New Funding Opportunity: MRA's Next Steps Program

Since 2007, MRA has awarded $150M to support more than 450 research projects led by scientists and clinicians across the globe in 19 countries. MRA will continue to release its annual Request for Proposals (RFPs) each year in August to support research across the different existing grant mechanisms including Team Science, Young Investigator, Pilot, Established Investigator and Dermatology awards.

MRA is excited to announce a new funding opportunity called **Next Steps**, a separate and distinct grant mechanism from the MRA's annual RFP call for applications. The intent of this research funding strategy is to help advance translation of discoveries into the clinic by supporting: 1) needed preclinical resources and tools for the research community to identify and begin to develop new therapies and 2) infrastructure to analyze and build large datasets to identify better diagnostic and prognostic biomarkers leading to hypothesis-driven research proposals for submission to MRA and other funding agencies.

Separate Requests for Application (RFAs) in the following three high priority research areas will be released throughout 2024 with key dates for each RFA listed in the table below:

- **Advancing Drug Discovery to Identify New Therapies:** Drug discovery efforts against validated targets to support new therapeutic entity identification, optimization and testing in preclinical models, with an emphasis on targets including adapter proteins, transcription factors, cell surface proteins, etc (ie: CRKL, TERT, GAB2, YAP, LZTR, B7H3);
- **Diagnostic and Prognostic Biomarker Identification:** Analysis and/or validation of large multi-institutional datasets to advance improvements in early detection and diagnosis across different skin types and identify prognostic biomarkers at different stages of the disease;
- **Characterization of Rare Melanoma Preclinical Models:** Characterization of rare melanoma cell lines and PDX models with different molecular assays and drug sensitivity tests with the goal of making the models and corresponding data available to the research community to enable more preclinical research in rare melanomas.

Key Dates	Advancing Drug Discovery to Identify New Therapies	Diagnostic and Prognostic Biomarker Identification	Characterization of Rare Melanoma Preclinical Models
RFA Released:	2/6/2024	4/1/2024	6/17/2024
Proposals due:	3/28/2024	6/6/2024	8/19/2024
Review:	4/8 – 5/14/2024	6/17 – 7/23/2024	9/3 – 10/8/2024
Decision dates:	6/1/2024	8/15/2024	10/15/2024

Awards through the Next Steps Program will be granted as milestone-based payments. Therefore, submitted applications will require the research proposal and budget, and a clearly defined milestone plan and timeline. Funding levels range from $50,000- $250,000 (specified in each Next Step priority area announcement) with study duration of 1-2 years. **Only researchers from academic medical centers and universities are eligible to apply including institutions in the U.S. and worldwide.**

Announcements of this program will be made via email and on the MRA website. If you have any questions please contact Joan Levy, MRA Chief Science Officer at jlevy@curemelanoma.org.

Next Steps Program RFA:
Priority Area Announcement:
Advancing Drug Discovery to Identify New Therapies

Background:

Treatment of advanced melanoma has dramatically improved over the past decade with 16 new therapies approved by the Food and Drug Administration (FDA). Even with these treatment advances, 50% of patients with advanced melanoma will either not respond to any of these treatments or their disease will progress. Furthermore, the approved therapies do not appear to be as effective in patients with acral, mucosal and uveal melanomas, 3 rare sub-types of the disease. Based on these reasons there is a critical need to find new therapeutics. Through extensive genomic analyses of the different types of melanoma, new targets have been identified and validated that have the potential to lead to novel therapeutic entities. Much of this discovery research was funded, in part, through prior MRA grant awards. Furthermore, in the last decade drug discovery has significantly advanced using new technologies and approaches showing promising results for targets that have previously been considered "undruggable", several of which have been identified in melanoma. **The goal of this RFA is to provide initial support to identify new therapeutic modalities including small molecules, antibodies and cell therapies against validated melanoma targets, with an emphasis on targets that are applicable to rare melanoma subtypes.** Support from this RFA will be geared towards early stages of the drug discovery continuum that could result in an optimized lead compound or biologic showing activity in appropriate melanoma preclinical models. It is anticipated that achieving the aims of the proposal may require the expertise from different departments in a given institution or collaborations across multiple institutions and core facilities.

