. For patients, this can mean unnecessary procedures, scarring, and even functional limitations.

One challenge to widespread adoption of this technology is that the field of dermatology doesn’t have standard image requirements. In response, Halpern, and others like him, are working hard to develop digital communication standards.

To help make this happen, Halpern leads the International Skin Imaging Collaboration (ISIC)—an academic and industry partnership designed to facilitate the clinical application of digital skin imaging in melanoma. The ISIC community invites people to download images and use them for educational purposes. They also host competitions to create algorithms to better spot early melanomas. “What’s exciting,” says Halpern, “is when we compared the algorithms against 510 clinicians including dermatologists from around the world, the algorithms outperformed the majority of them. While this ‘artificial experiment’ was performed without the clinicians interacting with the patients, it does demonstrate that current computer algorithms are already pretty powerful. As we give computers lots more data, including both images and clinical information, we anticipate that their performance will continue to improve.”

While the vast majority of past MRA-funded research projects have focused on later-stage melanoma treatments, work like Halpern’s is laying an important foundation for future awards needed to move the field forward



Dr. Allan C. Halpern at 2019 MRA Scientific Retreat

towards earlier detection and treatment. In particular, although early-stage melanoma is challenging for dermatologists to identify, AI might change that. Doing so would have significant benefits for patients as it would improve early diagnosis of melanoma.

“AI isn’t new,” Halpern says. “There have been multiple waves of AI. What’s different and exciting about this current wave is that it teaches computers like we teach kids, learning by example. This has been made possible because computers are much more powerful than they were years ago and now have nearly limitless storage.” Current AI uses what is known as “deep learning” one example of which are “convolutional neural networks.” These algorithms use multiple layers of analysis to learn directly from raw data. Such networks are particularly well suited for analysis of visual information, provided there are large enough collections of data for training. The recent availability of very large general image datasets give the algorithms a head start for analyzing new types of images, such as skin lesions.

Properly training AI for melanoma, however, will require a lot more imaging in clinical practice, collecting high-quality images, controlling for bias, and doing a better job applying what is learned so as to avoid unnecessary biopsies.

“It’s not a question of if we’ll use this technology, but when,” says Halpern. He is, however, quick to preface that this is not man against machine. AI, and those in support of it, are not trying to put people out of work. “What we want are better diagnoses,” says Halpern. “Even dermatologists do better when they know what the computer analysis is saying.”

Work like Halpern’s raises the bar of what is possible and begins to fill a critical niche: catching melanoma early when it is most treatable and survival rates are greatest. The implications are truly profound for patients and for professionals alike. “There are lots of opportunities for MRA to be involved in this work and to help implement it the right way,” says Halpern. Indeed, AI—much like MRA’s mission—requires collaboration.

The groundwork has started; the revolution is here; the technology is capable; and the time is now.

² U.S. Preventive Services Task Force. Screening for Skin Cancer: US Preventive Services Task Force Recommendations Statement. JAMA. 2016; 316(4): 429-435.

³ For more information, visit: www.isic-archive.com/#!/topWithHeader/wideContentTop/main

⁴ Halpern AC. Predicting the Future: AI, Machine Learning and Dermatology” at the 2019 American Academy of Dermatology Annual Meeting.

DOUBLING DOWN ON RARE MELANOMAS



Chromosomes, like the one pictured here, are important structures that contain the genetic information of an organism. Telomeres protect the ends of chromosomes from deteriorating

Recognizing the importance of accelerating research and improving outcomes for people diagnosed with rare melanomas, MRA has invested more than \$10.3 million through 22 awards specifically focused on these subtypes. This makes MRA the largest, non-profit funder research focused on rare melanoma worldwide.

Dr. Titia de Lange is hoping her research will help drive change in this rare melanoma space. de Lange is a recipient of The Black Family-MRA Team Science Award and is examining acral melanoma on the chromosome level to determine whether a process known as “telomere crisis,” which causes extensive damage to a cell’s genome,

When someone says “melanoma,” they think skin. Indeed cutaneous (skin) melanoma is the most common type of melanoma, accounting for roughly 90% of cases and receiving the lion’s share of funding. But what about the remaining 10% of melanomas?

