REQUEST FOR APPLICATIONS

MMRF Immunotherapy Networks of Excellence

June 29, 2017

1. FUNDING OPPORTUNITY DESCRIPTION

Purpose/Overall Goal:

The Multiple Myeloma Research Foundation (MMRF) is issuing this grant announcement to solicit applications for the formation of the **MMRF Immunotherapy Networks of Excellence**. Consistent with the MMRF's Precision Medicine Model and inspired by the rising number of approved immune-based therapies and additional immune approaches in clinical development for myeloma, there is a clear need to effectively tailor these treatments to the individual patient and his/her disease. Extensive analyses therefore must be performed at both the tumor and host immune levels in order to improve the efficacy of these immune agents and identify patients more likely to respond to specific immune approaches,

This grant is designed to bring together researchers from different institutions and laboratories to form **collaborative MMRF Immunotherapy Networks of Excellence** that will use state of the art tumor genomic and immune profiling technologies with high level computational capabilities to: 1) build a large database of information from tumor and immune analyses from a variety of different types of immune approaches; 2) generate and test hypotheses pertaining to response biomarkers and novel immune oncology (IO) targets and combination approaches; 3) rapidly translate the findings to execution of appropriately designed clinic trials. The investigators forming the Networks should therefore have a balance of basic, translational and clinical research expertise in various areas of immune therapy as it specifically pertains to the treatment of myeloma. In addition the Networks should have leaders representing a broad range of immune therapies including different types of antibodies, cell-based therapies and vaccine approaches. The MMRF will support **2** Immunotherapy Networks of Excellence that each will be composed of different institutions and laboratories and distinct from one another.

The long-term goals of each Network are to:

- Standardize immune monitoring assays for correlative analyses to be used across different immune-based therapies for myeloma
- Aid in the understanding of resistance mechanisms to existing IO treatments and treatments in development
- Predict the likelihood of response to particular therapies as well as the likelihood of toxicity
- Develop rational combination IO therapies for testing in clinical trials

In addition 1-2 representatives from each institution in the Networks will be part of an Immune Steering Committee. The Steering Committee will include members from the MMRF Immunotherapy Networks of Excellence but also include members from other oncology indications. The purpose of the Immune Steering Committee is to:

- Assist in the development of educational programs to better inform patients and caregivers of the effects and safety concerns of IO agents
- Provide recommendations for programs, in collaboration with other oncology groups, to address widespread safety concerns

- Work directly with the FDA to identify appropriate IO clinical endpoints

Specific Research Objectives:

The specific research objectives for the collaborative MMRF Immunotherapy Networks of Excellence project grant include, but are not limited to, the following areas:

- Development of SOPs for tissue processing of bone marrow and peripheral blood specimens to be used to assess both tumor and host immune factors that contribute to response
- Standardize and conduct biospecimen analyses with state of the art assay platforms including:
    - Genomic characterization of tumor and immune components in the microenvironment
    - Characterization of T and B cell receptors
    - Phenotypic and functional characterization of immune cells in both the bone marrow and peripheral blood by a variety of different assays
- Have access to samples from clinical trials and/or biobanks to initiate a pilot study(s) to:
    - Ensure that specimen processing, platforms, and data analytics for the different analyses are running properly
- Perform bioinformatic analyses and provide the appropriate interpretations for the different platforms being used
- Contribute to the creation of a public database that will include data from both tumor and immune analyses
- Develop or have access to cell lines, animal models and additional tools to support translational research to test different hypotheses

The MMRF Immunotherapy Networks of Excellence will be funded in 2 Stages:

Stage 1 is designed for data generation and hypothesis testing. Based on the results of Stage 1, Stage 2 will be used to move the findings into the clinic in the form of a novel immune clinical trial.