Deadlines:

Applications will be submitted through Proposal Central using this link and are due on **3/28/2024 by 11:59 PM EST.**

Award Duration:

1-2 years

Funding Level and Additional Support:

Up to $250,000 depending on the scope of the research project with potential for follow-on funding.

In addition to funding, MRA will provide additional support by connecting a program with outside resources that have drug discovery and drug screening expertise. For projects involving rare melanomas, MRA has created an Acral and Mucosal catalog of cell lines and patient-derived xenograft models from various institutions worldwide. The catalogs serve as a launching pad for research programs who need a variety of acral and mucosal melanoma preclinical models – providing awareness of models that have been created by other research laboratories. **Please note that model exchanges between research laboratories are not guaranteed and, in most cases, would require an MTA between institutions and potentially an approved model use research request.**

Payment Schedule:

Payments will be released after achieving specific milestone accomplishments clearly outlined in a milestone/timeline plan to be included at the end of the project proposal as part of the application. Payments will be approved after MRA's review of progress and determination that milestones and timelines have been met, at MRA's sole discretion.

Eligibility:

Researchers and clinicians within or outside the U.S. working in academic medical centers and universities or other non-profit research institutions are eligible to apply. Applications will **not** be accepted from for-profit companies.

General eligibility requirements:

- **MRA encourages applications from a diverse pool of investigators with respect to race, gender, sexual orientation, ethnicity, national origin, and disability.** MRA recognizes that diversity in the biomedical research workforce is critical for ensuring that the most creative minds have the opportunity to contribute to realizing our research goals and to ensuring more equitable health outcomes for all.
- **Principal Investigators (PIs) must hold a full-time faculty appointment at the level of Assistant Professor (or equivalent) or above.**
- Fellows/post-docs or those in other training or research support positions are not eligible to apply as a PI.
- Individuals employed by state or federal government agencies may reach out to Joan Levy, MRA Chief Science Officer (jlevy@curemelanoma.org) to determine their eligibility.
- **An investigator may serve as PI on only one proposal submitted to the Next Steps RFA call in any given calendar year.**
- Multiple applications will be accepted from a single institution, provided that each application has a different PI and represents a distinct project.
- Researchers who have not received prior MRA awards but who have projects that fit within the scope of this RFA are eligible to apply.

If there are any questions about eligibility, please contact Joan Levy Ph.D., Chief Science Officer, at jlevy@curemelanoma.org before applying. Applications from PIs who do not meet the eligibility criteria will not be reviewed.

Funding Priorities and Pertinent Accompanying Information:

The application should provide evidence either from published or unpublished data that the proposed target has been validated and expected to play some role in melanoma initiation or progression thereby qualifying it as a legitimate target for initial drug discovery efforts. The validated target may also play a role in other cancer types and this should be clearly stated in the research proposal.

Target suggestions to explore but are not limited to include:

- Adapter proteins and transcription factors
- Epigenetic regulators
- Cell surface proteins that can be targeted with antibodies or cell-based therapies

The RFA supports:

- High throughput screening (HTS) or high content screening (HCS) of the target including design and optimization of relevant HTS or HCS assays
- Medicinal chemistry efforts to optimize activity in cell-based assays and *in vitro* ADME and *in vivo* PK properties
- Testing of optimized lead compounds in relevant melanoma animal models for efficacy and PD assessments
- Optimization of biologics (antibodies and cell-based therapies) that can be tested in relevant melanoma cell-based and animal models

Funding from this award might support only portions of the early drug discovery screening continuum in the areas described above. Specific goals supported by this funding will depend on the starting point of the project (ie: starting with a target that needs to be screened vs. an initial compound or biologic that has to be further optimized vs. an optimized compound that needs further characterization in animal models).

