

The Melanoma Research Alliance: The Power of Patient Advocacy to Accelerate Research and Novel Therapies

Debra Black and Laura Brockway-Lunardi

Abstract

Patient advocacy organizations play a major role in accelerating research and are particularly important in a disease like melanoma, for which there is an urgent need for new tools and treatments. Melanoma is a growing public health burden. In the United States alone, the incidence of melanoma has tripled over the past 30 years, and one American dies every hour from the disease. To accelerate the field, the Melanoma Research Alliance (MRA) was founded in 2007 and is now the largest private funder of melanoma research, having invested more than \$48 million in innovative and translational research projects worldwide to date. This investment is bearing fruit in the recent transformation of the melanoma clinical landscape, which has brought new hope to patients and their families. Yet, even with new drugs on the market, much more needs to be done until melanoma is effectively addressed. MRA is part of a growing group of nonprofit disease research foundations collectively called "venture philanthropies" that are playing a powerful role in transforming the outlook for their disease by overcoming barriers that bog down progress, targeting key areas, and enhancing collaboration. MRA is leading an innovative agenda to accelerate efforts on behalf of patients. Our goal, while significant, is straightforward: to end suffering and death due to melanoma. *Cancer Immunol Res*; 1(6); 357–61. ©2013 AACR.

Founder's Story: Debra Black

"In 2003, I noticed a reddish spot on the bottom of my foot and quickly showed it to my dermatologist. I had an *in situ* melanoma removed several years before, so I was diligent about skin screenings. My doctor told me it was a wart and attempted to burn and freeze it off. However, it kept coming back and began to bleed. Eventually, I went to a podiatrist, who knew instantly that it wasn't a wart. After 4 years of dealing with this spot, a biopsy confirmed it was stage II melanoma. After surgery to remove the melanoma, two skin grafts, 6 weeks of keeping my foot elevated, and 4 months of using a walker and wheelchair, I was changed forever. I talked to numerous doctors and was shocked to learn how few treatment options were available for patients with late-stage melanoma and the dearth of funding for new research. My husband Leon Black and I vowed to do something to change that and, in 2007, founded the Melanoma Research Alliance (MRA). We have personally provided \$40 million in seed funding to launch MRA and are continuing to underwrite all operating costs of the organization, which allows 100% of every donation to MRA to fund melanoma research. Our goal is to fund the most prom-

ising science worldwide to find a cure and end the suffering and death caused by this disease."

Melanoma: A Growing Public Health Burden

The number of new cases of melanoma is increasing steadily and dramatically even at a time when incidence of other common cancers has declined (1). In the United States alone, the incidence of melanoma has tripled over the past three decades (2). This year, approximately 76,000 Americans will be diagnosed and more than 9,000 will die from the disease (2). The ability to spread widely to other parts of the body is a unique characteristic of melanoma that other types of skin cancers do not readily possess. This characteristic makes melanoma the deadliest of skin cancers, accounting for only 4% of diagnoses but 80% of skin cancer-related deaths. Although melanoma is highly curable with surgery if caught early, those with late-stage disease have a median life expectancy of less than 1 year.

In the last few years, the treatment landscape has changed dramatically. Since 2011, four new therapies have been approved by the U.S. Food and Drug Administration (FDA) for metastatic melanoma (ipilimumab, vemurafenib, dabrafenib, and tremetinib), which is a pace unparalleled in cancer drug development. Along with a new adjuvant therapy (pegylated IFN- α 2b) and tools for prevention and diagnosis, patients and those at risk have considerably better options. Yet, these approaches will not cure most patients and much more work needs to be done until melanoma is effectively addressed. Gaps still exist in the understanding of this disease, including finding ways to identify responders/nonresponders as early as possible and unraveling the problem of drug resistance. Although immunotherapies seem to exert fairly broad activity, melanoma

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Note: Debra Black is Co-founder and Chair of the Board for the Melanoma Research Alliance, and Laura Brockway-Lunardi is the Scientific Program Director.

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is becoming understood as a disease involving smaller subsets. The field is meeting these challenges with new research that reflects unprecedented opportunity for additional transformational progress, with hundreds of clinical trials under way (www.clinicaltrials.gov).