Acral, uveal, and mucosal melanoma – known collectively as ‘rare melanomas’ – represent a type of black hole for the clinical community. We know far less about them—what causes them, how they progress, and how to effectively treat them. Rare melanomas frequently appear in parts of the body that are shielded from the sun (such as palms, under fingernails, in eyes, or nasal cavities), and so their development is not directly related to sun exposure. And because these areas of the body aren’t traditionally associated with melanoma, patients with rare melanomas are more likely to have late diagnoses and poorer prognoses.

contributes to acral melanoma development and progression. de Lange, who is Director of the Anderson Center for Cancer Research, a Leon Hess professor, and the head of the Laboratory of Cell Biology and Genetics at Rockefeller University, has spent more than 25 years researching telomeres, the protective elements at the ends of chromosomes.

Telomeres look like broken DNA but are not broken DNA at all. Instead, they are, in fact, critical for the stability and maintenance of genetic information. Telomeres are shielded by a dynamic complex of six proteins, which de Lange has dubbed “shelterin,” which helps regulate the length of telomeres and shelters them from DNA repair processes—an incredibly important but complex and still somewhat mysterious process.

⁵ To learn more about rare melanomas and melanoma subtypes, visit www.curemelanoma.org/about-melanoma/types/

This type of research is so important because if you only fund research on existing treatments then you will never find the next big breakthrough.

Flawed telomere function, however, can generate genome instability and drive cancer progression. “Cells are programmed to go through regeneration but cells that go through too many divisions are likely associated with cancer,” explains de Lange. “Eventually cells peel off and die; however, some cells break through this ‘death order’ and can create tumors and chaos.” This telomere crisis is very frequent in early stage cancers and telomere dysfunction also contributes to genome rearrangements in tumors.

de Lange, who studies telomere function became interested in acral melanoma because it occurs in parts of the body that receive little sun exposure (and correspondingly little UV damage) and as a result, acral tumor cells have fewer mutations. Instead, acral melanoma cells often have large-scale changes to their genomes – for instance, large sections of chromosomes are either deleted or increased in number – changes that may result because of alterations to telomeres, which regulate so-called ‘genome stability’.

de Lange’s 3-year research project is examining how acral melanomas arise and what causes these chromosomal changes. She is also hoping to identify molecules that can be targeted with future therapies. de Lange says it’s critical to keep an open mind for hypothesis-driven, basic research of what happens inside cells.

“What I hope patients know is that we are working as hard as we can to better understand this disease,” says de Lange. “Our highest hope is that we have greater insight into how melanoma chromosomes and tumors function so that we can develop biomarkers for disease staging and predictive information to help us with prognosis, diagnosis, and so on,” says de Lange.



Dr. Titia de Lange

de Lange underscores the importance of organizations like MRA providing funding for preliminary research to let initial pilot projects mature: “I want everyone to know just how important it is that MRA is willing to take risks and fund research like this in its early stages. I don’t think our project would have been funded by the NIH. This type of research is so important because if you only fund research on existing treatments then you will never find the next big breakthrough.”



RARE MELANOMAS, REAL PEOPLE: MEET DAVID

Kellie Gardner, David Marx, Linda Marx, and Dr. Michael Atkins

David Marx was shocked when he was diagnosed with Stage 3 melanoma in 2018. He always thought melanoma was ‘skin cancer’ and had no idea it could develop in areas that aren’t regularly exposed to the sun like his toenail.

Following surgery to remove his primary melanoma and affected lymph nodes, David’s oncologist, chair of MRA’s Medical Advisory Panel, Dr. Michael Atkins suggested adjuvant therapy. Adjuvant therapy is additional treatment given after surgery, with the goal of reducing the risk of melanoma returning. For patients with Stage 3 melanoma like David, up to 60% will relapse within three years of surgical resection without adjuvant therapy.¹

After talking with Dr. Atkins, David and his wife Linda decided to move forward with monthly infusions of the immunotherapy, nivolumab. He began a year-long course of adjuvant therapy about five weeks after surgery.

“The side effects I’ve experienced - itchiness and feeling tired have been a minor inconvenience,” says David. “I also know that I’m doing everything I can to keep melanoma from returning.”