The award specified in this RFA is to support Stage 1 of the Network's goals and objectives. In Stage 1 the Network will be required to:

- Perform a designated pilot study to ensure that all molecular and immune assays, platforms and analytics are working properly within the Network. This could be done with banked samples in a retrospective analysis or prospectively collected samples. If the samples are part of a clinical study, permission to share the data and results with the MMRF would have to be secured.
- Use the specified resources and tools within the Network to address different critical well-defined research questions at the pre-clinical level (i.e.: resistance mechanisms to IO agents; novel IO combination approaches, etc.) that would generate the data needed to move forward with a novel IO trial concept

At any point and up to no longer than 18 months after initiation of the Stage 1 award, the Network can propose a novel clinical trial concept and apply for additional funding for the trial. This application will be separate from this RFA and additional funding will be added. It should be noted that the

MMRF will provide partial funding for the trial and it is expected that the Network will seek additional financial support from pharma/biotech and other sources to support the entire trial.

2. KEY DATES:

Release of RFA	June 29th
LOI Due Date	July 21st
Application Due Date	September 15th
Peer Review	Mid-September-Mid-October
Award Announcement	By end of November

3. Funds Available

The MMRF intends to fund 2 awards thereby creating **two** MMRF Immunotherapy Networks of Excellence**.** For each Network, the Stage 1 grant funding award will be for **two** years, at no more than **1.5M/year** including direct and indirect costs (indirects may not exceed 10% of directs). Funding for the second year will be contingent upon completion of well-defined milestones specified for Year 1. After the first **18 months** the Network will be able to apply for Stage II funding which will be to execute a **novel** immune-based clinical trial. It should be noted that the MMRF will provide partial funding for the trial and it is expected that the Network will seek additional financial support from pharma/biotech and other sources to support the entire trial.

Permissible direct costs include:

- Personnel Expenses of the Principal Investigator and co-Principal Investigators, post-doctoral researchers, and non-administrative staff including salary, wage, or stipend with fringe benefits. No more than 40% of the direct costs may be requested for the salary and fringe benefit expenses of professional staff with a post-graduate degree (Ph.D., M.D., D.V.M.). The 40% limit does not include the salary and fringe of technical research staff.
- Supplies and materials as itemized in the budget
- Annual travel expenses of no more than $2000/meeting for 1 researcher/institution for attendance to a nationally-recognized scientific/medical conference

Permissible indirect (also referred to as institutional) costs:

- May not exceed **10%** of direct costs.

Impermissible Costs:

- Membership dues, books, journals, publication costs and tuition

The funds awarded shall be used solely for the purposes specified in the application submitted to the MMRF as executed by the Principal Investigator, co-Principal Investigators, collaborating staff and institution in compliance with the budget annexed to the application, or any subsequent budget approved by the MMRF.

4. ELIGIBILITY

Requirements:

This purpose of this RFA is to support **2** distinct MMRF Immunotherapy Networks of Excellence focused around a **collaborative, multi-institutional program (at least 3 separate research institutions/ laboratories) to collectively assemble the appropriate assays, tools and models in order to study critical research questions that will drive new immune treatments into the clinic for myeloma patients.** Each Network should include investigators with expertise in basic, translational, and clinical research focused on different types of immune therapeutic approaches.
Since 2 distinct Networks will be awarded they will each be required to agree to:

- Share resources, reagents, methods and SOPs for the different assays and tools being developed within the two Networks
- Contribute to the establishment of an immune-profiling database first to share between the institutions in the two Networks and the MMRF and eventually to be released more broadly into the public domain
- Meet on a semi-annual basis to discuss results

Each MMRF Immunotherapy Network of Excellence will be judged as a unit and funding will not be available for otherwise meritorious parts of the application. The quality of all the projects and cores and the enhancement to be achieved by linking them together will determine the likelihood of funding. The MMRF Immunotherapy Networks of Excellence grant applicants will be judged principally, although not solely, on three main features of the application: 1) the significance of the research to the overriding goal of a better understanding of identifying more optimal immune approaches for the treatment of myeloma in patients more likely to respond as well as approaches that could overcome resistance mechanisms 2) prior accomplishments of the investigators in the field of immune biology and therapeutics more specifically in the field of myeloma research and 3) the synergy and collaboration that would result from knitting the different institutions together into an interactive program.