The Melanoma Research Alliance

The mission of the MRA is to accelerate the pace of scientific discovery and its translation to eliminate suffering and death due to melanoma. MRA is funding the most promising research worldwide to accelerate progress and improve outcomes for patients and all who are at risk. MRA was founded under the auspices of the Milken Institute and its affiliates, including the Prostate Cancer Foundation, the largest philanthropic source of funds for prostate cancer research, and FasterCures, which is an "action tank" that aims to remove barriers to medical progress. Applying the proven business framework of the Milken Institute, MRA has become the largest private funder of melanoma research, having awarded more than \$48 million to 116 innovative research projects to find better preventative, diagnostic, and therapeutic approaches to the disease. At the time of this writing, MRA will make available at least an additional \$8 million for new research awards to be funded in 2014.

MRA is part of a growing group of nonprofit disease-research foundations collectively called "venture philanthropies" that applies concepts from venture capital finance and business practices to philanthropic efforts (3). Venture philanthropies have a singular focus on their disease and put the patient at the center of everything they do. MRA, like other venture philanthropies, aims to overcome barriers that bog down progress, reorienting the research and grant-making processes with a sense of urgency and accountability, targeting key areas, and enhancing collaboration to speed translation to the clinic.

Focus on key scientific and clinical needs

The MRA's research portfolio focuses on translational research in the so-called "valley of death," which is the type of research aimed at turning scientific discoveries into new tools and treatment for patients and those at risk. Since its inception, MRA has emphasized its grant making in key scientific and clinical areas. In 2007, upon its launch, the MRA convened a "call to action" meeting that was held with key leaders in the field, which identified 17 areas of focus (4). In 2011, MRA updated its scientific agenda, which reflected new opportunities and needs and acknowledged the progress that was made in these areas as a result of funding by MRA and other stakeholders (ref. 5; Table 1). With this as a guide, MRA has invested or is investing research funding in every one of

Table 1. Current MRA strategic research plan

Prevention

- Further elucidate the genetic basis of risk and apply this information for identification and management of high-risk groups
- Develop new agents for melanoma prevention, including topical or oral compounds for high-risk groups

Diagnosis and staging

- Develop a more accurate, molecularly based staging system for melanoma
- Design new imaging agents for detection and staging of metastatic melanoma, including new PET agents
- Support a centralized, large-scale effort to extract and map molecular data from melanoma cell lines and tumor samples to clinical outcomes to identify new prognostic and therapeutic targets and to optimize current therapies
- Identify prognostic biomarkers for patients with stage I–IIIA melanoma to guide clinical management
- Develop serologic biomarkers to detect early-stage melanoma

Treatment

- Develop combinatorial treatment strategies for patients with stage III–IV melanoma, including combinations of immunologic and molecularly targeted agents
- Identify and characterize new biomarkers of treatment response and nonresponse to therapies
- Elucidate the prognostic and therapeutic value of tumor microenvironmental factors, including using a "systems biology" approach
- Promote research on immunotherapies, including vaccines and immune-modulating antibodies, for single-agent use and in combination
- Create new adjuvant therapies
- Explore mechanisms of resistance to immunotherapies or molecularly targeted therapies and methods to overcome resistance
- Identify new molecular targets and therapeutics for melanomas not expressing BRAF mutations or BRAF-mutant melanomas not responsive to BRAF inhibitors
- Explore epigenetic targets including methylation and microRNAs for the development of new therapies
- Identify and target factors driving the process of melanoma invasion and metastasis

Abbreviation: PET, positron emission tomography.

these areas. MRA research awards in prevention have worked toward a better understanding of the biologic mechanisms of melanoma carcinogenesis, including identification of risk genes, as well as to support the development of prevention agents. In diagnosis and staging, MRA has supported programs to improve skin screening, identify new prognostic biomarkers, and improve imaging of metastases. Of awards in treatment, MRA supports research to advance immunotherapies, molecular-targeted drugs, and combination therapies and research into new biomarkers of response to therapy. Now, with even more recent progress dramatically altering the field, MRA is currently updating its scientific strategy to ensure dollars are deployed toward those areas in which MRA can make a significant and important contribution in such a rapidly changing environment.