¹ Long, Georgina. “Adjuvant Dabrafenib plus Trametinib in Stage III BRAF-Mutated Melanoma.” *The New England Journal of Medicine*. (Nov. 9, 2017)

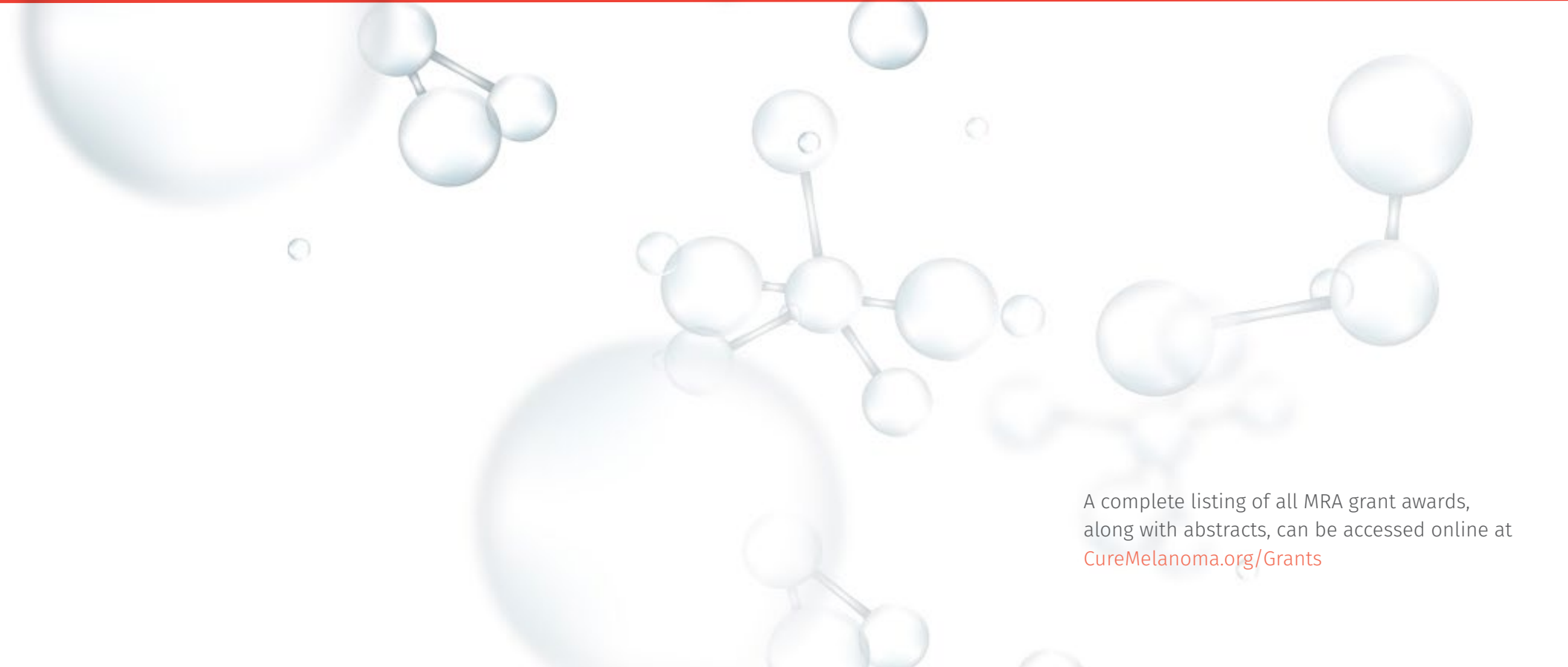
A graphic of a molecular structure with blue and red spheres connected by grey rods, set against a white background with a red horizontal band. The spheres are semi-transparent and have a slight glow.

MRA'S CHARGE

For patients for whom treatments and outcomes have been less certain and less successful, for researchers with big ideas that provide promise but need piloting, for cross-industry and cross-discipline projects that could change the landscape as we know it, MRA is here championing for you each step of the way. Together, we are raising the bar—standing on the shoulders of those who have fought before us and setting the precedent for those who have yet to come.

The top half of the image features a solid red background. Scattered across this background are several semi-transparent molecular models. These models consist of spheres of varying sizes connected by thin lines, representing chemical structures. Some models are in sharp focus, while others are blurred, creating a sense of depth. The overall aesthetic is scientific and modern.

2019 RESEARCH AWARDS

The bottom half of the image features a solid white background. Similar to the top half, it contains several semi-transparent molecular models. These models are rendered in a light blue or cyan color. They are scattered across the white space, with some appearing more prominent than others. The models are identical in structure to those in the red section, maintaining a consistent scientific theme.

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

Established Investigator Awards

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

Epigenetic Regulation of Resistance to Targeted Therapies in

Melanoma: Dissects a molecular pathway of a treatment-resistance to BRAF inhibitors and tests specific inhibitors to overcome treatment resistance.

MRA Established Investigator Award

Rhoda Alani, Boston University

Targeting MAPK and PI3K Signaling via CK2 Inhibition in Acral

Melanoma: Investigates the possibility of using CK2 inhibitors, in combination with currently used therapies, to improve treatment outcomes in NF1 mutant acral melanoma.