Leadership and staffing:

Each MMRF Immunotherapy Network of Excellence shall have a Principal Investigator who is responsible for the preparation and submission of the application and budget, the conduct of the research programs and for adherence with all stipulations in the MMRF's guidelines. Each institution in the Network should have a co-Principal Investigator responsible for the management of their institution's contribution to the Network under the overall direction of the Principal Investigator. A detailed management plan must be provided with the application that clearly defines the roles and responsibilities of the Principal Investigator and co- Principal Investigators at each of the institutions of the Network. The Principal Investigator and co-Principal Investigators must hold an M.D., Ph.D., or equivalent degree, and be from not-for-profit 501(c) 3 organizations, or their international counterparts/equivalents, including universities, colleges, hospitals, research organizations and/or clinical laboratories.

5. Submission of LOI

- A 1-2 page letter of intent should be submitted by **5 PM EST on July 21, 2017** and include the following information:
  - Name of Principal Investigator and Institution
  - Name of other Co-Investigators and their respective institutions
  - Brief summary of expertise/value add from each investigator and institution
- Submission by email to:

  Daniel Auclair, Ph.D.
  Senior Vice President Research
  Multiple Myeloma Research Foundation
  383 Main Ave., 5th Floor
  Norwalk, CT 06851
  Tel. (203) 652-0218
  Email: Auclaird@themmrf.org
- Full application will be due on **September 15th by 5 PM EST**

6. Review Process

Each application will undergo a thorough review that consists of two parts: an internal review by the MMRF for compliance with guidelines, eligibility, and appropriateness; and a second more extensive external peer review by recognized experts in both the myeloma and immune oncology fields.

The review criteria include:

1. Importance of the research to contribute to a better understanding of response and resistance to immune therapeutic agents and identification of more optimal immune combination approaches to test in the clinic
2. Integration and application of state of the art technologies to be used to comprehensively assess both host and immune parameters that contribute to response to different agents. Incorporated into this assessment is the need for standardization of: 1) tissue processing, 2) genomic and immune monitoring assays, and 3) bioinformatics analyses
3. Demonstration of the synergy and interdisciplinary nature of the proposed collaborative projects that encompass a broad range of expertise in different immune therapeutics compared to the team members working independently
4. Clarity of thought and written presentation of the overall program goals and research projects
5. Likelihood of technical success as balanced by scope of work and novelty of the proposed collaborative program
6. Experience, background, and qualifications of investigators (Principal Investigator(s) and co-Principal Investigator)
7. Appropriateness of the budget
8. Quality of the resources and environment (facilities, special equipment, patient population, etc.)
9. Adequacy of provisions for protection of human subjects, laboratory animals and investigators and staff using biohazardous materials or procedures

Written review critiques of the application are not provided back to applicants.

7. Progress Report and Second Year Continuation of Funding

A first year milestone-driven progress report is strictly required for second year funding of the program. The Principal Investigator must submit a report (limit of 10 pages) of the progress of the Network 60 days prior to the first year grant anniversary date. The report should briefly review both the initial pilot project and research progress during the first year. Furthermore there should be a list of any publications and a disclosure of intellectual property that were derived from the Immune Network. The report should include a report from the Financial Officer of the Sponsoring Institution detailing how the grant funds were expended over the course of the year. Finally, the Principal-Investigator and co-Principal-Investigators of each Network will be expected to have joint semi-annual meetings with each other, the MMRF and a Steering Committee.

The written reports shall be reviewed by the MMRF in order to evaluate the research progress of each program in the Network. The MMRF will use that report as the basis for continuation of the Network for the second year of funding.

Although awards are for a two-year period, the MMRF reserves the right to terminate any grant if it determines that there has been inadequate research progress or if progress reports are delinquent for more than 30 days.