A hallmark of the MRA research portfolio is its focus on developing new treatment approaches for metastatic melanoma, with 85% of funding to date invested in this area of urgent need. Given the importance that immunology and immunotherapy research is playing in melanoma, a large proportion of MRA funding is supporting these studies (Fig. 1). As the basic understanding of how the immune system responds to tumors continues to expand, so do the opportunities for advancing these approaches to combat melanoma and other cancers. To date, MRA has invested more than \$10 million in projects to improve the current arsenal of immune checkpoint blockade agents, ipilimumab and anti-PD-1 approaches, through studies on biomarkers of clinical response and nonresponse and strategies to combine these agents with other therapies, including kinase inhibitors/small molecules, radiation, and other immunotherapies. Other funded areas in immunology and immunotherapy include adoptive cell transfer therapy, melanoma vaccines, and other immune system-modulating agents.

The development of specific inhibitors of mutation-activated BRAF has been a major breakthrough in the treatment of a

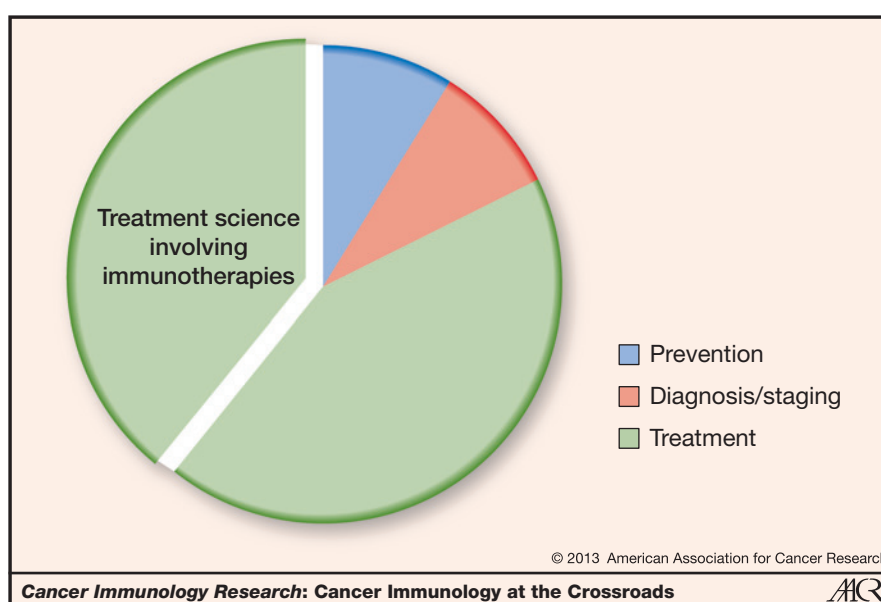
subset of patients with advanced melanoma. In recent years, researchers have made tremendous strides in the identification of additional melanoma molecular targets. This research is critical not only for patients whose melanomas do not express V600E BRAF mutations but also to set the stage for future combination therapy with BRAF inhibitors. In fact, the development of combination therapies to counter drug resistance and improve clinical responses to single-agent therapies is an area of critical importance and one that MRA has prioritized. These efforts include studies to inform rational combinations of molecularly targeted agents and immunotherapies.

Beyond treatment science, the remainder of the MRA portfolio supports research to form the basis for better preventative and diagnostic approaches. Very early diagnosis has the potential to save the most lives from melanoma, but it would be better to prevent the disease from forming at all. To this end, MRA is supporting studies to better understand the biologic basis of melanoma formation, including the interaction of genetic risk factors and the environment, and the development of biologically based preventative strategies. Additional projects include skin screening approaches and research to improve melanoma diagnostic and prognostic tools.

