Demonstrating the Impact of MRA-funded Research: A Case Study

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HRA Spring Members Meeting
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Mission

This mission of the Melanoma Research Alliance 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.
MRA Grant Portfolio Overview

- 312 Awards Granted
- $111 Million Invested
- 144 Institutions
- 18 Countries
MRA Grant Solicitation and Selection Process

• **Release Annual Request for Proposals (RFP)** – includes Special Emphasis Areas, Special Opportunities

• **Grants Reviewed by standing Grant Review Committee:**
  – Online triage step
  – In-person Grant Review Committee meeting

• **Slate of grants approved by MRA Board of Directors**
**MRA Grant Award Mechanisms**

**Team Research:** requires multidisciplinary teams and involvement of a Young Investigator. $900k and up over 3-years

**Established Investigator:** past their first four years of appointment with an established record of scientific productivity. $375k over 3-years

**Young Investigator:** within four years of first faculty appointment, requires a mentorship commitment from a senior investigator. $225k over 3-years

**Pilot:** test potentially transformative ideas that may not have extensive data, but articulate a clear hypothesis – “high-risk, high-reward.” $100k over 2-years

**Dermatology Fellow:** engaging clinical dermatologists in melanoma research, requires mentorship and fellowship in Dermatology Department. $35k for 1-year; year 2 possible
How do we assess MRA’s multi-million dollar investment in melanoma research?
Patient outcomes have changed dramatically since MRA’s founding.


Schadendorf et al. JCO 2015;33:1889-1894
5-year survival >50%, 12 new treatments approved
• **IMPACT 2015**: Evaluated progress towards Scientific Aims for the first 63 completed awards from MRA’s portfolio in 2015-2016.

• **IMPACT 2018**: Took a 3-pronged approach:
  
  1. Evaluated progress towards Scientific Aims for the projects completed after IMPACT 2015 and before 2017 (44 total)
  2. A post award survey was sent to the 93 admin PIs with awards evaluated as part of IMPACT 2015 and IMPACT 2018 (response rate = 74%)
     • Quantitative success measures such as follow-on funding, patents and publications
     • Feedback from funded investigators
  3. Assessment of qualitative and quantitative outcomes for 107 awards evaluated as part of IMPACT 2015 and IMPACT 2018
     • Used combination of data from Progress Reports, Dimensions, PubMed, www.uspto.gov, Post Award Survey

**Together, IMPACT 2018 allowed us to:**

• Highlight key results from MRA’s research funding on melanoma and cancer; and,

• Develop lessons learned and opportunities for improvement.
Results from IMPACT 2018 were presented to the MRA Board in November, 2018.

The full report included:

1. Executive Summary
2. PowerPoint presentation of key summary data
3. Key Award Examples
4. Detailed 17 page report
5. Individual 1-2 pg project summaries for each award assessed

The results were also presented publicly at the international conference *AACR Melanoma: Biology to Target* and 2019 MRA Scientific Retreat.
### IMPACT 2018: Outcomes Summary

<table>
<thead>
<tr>
<th>Award Mechanisms</th>
<th>Number of Awards</th>
<th>Amount Funded</th>
<th>Amount of Follow-on Funding</th>
<th>ROI (Additional Funding/Award Funding)</th>
<th>Number of Patent Applications</th>
<th>Number of Patents Awarded</th>
<th>Number of Publications</th>
<th>Number of Presentations</th>
<th>Number of Collaborations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pilot</td>
<td>13</td>
<td>$1.1M</td>
<td>$5.2M</td>
<td>4.7</td>
<td>4</td>
<td>2</td>
<td>26</td>
<td>23</td>
<td>26</td>
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<tr>
<td>Established Investigator</td>
<td>31</td>
<td>$7.5M</td>
<td>$51.4M</td>
<td>6.8</td>
<td>10</td>
<td>4</td>
<td>136</td>
<td>332</td>
<td>77</td>
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<tr>
<td>Team Science</td>
<td>32</td>
<td>$27.4M</td>
<td>$70.8M</td>
<td>2.6</td>
<td>26</td>
<td>16</td>
<td>212</td>
<td>306</td>
<td>123</td>
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<tr>
<td>Young Investigator</td>
<td>28</td>
<td>$4.8M</td>
<td>$26M</td>
<td>5.4</td>
<td>10</td>
<td>6</td>
<td>127</td>
<td>152</td>
<td>77</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>107</strong></td>
<td><strong>$42.7M</strong></td>
<td><strong>$153.6M</strong></td>
<td><strong>3.6</strong></td>
<td><strong>50</strong></td>
<td><strong>28</strong></td>
<td><strong>543</strong></td>
<td><strong>827</strong></td>
<td><strong>307</strong></td>
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<tr>
<td>Award Mechanism</td>
<td>Title</td>
<td>Year</td>
<td>Journal</td>
<td>Citations</td>
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<tr>
<td>Young Investigator</td>
<td>Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients</td>
<td>2017</td>
<td>Nature Medicine</td>
<td>139</td>
<td></td>
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<tr>
<td>Pilot</td>
<td>Phosphoenolpyruvate Is a Metabolic Checkpoint of Anti-tumor T cell Responses</td>
<td>2015</td>
<td>Cell</td>
<td>250</td>
<td></td>
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<td>Team Science</td>
<td>Commensal Bifidobacterium promotes antitumor immunity and facilitates anti–PD-L1 efficacy</td>
<td>2015</td>
<td>Science</td>
<td>487</td>
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<td>Team Science</td>
<td>Melanoma-intrinsic β-catenin signalling prevents anti-tumour immunity</td>
<td>2015</td>
<td>Nature</td>
<td>458</td>
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<tr>
<td>Established Investigator</td>
<td>The Genetic Landscape of Clinical Resistance to RAF Inhibition in Metastatic Melanoma</td>
<td>2014</td>
<td>Cancer Discovery</td>
<td>376</td>
<td></td>
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<tr>
<td>Established Investigator</td>
<td>Highly Recurrent TERT Promoter Mutations in Human Melanoma</td>
<td>2013</td>
<td>Science</td>
<td>782</td>
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<tr>
<td>Young Investigator</td>
<td>Immunologic correlates of the abscopal effect in a patient with melanoma</td>
<td>2012</td>
<td>New England Journal of Medicine</td>
<td>881</td>
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<tr>
<td>Established Investigator</td>
<td>Modelling vemurafenib resistance in melanoma reveals a strategy to forestalldrug resistance</td>
<td>2013</td>
<td>Nature</td>
<td>363</td>
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<tr>
<td>Young Investigator</td>
<td>Radiation and dual checkpoint blockade activate non-redundant immune mechanisms in cancer</td>
<td>2015</td>
<td>Nature</td>
<td>592</td>
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<tr>
<td>Young Investigator</td>
<td>Evaluating cell lines as tumour models by comparison of genomic profiles</td>
<td>2013</td>
<td>Nature Communications</td>
<td>418</td>
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<tr>
<td>Team Science</td>
<td>Tumour exosome integrins determine organotropic metastasis</td>
<td>2015</td>
<td>Nature</td>
<td>775</td>
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## IMPACT 2018: Respondents Ranked List of Impact of MRA Awards on Career and Research Trajectory