MRA Established Investigator Award, collaboratively funded by Columbia University

Angela Christiano, Columbia University

Applying AI to Assess Histologic Features to Improve Melanoma

Diagnosis: Uses novel computational techniques to improve the ability to accurately and reproducibly diagnose melanoma, and ultimately enhance patient care.

Michael and Jacqueline Ferro Family Foundation - MRA Established Investigator Award for Artificial Intelligence Applied to Melanoma

Joanne Elmore, David Geffen School of Medicine at UCLA

DGAT1 is a Novel Melanoma Oncogene: Aims to dissect how fatty acid metabolism affects melanoma cells and whether targeting this pathway therapeutically can hamper melanoma growth.

MRA Established Investigator Award

Adam Hurlstone, University of Manchester

Eradicating Melanoma Drug-Tolerant Cells: Aims to understand and therapeutically target the nongenetic strategies tumors use to evade treatment.

MRA Established Investigator Award

Jean-Christophe Marine, VIB (Vlaams Instituut voor Biotechnologie)

Enhanced-OCT for Discriminating Nevi from Melanomas: Aims to improve the accuracy of melanoma diagnosis by applying artificial intelligence to optical coherence tomography imaging.

Michael and Jacqueline Ferro Family Foundation - MRA Established Investigator Award for Artificial Intelligence Applied to Melanoma

Mohammadreza Nasiriavanaki, Wayne State University

Developing a Predictive Tool Using Machine Learning Algorithm in

Melanoma: Will apply artificial intelligence to microscopic images to predict which Stage III patients will benefit from additional treatment after surgery.

MRA Established Investigator Award, collaboratively funded by New York University School of Medicine

Iman Osman, New York University School of Medicine

Metabolic Control of T Cell Senescence for Melanoma Immunotherapy:

Will uncover how altered energy usage leads to T cell dysfunction and will develop strategies to overcome this in melanoma.

MRA Established Investigator Award

Guangyong Peng, Saint Louis University



Dr. Antoni Ribas at the 2019 MRA Scientific Retreat

Preclinical Development of a Disrupter of BRAF-Containing Dimers: Aims to determine how best to use a next-generation BRAF inhibitor to maximize its antitumor activity with the goal of advancing these findings to the clinic.

MRA Established Investigator Award

Neal Rosen, Memorial Sloan-Kettering Cancer Center

Studying the Effects of Intra-tumor Heterogeneity on Anti-tumor Immunity: Uses a novel melanoma mouse model to better understand the body's anti-tumor immune response, which could lead to strategies to enhance response rates to therapy.

MRA Established Investigator Award

Yardena Samuels, Weizmann Institute of Science

Nanomedicine Targeting Melanoma-Astrocytes Interplay in 3D Brain Metastases: Will establish 3D-printed models of melanoma brain metastases to elucidate how melanoma spreads to the brain and to evaluate the efficacy of novel therapeutics.

MRA Established Investigator Award

Ronit Satchi-Fainaro, Tel Aviv University

Targeting CD39 in Melanoma: Will test whether targeting the cell surface enzyme CD39 either alone or in combination with approved immunotherapies is a promising therapeutic strategy for melanoma.

MRA Established Investigator Award

Mark Smyth, Queensland Institute of Medical Research

Mechanism of EBF3 Tumor Suppression in Melanoma: Seeks to better understand how alterations in the protein EBF3 drives melanoma formation and responsiveness to immunotherapy.

MRA Established Investigator Award

Hensin Tsao, Massachusetts General Hospital

Proof of Practice: Melanoma Screening Using Computer Vision:

Addresses major barriers holding back the use of computer-assisted diagnostic devices in the clinic to improve melanoma detection.

MRA Established Investigator Award, collaboratively funded by University of California, San Francisco

Maria Wei, University of California, San Francisco

Understanding and Targeting Metabolic Heterogeneity in Melanoma:

Examines the differences in energy usage among melanoma cells and how this impacts responsiveness to therapy.

MRA Established Investigator Award

Bin Zheng, Massachusetts General Hospital

Finding Pathways That Drive T Cells Into Melanoma: Aims to find drugs that can enhance T cell recruitment to the tumors and to decipher how they work using a zebrafish model.

MRA Established Investigator Award

Leonard Zon, Harvard University



Dr. Sancy Leachman at the 2019 Scientific Retreat

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.