The RFA DOES NOT Support:

- Identification and validation of new targets
- Testing of repurposed drugs, FDA approved or drugs being clinically tested in other cancer and disease indications
- Development and characterization of new cell lines, organoid and xenograft models for preclinical drug testing (a separate priority funding announcement from the Next Steps Program will be released to support these activities)

Evaluation Criteria:

All proposals will be evaluated on:

- Rational biological connection and validation of the target to melanoma
- Strength of the scientific approach and research design of proposed experiments
- Qualifications of the research team and adequacy of resources and environment
- Appropriateness of budget tied to a reasonable milestone/timeline plan

Application Format:

All applications are due by 11:59 PM. Eastern Time on March 28, 2024. Proposals will not be considered after the deadline. Applicants must utilize the Proposal Central online application tool at https://Proposal Central.com/ and the document templates and requirements therein. Please carefully follow the instructions in Proposal Central and below. Applications include the following steps and components:

1. **Title Page:** Enter the project title. Please note: the grant title (along with the PI's name and institution) will become public if the award is selected for funding, therefore, it should not contain any proprietary information.

2. **Templates and Instructions:** Download RFP and templates.

3. **Enable Other Users to Access this Proposal:** Allow others (e.g., institutional administrators or collaborators) to view, edit, or submit your proposal. Electronic signatures are required to submit the application for submission. ***The Signing Official from the applicant's institution must be provided at least 'Edit' access on this screen to be able to sign.*** Please review the Signature Page to confirm the signature roles required and add as appropriate on this page.
   ***PLEASE MAKE SURE TO GRANT ACCESS AHEAD OF TIME TO YOUR INSTITUTION'S SIGNING OFFICIAL TO AVOID ANY LAST-MINUTE ISSUES WITH SIGNING AND SUBMITTING YOUR APPLICATION. ***

4. **Applicant/PI:** Key information about the applicant PI.

5. **Organization/Institution:** Key information about the PI's institution, including name and email address of the signing official who, in addition to the PI, will be contacted if the award is selected for funding. If your institution has a ROR (Research Organization Registry ID), please include.

6. **Key Personnel:** List and provide contact information for key persons. Include everyone **except the applicant** who will contribute to the scientific development or execution of the project in a substantive, measurable way whether they receive salaries or compensation under the grant. ORCID ID is required only for the PI.

   Descriptions of Key Personnel roles:

   Principal Investigator (PI): This is the applicant for this award who will also serve as project leader and primary point of contact for MRA Staff if multiple investigators and collaborators are involved. The PI will ensure that the team complies with the terms of the award, including all reporting, contractual, and financial obligations. Co-PIs are **not** allowed.

   Co-Investigator: Co-I's are vital scientific contributors (at the same or a different institution from the PI), often bringing a needed expertise to the research team. They commit some level of measurable effort to the project and are, therefore, always designated as Key Personnel whether being compensated or otherwise.

   Collaborator: Play a lesser role in the thinking and logistics of the project than a Principal Investigator or Co-Investigator. Depending on the role and effort, a collaborator may be designated as Key Personnel (although not required) and may be compensated.

   Consultant: Provides guidance on specific aspects of the research project, as their expertise applies. A consultant may be designated as Key Personnel (although not required) and may be compensated.

   Others: Key Personnel may also include (but are not required) people at the master's or baccalaureate level (such as Project Managers, Technicians, Postdoctoral Associates, Fellows, Research Assistants or Graduate Students), if they will contribute to the scientific development or execution of the project in a substantive, measurable way whether they receive salaries or compensation under the grant.

REQUIRED SUPPORTING DOCUMENTS FOR KEY PERSONNEL					
Personnel	**Include in KP Section**	**Biosketch**	**Current/Pending Support**	**Letter of Support**	**ORCID ID required**
Principal Investigator	Yes (All)	Yes	Yes	N/A	Yes
Co-Investigator	If applicable	Yes	No	Optional	No
Collaborator	If applicable	Yes, if included as KP	No	Optional	No
Project Manager	Optional	Yes, if included as KP	No	No	No
Technician	Optional	Yes, if included as KP	No	No	No
Consultant	If applicable	Yes, if included as KP	No	No	No
Postdoctoral/Fellow	Optional	Yes, if included as KP	No	No	No
Graduate Student	Optional	Yes, if included as KP	No	No	No
Other (such as research asst, etc)	Optional	Yes, if included as KP	No	No	No

7. **Data and Renewable Reagent Sharing Plan:** In order to promote rapid research advancement, transparency, reproducibility, and collaboration, MRA encourages the open sharing of data and resources generated from its funded awards. Provide information for the types of data and renewable reagents that will be generated as part of the award and how they will be shared.