8. Final Reports

Within 90 days of the expiration of the grant period, the grantee shall submit a summation of the research, together with copies of all publications and/or disclosure of intellectual property derived from the research. A one paragraph summary of the research project must be included for the lay public. The final payment shall be made only after the receipt by the MMRF of a satisfactory final research report and a satisfactory final accounting report.

9. Application Information

Applications should be submitted through the proposalCENTRAL Application System.

For scientific inquiries contact:

Daniel Auclair, Ph.D.
Senior Vice President, Research
Multiple Myeloma Research Foundation
383 Main Ave., 5th Floor
Norwalk, CT 06851
Tel. (203) 652-0218
Email: Auclaird@themmrf.org

For administrative and budget inquiries contact:

Jeannie Calcano Peare
Clinical and Research Executive Assistant

Multiple Myeloma Research Foundation
383 Main Avenue, 5th Floor
Norwalk, CT 06851
Phone: 203-652-0464
Email: pearej@themmrf.org

10. Contract and Terms of Award:

Upon receipt of the Notice of Grant Award, the applicant organization will provide the MMRF with the name and contact information for a legal representative who is authorized to negotiate on behalf of the institution. The MMRF reserves the right to withdraw the grant award if the parties fail to agree to grant terms within **60** days of the Notice of Grant Award**.**

The failure of the grantee and/or the sponsoring institution to adhere to any of the terms and conditions in the contract shall constitute sufficient grounds for the MMRF, in its discretion, to withhold any or all funds due until the deficiency is corrected. Either the MMRF or the sponsoring institution may terminate the contract upon giving 90 days written notice, if the deficiency cannot be corrected. In such case, any unexpended balance of funds must be returned to the MMRF.

11. Assurances

Human Investigation

The grantee (Program Director and/or Project Leaders) must obtain approval from the sponsoring institution's Institutional Review Board on use of human subjects in research if the project requires the use of human materials or subjects. Written approval of the Institutional Review Board on use of human subjects must be submitted to the MMRF. Failure to notify the MMRF of use of human materials or subjects in a grantee's research may result in termination of the grant.

Laboratory Animals

The MMRF adheres to the most current guidelines applicable to the care and the treatment of animals in laboratory work as outlined by the National Institutes of Health. For projects which involve laboratory animals, approval from the Sponsor's Institutional Animal Care and Use Committee (IACUC) must be obtained. The approval date and Animal Welfare Assurance number must be provided to the MMRF. Non US applicants should submit approval documentation from the Animal Ethics Committee. The grantee must include in the application a statement that the sponsoring institution meets and adheres to these policies whether or not the use of laboratory animals is planned in the proposal. Failure to notify the MMRF of compliance with these guidelines on the use of laboratory animals may result in termination of the grant.

Biohazards

The grantee must include in the application a statement about any potential biohazards and a description of the safeguards planned where such hazards to the investigator, other personnel or any other individuals may be encountered. The MMRF assumes no responsibility or liability for any such biohazards and shall be held harmless from the results of the use of any such biohazards.

12. About the MMRF

The mission of the Multiple Myeloma Research Foundation (MMRF) is to find a cure for multiple myeloma by relentless pursuing innovation that accelerates the development of next-generation treatments to extend the lives of patients. Founded in 1998 by Kathy Giusti, a multiple myeloma patient, and her twin sister Karen Andrews as a 501 (c) (3) nonprofit organization, the MMRF is a world-recognized leader in cancer research. Together with its partners, the MMRF has created the only end-to-end solution in precision medicine and the single largest genomic dataset in all cancers. The MMRF continues to disrupt the industry today, as a pioneer and leader at the helm of new research efforts. Since its inception, the organization has raised over $350 million and directs nearly 90% of the total funds to research and related programs. As a result, the MMRF has been awarded by Charity Navigator's coveted four-star rating for 12 years, the highest designation for outstanding fiscal responsibility and exceptional efficiency.