Development of Novel YAP-TEAD Inhibitors for Uveal Melanoma: Seeks to develop a novel, first-in-class drugs for the treatment of melanoma of the eye .

MRA Pilot Award

Fernando Camargo, Children’s Hospital Boston

Mitochondrial Control of Melanoma Initiation: Aims to delineate how changes to mitochondria, the body’s energy-producing cellular machines, impact melanoma initiation, progression and treatment.

MRA Pilot Award, collaboratively funded by Icahn School of Medicine at Mount Sinai

Jerry Chipuk, Icahn School of Medicine at Mount Sinai



Dr. Paul Chapman at the 2019 MRA Scientific Retreat

Blood Vessel Co-option by Brain Tropic Melanoma Cells: Seeks to better understand how melanoma cells invade the brain via their ability to interact with the brain's blood vessels, and target this process therapeutically.

MRA Pilot Award

Andrew Dudley, University of Virginia School of Medicine

Spliced Immune Receptors for Immune Regulation and Melanoma Immunotherapy: Aims to explore the mechanism of action on potential therapeutic applications for a novel immunostimulatory molecule.

MRA Pilot Award

Michal Lotem, Hadassah Medical Organization

Targeting Ferroptosis to Combat Resistant Forms of Melanoma:

To determine whether a novel pathway of cell death can be therapeutically manipulated to kill melanoma cells.

MRA Pilot Award

James Olzmann, University of California, Berkeley

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.

Identification of Metabolic Liabilities of Melanoma Cells: Seeks to understand how melanoma metabolism changes when a tumor first forms and eventually spreads to other areas of the body.

MRA Young Investigator Award

Kivanc Birsoy, The Rockefeller University

Discovering Unconventional CD8+ T Cell Epitopes in Metastatic Cutaneous Melanoma: Aims to develop cell-based therapies targeting a novel class of tumor antigens.

Bristol-Myers Squibb - MRA Young Investigator Award in Immunotherapy

Yiwen Chen, University of Texas MD Anderson Cancer Center

Optimization of GITR Antibodies for Melanoma Immunotherapy: Focuses on enhancing the therapeutic activity of an immunostimulatory antibody to improve its anti-cancer activity.

MRA Young Investigator Award, collaboratively funded by Weizmann Institute of Science

Rony Dahan, Weizmann Institute of Science

Targeting Copy Number Alterations to Overcome Immune Evasion in Melanoma: Will study how large scale deletions and amplifications of melanoma cell genomes contributes to therapeutic response and resistance.

Julie and Edward J. Minskoff - MRA Young Investigator Award

Teresa Davoli, New York University School of Medicine

The Multifaceted AMBRA1-based Signaling in Melanoma Response to Therapy: Seeks to understand how the novel tumor suppressor gene AMBRA1 contributes to melanoma progression and responsiveness to treatment.

MRA Young Investigator Award

Daniela De Zio, Kraeftens Bekaempelse

Microbial Metabolites in Immunotherapy of Malignant Melanoma: Investigates how a bacterial product found in the gut influences the responsiveness of melanoma to immunotherapy.