### Areas of highest impact

- Expanding an existing collaboration
- Establishing a new collaboration
- Receiving additional funding
- Using a new method or technique
- Expanding the lab

### Areas of least impact

- Applying for or receiving a patent
- Transitioning from clinical to basic research
- Starting a biotech company
## IMPACT 2018: Key Examples/Award Summaries

### Other Summary Components

- Aims Summary
- Progress of Scientific Aims
- List of Quantitative Metrics
- Feedback from Survey

<table>
<thead>
<tr>
<th>TITLE</th>
<th>Publications 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEAM MEMBERS AND INSTITUTION</td>
<td>Presentations 27</td>
</tr>
<tr>
<td></td>
<td>Patent applications 2</td>
</tr>
<tr>
<td>Team Science Award (TSA)</td>
<td>Clinical trials 2</td>
</tr>
<tr>
<td>7/1/2013 – 6/30/2016</td>
<td>Collaborations 6</td>
</tr>
<tr>
<td>Budget Proposed: $1,000,000</td>
<td>Follow-on grants 6</td>
</tr>
<tr>
<td><strong>Budget Actual: $900,000</strong></td>
<td>Follow-on funding</td>
</tr>
<tr>
<td>Budget Notes: Budget reduction</td>
<td>$4,260,000</td>
</tr>
<tr>
<td>Status: 2 years post completion</td>
<td></td>
</tr>
</tbody>
</table>

### Progress Summary

Immunotherapy, especially strategies to enable the immune system to overcome immune checkpoint inhibition, provide remarkable benefit, but only in a subset of melanoma patients. Clinical responsiveness to immune checkpoint inhibitors may depend on if the patient has tumors with spontaneously occurring inflammatory features and a pre-existing immune response at the tumor sites. This project used patient samples, existing data in TCGA (The Cancer Genome Atlas), and animal models to characterize 3 mechanisms that enable this “smoldering” immune response. They identified 3 mechanisms. (i) Increased
The evolution of research topics funded by MRA reflects the progress of melanoma research as a whole over the past 11 years.

MRA funded research impacts clinical practice.

MRA funded research informs current thinking in the field.

MRA funding positively impacts the careers of funded researchers and leveraged significant dollars.

The majority of MRA’s funded awards are successful, but modifications to the original aims occur, as well as technical hurdles.

Many of the conclusions drawn from IMPACT 2015 are supported by the IMPACT 2018 evaluation.
• Continue to fund a diverse range of award mechanisms
• Maintain a rigorous GRC-driven peer review process to ensure MRA awards continue to advance melanoma research and clinical practice
• Evaluate if MRA should modify its approach to funding clinical trials
• Consider expanding the number of Pilot and Young Investigator Awards MRA makes each year
• Consider broadening portfolio to fund a greater number of awards focused on prevention and diagnostics
• Evaluate the impact of the collaborative funding program, co-funding awards with other non-profits, as well as geographically-focused and topic-focused programs
• Evaluate how MRA partners with industry to fund research
• Significant amount of work – consultant/additional staff/dedicated staff needed
• Need staff that can go deep on the science but have a broad understanding of the field
• Important to understand needs and interests of audience
• Mix of quantitative and qualitative outcomes are often important
• Mix of platforms are necessary for the analysis if assessing program at the level of individual grants
• Organization-specific considerations: MRA is a relatively young organization, relatively small number of awards
• Field specific considerations: Melanoma research field is unique, particularly during the time period assessed in this analysis
Acknowledgements

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