Investing in human capital and team science

MRA is committed not only to funding melanoma research projects but also to investing in human capital to build the field of researchers devoted to melanoma. To date, MRA has supported 169 principal investigators at 80 institutions in 14 countries. These include both early-career and established investigators. MRA is particularly proud of its Young Investigator Award program, which funds the next generation of melanoma research leaders. Young investigators (defined by MRA as those within the first 4 years of their first faculty appointment) are at a critical time in their career as they build their laboratory and seek funding, which is particularly difficult

Figure 1. Distribution of MRA research funding by scientific area.



in today's declining NIH funding environment. To date, MRA has funded 40 of these early-career investigators and plans to continue emphasizing this important program into 2014 and beyond.

With a focus on enhanced collaboration, MRA also supports the Team Science Awards, which are given to multidisciplinary research groups; these awards account for two thirds of MRA's funding to date. Recognizing the value of enhancing relationships between the academic and industrial research sectors, MRA also offers Academic-Industry Partnership Awards, which support projects focused on clinical translation in conjunction with matched contributions from an industry partner whose participation is essential to the project. Building the field of scientists dedicated to melanoma research and facilitating collaboration among them as well as across fields and sectors is essential to driving progress.

Measuring progress and ensuring accountability

In just a few years of active research, the productivity of MRA-funded investigators has been high, as measured by tangible outcomes and promising early research results. One of MRA's goals is to invest in novel ideas that will form the basis for investigators to secure additional funding from other sources. This approach has been very successful, with more than \$46 million in additional research funding leveraged from other sources by MRA investigators, including NIH, industry, and other foundations. In 2013 alone, industry funding of \$2 million matched \$1.7 million of MRA funds in the Academic-Industry Partnership Awards program. Taking these programs together, the impact of the MRA investment is approaching a total of \$100 million in melanoma research funding to date. In addition, the high level of patents and new invention disclosures, clinical trials, and research papers resulting from funded research are tangible indicators of the MRA's impact. Rigorous peer review and oversight of funded research ensure MRA's dollars are deployed with maximum impact.

Encouraging collaboration

Collaboration is at MRA's core—from the team approaches to research to the engagement of partners to help realize MRA's vision. MRA has cofunded melanoma research with other premier foundations, including Stand Up To Cancer, Cancer Research Institute, and others. MRA's annual scientific retreat brings together several hundred leaders in melanoma and oncology including those from academia, industry, government, and nonprofit to share early research findings (including both negative findings and positive data) and explore issues of mutual interest with the goal of accelerating collaboration between and among sectors.

In addition to working with stakeholders that share our mission, MRA has been engaged in a series of public awareness initiatives educating the public about the risks of melanoma and ways to protect their skin as well as helping to raise funds to

support melanoma research. MRA's corporate allies help reach approximately 20 million people in the United States and abroad each May during Melanoma and Skin Cancer Awareness Month. Over the past 3 years, MRA has raised more than \$500,000 per year through these programs, and participation has grown from 10 allies in 2011 to more than 25 companies in 2013.

Patient advocacy in the policymaking process

Although research funded by the MRA continues to advance the understanding of melanoma, involvement in the policymaking process is critical in the fight against cancer. Working with senior policymakers at the NIH, FDA, Department of Health and Human Services, and Congress, MRA contributes a trusted and credible scientific voice to issues of relevance to the melanoma and broader cancer community. As an investor in the research, MRA is involved in addressing key regulatory roadblocks that challenge the development of new cancer therapies and devices. For example, MRA has contributed to discussions about the development of combination therapies (6) and diagnostic tools and issues in clinical trial design. In the area of public health, MRA has been a leader in calling for restrictions on and greater regulation of tanning beds and supporting government agencies' efforts to raise the profile of melanoma prevention among the general public.

Building upon our success

Every hour, melanoma takes another life in the United States. But the exciting clinical and research advances have provided new hope for patients and those at risk. Immunotherapeutic approaches have historically been an important area for melanoma, and the new antibodies against PD-1 and PD-L1 are particularly exciting for melanoma as well as for other cancers. Melanoma has truly become a case study for other cancers, serving as a proving ground for the development of molecularly targeted drugs, companion diagnostics, and combination therapies. MRA is proud to support the scientific community and lead an innovative and collaborative agenda to accelerate efforts on behalf of patients. Our goal, while significant, is straightforward: to end suffering and death due to melanoma.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: L. Brockway-Lunardi

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