



TEAM SCIENCE
AWARD

M2Gen Funding Opportunity Announcement

Spring 2018

April 4, 2018

M2GEN[®]



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Background

The Oncology Research Information Exchange Network (ORIEN) is a unique alliance to integrate data sharing and collaborative learning to accelerate cancer research and care. ORIEN was founded by the Moffitt Cancer Center and The Ohio State University Comprehensive Cancer Center in May 2014, and now includes 17 members (ORIENCancer.org). The foundation of the alliance is the common Total Cancer Care® (TCC) protocol, a longitudinal surveillance study of cancer patients, which allows for lifetime consent to access clinical data, perform laboratory analysis of specimens, and the ability to re-contact the patient. Following patient consent, patients agree with the Member Institution to three basic principles: 1) Follow the patient throughout their lifetime, permitting sharing of data and information; 2) Study the patient's specimens and, 3) Maintain contact with the patient.

The ORIEN Avatar Research Program, launched in 2016, generates molecular (NGS) data on patients with high risk cancers and links longitudinal clinical data throughout a patient's lifetime to learn and anticipate patient needs. With ORIEN Avatar, the pace of development can be accelerated by taking a proactive approach to study the molecular and clinical nature of patient's disease and anticipating needs for clinical trials. The results: reduced timelines, reduced costs and better outcomes for patients.

Through ORIEN, members collect and share clinical data as well as patient specimens for analysis and have access to robust molecular data to foster and enable translational research. M2Gen has developed a network data model system to integrate data from multiple sources and institutions to support team science and address complex problems. Centrally managed by M2Gen, the ORIEN system provides the ability to identify patients for target-based clinical trials, and to query the data system to conduct research projects.

ORIEN's Patient Advisory Council supports the position that patients enrolled in the Total Cancer Care Protocol be informed of the necessity for data sharing and fostering collaboration among top scientists to promote progress in cancer care. The Advisory Council also endorses the development of a "forum" for patient education and how their donated data is being studied to support cancer research. As a means of "giving back" to patients who have consented to TCC, enrollment of patients in the Total Cancer Care Protocol offers patients increased probability of being matched to the most appropriate, precise, clinical trial.

Purpose

M2Gen is inviting members of the Oncology Research Information Exchange (ORIEN) to apply for the new ORIEN NOVA Awards for the purpose of:

1. Supporting the ORIEN mission through collaborative learning – Team Science.
2. Encouraging the ORIEN founding principle of data sharing and collaborative learning.

Eligibility

This Funding Opportunity is only open to faculty from ORIEN members. Applications must include participation of two (2) or more ORIEN member institutions. Applications will be accepted in two categories:

1. Request for Application (RFA) addressing an **ORIEN Avatar Question (OAQ)** using the ORIEN Avatar Research Program; and
2. **Investigator-initiated Proposals (IIP)**. The IIP category is limited to ORIEN member institutions participating in Total Cancer Care Protocol. IIP proposals will use TCC data and/or ORIEN Avatar data to address a wide spectrum of research including, but not limited to, basic and translational research, population science, and development of new data acquisition and data analysis tools.

PROCESS FOR APPLYING FOR AN ORIEN NOVA AWARD:

Pre-Submission Letter of Intent

ORIEN members interested in submitting an ORIEN NOVA Award application must complete a Pre-Submission Letter of Intent (LOI) no later than **May 9, 2018** for the purposes of assessing feasibility and scientific impact of the proposed submission. The on-line LOI form is available at <http://www.oriencancer.org/nova-award.php>. Supplemental narrative information accompanying the LOI should be in PDF format, not exceed two (2) pages in length. Only one attachment may be submitted with each LOI.

The following information should be included in the LOI on-line application and accompanying narrative:

- **Category** of NOVA Award the researchers intend to apply: ORIEN Avatar Question or Investigator-initiated Proposal;
- **Name(s)** and rank of Principal Investigator and Co-Investigators, proposals including junior faculty will be reviewed favorably;
- Names of participating **ORIEN member institutions**, including name of designated lead member submitting the LOI. Only one LOI will be permitted per project;
- **Project Title**, and/or the specific **ORIEN Avatar Question** the proposal intends to address:
 - A. What are the treatment response predictive biomarkers and optimal combination treatment strategies for immuno-oncology?
 - B. What are the treatment response predictive factors for Non-Hodgkins Lymphoma (NHL) and how might this information lead to new target discovery or rationale for combination therapies?
- **Project Summary/Abstract** that describes the question or goal being addressed, the project's potential scientific and/or clinical impact, specific aims, and a brief description of the research design and methods;