   MRA will incur costs associated with policy compliance, provided these fees (e.g., article processing charges, data storage), are included in the original grant application budget.

8. **Abstracts and Keywords:** Provide a general audience abstract (non-technical) and a technical abstract (2,000 characters, *including spaces,* maximum each) and keywords. Please note: the general audience abstract will become public if the award is selected for funding, therefore, it should not contain any proprietary information.

9. **Budget Period Detail:** Enter budget details for each award period requested. Awards will not support indirect costs, overhead costs, or other similar institutional charges. Fringe benefits for personnel salaries are allowable. Please also include any costs associated with compliance with MRA's data sharing policy. Furthermore, the budget should align with the milestone/timeline plan proposed in the project description section of the application. Therefore, if applying for a 2-year award, the budget does **not** have to be split evenly over the two years.

10. **Budget Summary and Justification:** A summary of the budget details will be shown in this step. In addition, provide sufficient detail for the evaluation of the major portions of the budget that are being requested. If more space is required than is provided in the Proposal Central forms (2,000 characters), applicants may upload the budget justification in document form in step 13.

11. **Current and Pending Research Support:** Please list all current and pending support for the Applicant.

    Any overlap of current or pending support with the MRA Next Step proposal must be described and explained. Current and pending support can be added to your (and other Key Personnel's) Professional Profile on Proposal Central by clicking on the 'Professional Profile' tab and going to Step #6: Other Support.

    To add your entries, please click on the "+" link and all entries previously saved in your Professional Profile will show. Please select the applicable support and save.

12. **Organizational Assurances:** IRB and IACUC approvals, if applicable.

13. **Upload Attachments: Upload the following:**
    a. **Biosketch for PI and Key Personnel:** Please upload an NIH format biosketch for yourself and all Key Personnel listed in step #6. Biosketches for research support staff, students, postdocs, and other training positions are not required. Applicants who do not have an NIH biosketch may use the template provided in Proposal Central. Besides publications, MRA welcomes the inclusion of research outputs such as datasets, code, patents, and papers posted to preprint servers.

    b. **Current and pending research support:** Whenever possible, please enter PI current and pending support directly into Proposal Central in the "Current and Pending Support" section (step #11). Any overlap of current or pending support with the Next Step proposal must be described and explained.

    c. **Project description:** Must be formatted in Arial 11-point or Times New Roman 12-point font with no less than ½ inch margins. The project description should be **5 pages maximum**, inclusive of the following: Background for selecting target and evidence of target validation, specific aims of the proposal which should clearly indicate the portion of the drug discovery cascade being addressed in the proposal (ie: identification of starting entity(ies) or 'hits", hit to lead identification, lead optimization in preclinical models), pertinent preliminary data, experimental design including resources available, detailed milestone plan incorporating a timeline, and rationale/fit with potential for clinical impact. Any figures to be included can be embedded within this section.

    d. **Literature references:** A list of up to 30 references supporting the project description is allowed, in addition to the 5-page project description.

    e. **Application checklist:** Please complete the checklist to ensure that all application materials are provided, and that the applicant is eligible to apply.

14. **PI Data Sheet:** Please enter your ORCID ID and other requested demographic information. If you do not have an ORCID ID, you can register for one here: **https://orcid.org/register**. Please note that requested demographic information will NOT be used by MRA in any way during the selection process. Having such information will help MRA better understand its applicant and awardee pool and detect and address any inequities identified.

15. **Validate:** Check for any missing required information.

16. **Signature Page(s):** *Before submitting the application*, an electronic signature is required from both the Applicant/PI and a Signing Official from the applicant's institution. Type your name in the text box and click the green 'Sign' button. A date and time stamp will appear next to the button indicating that the electronic signature was successful. To give the Signing Official access to sign this application, enter their information in Step #3: "Enable other users to access this proposal" and grant them at least "Edit" access.

17. **Submit:** Please note that no proposals will be able to be submitted past their deadline. Technical support for the on-line application system is not available after 11:59 p.m. Eastern Time or on weekends.