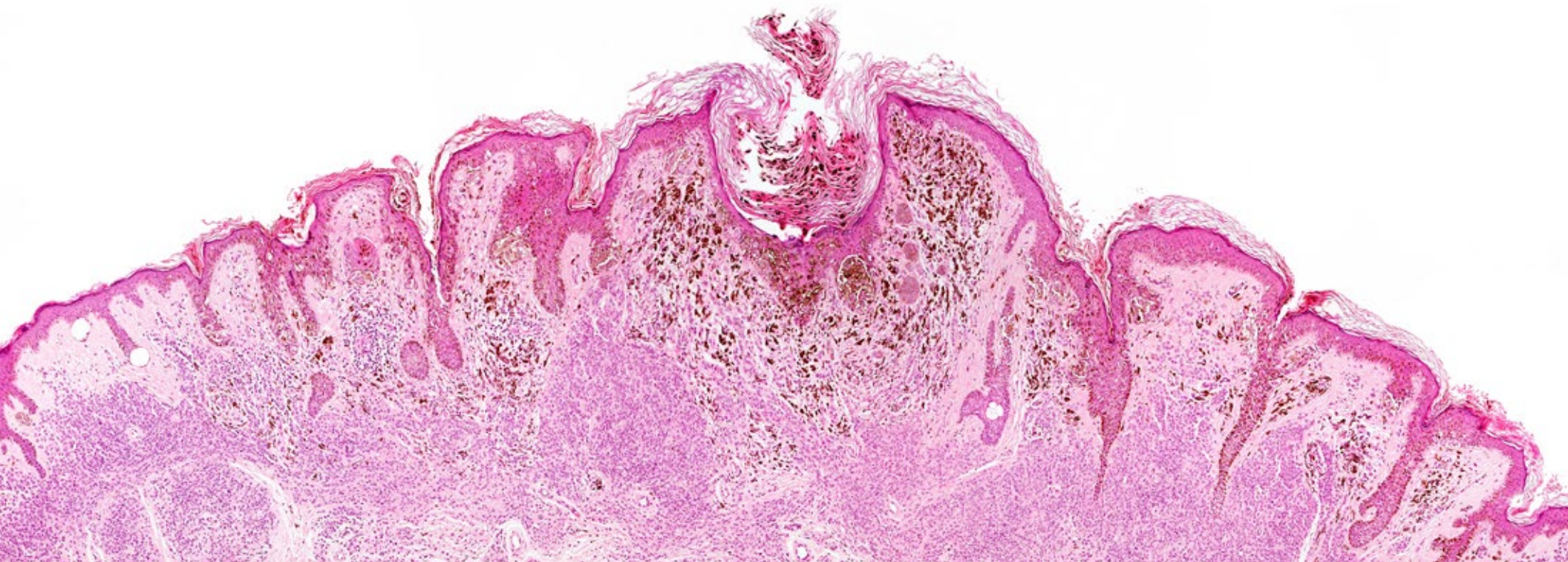
Bristol-Myers Squibb - MRA Young Investigator Award in Immunotherapy

Simon Heidegger, Technical University Munich

TANK-Binding Kinase 1 (TBK1) As A Novel Cancer Immunotherapy Target: Will explore whether inhibiting the protein TBK1 can help enhance responsiveness and overcome resistance to anti-PD1 blockade.

Tara Miller Melanoma Foundation - MRA Young Investigator Award

Russell Jenkins, Massachusetts General Hospital



Histological section of melanoma tissue

Transcriptional and Epigenetic Regulators of Melanoma Initiation: Aims to use a zebrafish model of melanoma to identify the molecular events that drive the transition of normal melanocytes to malignant melanoma.

MRA Young Investigator Award

Charles Kaufman, Washington University in St. Louis

Investigating Host Immune Factors in Mediating Immune Related

Adverse Event: Will conduct studies to gain a better understanding of immune-related adverse events (irAEs) to expand immunotherapy use and prevent toxicities in patients.

Society for Immunotherapy of Cancer – MRA Young Investigator Award

Shaheen Khan, UT Southwestern Medical Center



Dr. Eva Hernando at the 2019 MRA Scientific Retreat

Dissecting Tumor-Immune Cell Interactions in Uveal Melanoma:

Investigates how the immune system interacts with ocular melanoma cells and modulates their metastatic potential.

Ellen and Gary Davis - MRA Young Investigator Award

Ashley Laughney, Joan & Sanford I. Weill Medical College of Cornell University

Identifying New Molecular Targets and Drugs to Treat Resistant

Melanoma: Uses a unique chemical platform to identify novel drug leads to treat therapy-resistant melanoma.

Jill and Jay Bernstein - MRA Young Investigator Award

Nir London, Weizmann Institute of Science

Factors that Influence Artificial Intelligence-based Melanoma

Diagnosis: Uses artificial intelligence (AI) approaches to combine clinical images with patient metadata to improve melanoma diagnosis.

Michael and Jacqueline Ferro Family Foundation - MRA Young Investigator Award for Artificial Intelligence Applied to Melanoma

Veronica Rotemberg, Memorial Sloan-Kettering Cancer Center

Elucidating Cross-Presentation of Melanoma-Derived Antigens: Aims to understand at a cellular level why some patients do not respond to checkpoint immunotherapy.

Lee Grinberg Family-MRA Young Investigator Award

Stefani Spranger, Massachusetts Institute of Technology



MRA Young Investigator Awardees at the 2019 Scientific Retreat

MELANOMA > EXCHANGE

Available at www.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. Together, these community leaders have cultivated a unique environment where patients can get true insight into key milestones such as being diagnosed, choosing and going through treatment or finding the right clinical trial, and addressing any implications with friends and family.