- **Approach**, to include description of:
 - Relevant resources (patient clinical data, molecular data, patient specimens) that are needed to address the question.
 - Whether resources needed currently exist or will require new specimens and/or data.
 - Expected number of cases needed to complete the project
 - Description of the NOVA Award scientific team, including number of ORIEN member participants and plan for collaboration in addressing the scientific question.
 - Description of how the approach will enrich and improve the TCC and/or Avatar data for future scientific benefit.
 - Other key information that will inform the feasibility assessment of the pre-proposal LOI
- Resources needed from M2Gen during the award period in support of the project.
- Estimated funding needed.

M2Gen will provide support to the NOVA applicant teams in gathering the feasibility data needed for the Letter of Intent. Questions or assistance with Letters of Intent can be sent to ORIENprojects@m2gen.com.

Pre-submission LOIs will undergo a review by the ORIEN NOVA Award Peer Review Subcommittee for:

- Overall scientific impact: does the proposal have the potential to influence the research field?
- Relevance: are the proposal methods relevant to addressing the research question?
- Feasibility: is it feasible to achieve the project aims in a two year funding period?

The ORIEN NOVA Peer Review Subcommittee will select the LOIs for which full applications will be solicited.

Full Application Review Process

Once applications have been solicited, based on the Pre-Submission LOI, ORIEN NOVA applications will be reviewed by the ORIEN NOVA Award Peer Review Subcommittee. Applications will be reviewed on the strength of their scientific merit, innovation (the degree to which the project does not repeat, reproduce, or is not extensively derived from existing science documented in the literature), and strength of collaboration and team science, potential to obtain extramural funding, and feasibility to conduct the proposal within the funding period. ORIEN Avatar Research Question application review will also include the strength of the proposal in addressing the specific topics addressed in the RFA.

Proposal Criteria

The ORIEN NOVA Team Science Awards will be funded in two categories:

- [Category I. RFA addressing ORIEN Avatar Research Question \(OAQ\)](#)

M2Gen has identified research areas where team applications will be accepted in response to specific research questions. An individual application should address a specific research question and clearly outline the proposed approach to answer the research question through use and expansion of the ORIEN Avatar resources. Applicants should be familiar with the intent, background, and address feasibility and implications of the proposed answer to the research question being addressed. An “Intent Statement” is included below describing details for each OAQ proposed in the RFA.

For the Spring 2018 cycle, there are two RFAs associated with the ORIEN Avatar Research Questions:

- A. RFA 1. What are the treatment response predictive biomarkers and optimal combination treatment strategies for immune checkpoint inhibitors?

Intent: Immuno-oncology therapies, especially immune checkpoint inhibitors, have shown impressive results in some patients, especially patients with advanced lung cancer, melanoma and several other cancers, but it is beneficial in only a minority of patients. Immune checkpoint inhibitors, including anti-cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and anti-programmed cell death protein 1 (PD-1) or its ligand 1 (PD-L1) monoclonal antibodies (mAbs), unleash a patient’s immune system to attack and kill cancer cells. Checkpoint inhibitors have had a significant impact in cancer treatments in several cancers, and FDA approval has been granted for mono- and combinational therapies in advanced melanoma, advanced non-small cell lung cancer, classical Hodgkin lymphoma, head and neck squamous cell cancer, advanced urothelial bladder cancer, advanced gastric cancer, advanced renal cell carcinoma, liver cancer (HCC), and multiple tumor types with MSI-high. Even with the impressive success of checkpoint inhibitors, not all patients or all tumor types respond to checkpoint inhibitor treatment. For most of the approved indications, patient response rates vary from 20 to 50%. In addition, many patients who initially respond to checkpoint inhibitors will develop acquired resistance during treatment.

This Request for Application invites research applications to address the following questions:

- 1) What are the predictive biomarkers and biological mechanisms for immune checkpoint inhibitors that determine patient response? Currently the degree of immune cell infiltration, PDL1 level, tumor mutation burden (TMB) and MSI-H are considered to be predictive biomarkers, but typically less than 50% of “biomarker high patients” respond to the therapy.