Community Leaders:

Tracy Callahan

T.J. Sharpe

Jamie Troil Goldfarb

Cheryl Trocke



Lisa Simms Booth, Dr. Sapna Patel, and T.J. Sharpe at the Melanoma > Exchange Forum



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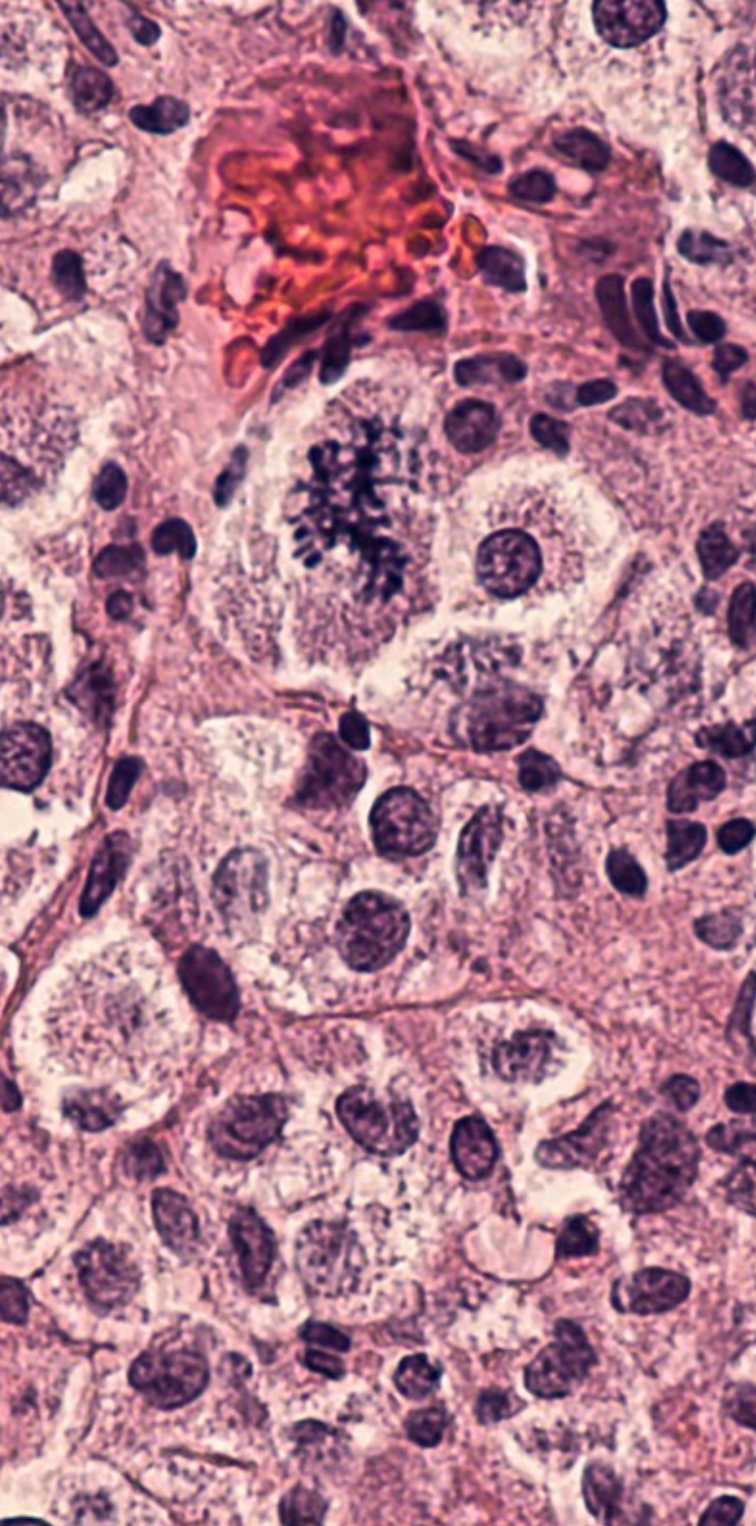
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Jeff Rowbottom at the 2019 Leveraged Finance Fights Melanoma event



STATEMENT OF FINANCIAL POSITION

ASSETS	Total 2018	Total 2017
Cash and Cash Equivalents	\$13,299,317	\$14,121,998
Investments	10,187,383	10,219,557
Contributions Receivable (Net)	13,734,662	18,009,454
Prepaid Expenses and Other Assets	51,403	75,043
TOTAL ASSETS	\$ 37,272,765	\$ 42,426,052

LIABILITIES	Total 2018	Total 2017
Accounts Payable	\$65,314	\$137,004
Grants Payable (Net)	17,294,177	11,848,581
Deferred Revenue	280,000	57,240
Due to Affiliate	109,159	16,744
TOTAL LIABILITIES	17,748,650	12,059,569

NET ASSETS	Total 2018	Total 2017
Unrestricted	\$5,789,453	\$12,357,029
Temporarily Restricted	13,734,662	18,009,454
TOTAL NET ASSETS	19,524,115	30,366,483
TOTAL LIABILITIES AND NET ASSETS	\$37,272,765	\$ 42,426,052

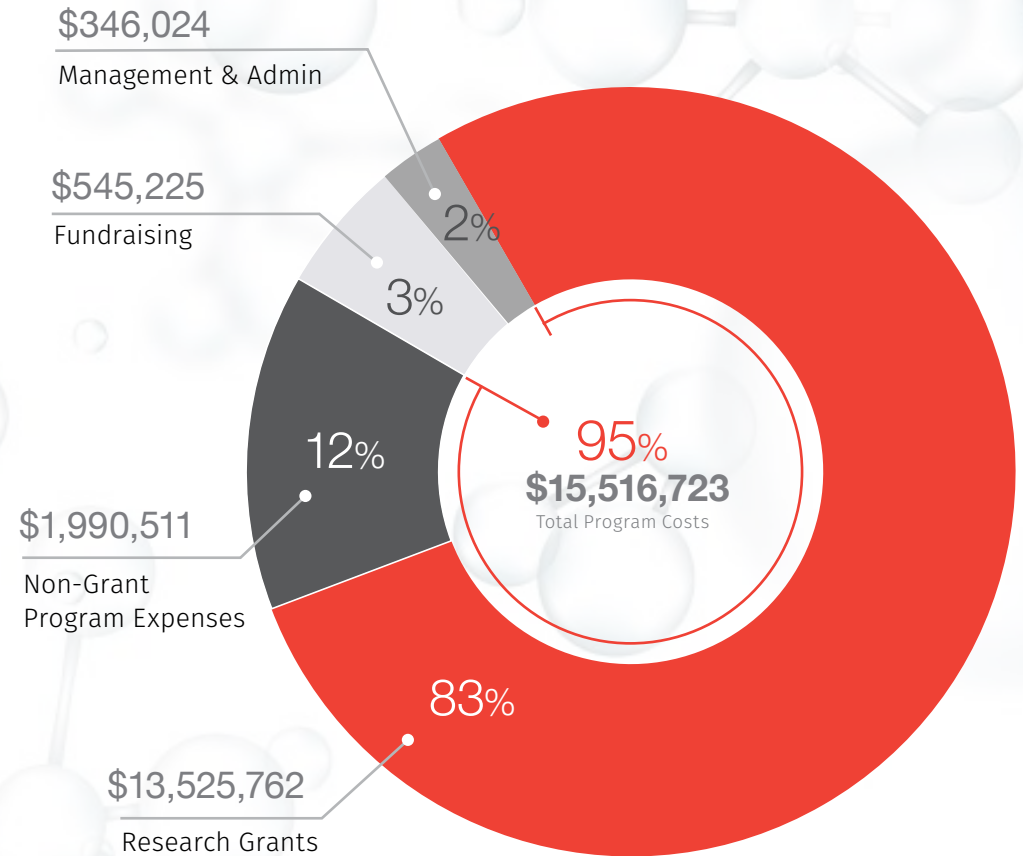
STATEMENT OF ACTIVITIES

REVENUE & EXPENSE STATEMENT

REVENUE	Total 2018	Total 2017
Contributions (Collectible Net)	\$2,895,365	\$2,841,125
Special Events (Net)	\$2,038,435	\$20,832,080
Sponsorship	\$514,710	\$455,000
Interest/Investment	\$114,094	\$291,322
Other Income	—	\$21,100
TOTAL REVENUES	\$5,562,604	\$24,582,963

EXPENSES:	Total 2018	Total 2017
Research Grants	\$13,525,762	\$9,079,591
Personnel Costs	\$1,588,653	\$1,412,640
Travel & Entertainment	\$350,487	\$309,836
Other Expenses	\$354,131	\$306,803
Meetings & Conferences	\$277,208	\$251,405
Professional Fees	\$163,814	\$210,636
Occupancy	\$144,917	\$138,887
TOTAL EXPENSES:	\$16,404,972	\$11,709,798
NET INCOME/(LOSS)	(\$10,842,368)	\$12,873,165

MRA FUNCTIONAL EXPENSES





Leon Black at the 2019 Leveraged Finance Fights Melanoma event

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