Why do some “inflamed” tumors that might be expected to respond to checkpoint inhibitors (for example, triple-negative breast cancer), not respond? What other factors, such as specific tumor genetic mutations and/or the tumor microenvironment, influence patient response to check point inhibitors?

- 2) What approaches would convert a tumor from a “non-inflamed” tumor to an “inflamed” tumor? There are variable degrees of tumor infiltrating immune cells across tumor types, and within specific cancer types. What measurements might predict conversion from a “non-inflamed” tumor to an “inflamed” tumor and what is the evidence that this conversion will lead to treatment response?
- 3) What are possible mechanisms of acquired resistance to checkpoint inhibitors? Long-term response is critical to patient treatment, but patients often develop acquired resistance following initial objective response. What are the escape mechanisms that occur during checkpoint inhibitor treatments and how might this information improve design of next generation of immuno-oncology treatments.
- 4) What are optimal combinational therapies with immune checkpoint inhibitors? Early studies suggest that combination therapies with check point inhibitors may improve response rates compared to the use of checkpoint inhibitors alone. Using the ORIEN Avatar system, what evidence can be derived to support rationale combination therapy that would result in not only improved response rates, but also improved duration of response?

And lastly, we are also open to unconventional approaches to this RFA, for example:

- 5) Can physics and mathematical models impact the development of tumor immunotherapy? For these types of response, we would like to focus on practical solutions that could lead to improved treatment responses.

The ultimate goals of this RFA are to expand the Avatar population and provide clinically validated biomarkers/mechanisms that may inform clinical trial design, and guide physicians to select and combine or sequence therapies involving immune checkpoint inhibitors resulting in improved patient outcome.

Applications that do not explore questions presented in this Intent Statement will be considered nonresponsive to this RFA.

Background: The immune system is a body’s natural defense system against any disease, including cancer. Tumor cells gradually escape or hide from an immune response through multiple mechanisms, including elevated expression of inhibitory checkpoint molecules such as PD-L1 on tumor cells and CTLA-4 and PD-1 on infiltrated T lymphocytes in the tumor microenvironment. Suppression of tumor mediated immune checkpoints results in anti-tumor immunity in a variety of cancer types. Several checkpoint inhibitors have been developed and gained FDA approval, such as Nivolumab (Opdivo), Pembrolizumab (Keytruda), Atezolizumab (Tecentriq), Avelumab (Bavencio), Durvalumab (Imfinzi), Ipilimumab (Yervoy).

Checkpoint inhibitors as single agents, and more recently in combination with standard-of-care cancer therapies, have demonstrated enhanced response rates with improved durability of treatment responses in several tumor types. However, most cancer patients do not benefit from current checkpoint blockade therapies. Similar to tumor cells initially escaping immune surveillance during tumorigenesis, there are multiple mechanisms that influence response or non-response to checkpoint inhibitors. It is of great importance to the treating physician to know who will respond or not respond, and more importantly to define better treatment strategies to increase the response rate and duration. The mechanisms of response and non-response, and predictive biomarkers, are also equally important to define clinical trial strategies, and to design next generation therapies.

The research intent of this RFA can only be achieved by multiple ORIEN cancer centers that agree to build the Avatar and share data and conduct collaborative learning. We would anticipate that as this research effort evolves and becomes successful that most, if not all, ORIEN members would be invited to participate in addressing this important question.

Feasibility: In response to this RFA, multidisciplinary teams of investigators from multiple ORIEN institutions are invited to submit research proposals toward the intent of this RFA. We especially encourage researchers to enrich and utilize the ORIEN Avatar for this project. The immuno-oncology treated patients included in this RFA should be enrolled to the ORIEN Avatar program that covers the cost of generating molecular data (WES for tumor and matched normal, RNAseq for tumor) and collecting clinical data from patients assigned to the Avatar program. In addition to the current Avatar data, applicants who possess enough patient specimens (as demonstrated by power calculation) may propose and request funding for the following:

- Immunophenotyping of tumor and blood
- Circulating tumor DNA sequencing from blood, collected longitudinally during IO treatment
- T-cell receptor repertoires, from tumor and blood
- Microbiome sequencing/profiling
- Methylation, proteomics
- Refractory/relapse tumor/blood samples for additional sequencing

Applicants are also encouraged to discuss with M2GEN about defining and collecting additional IO response/AE related clinical data in order to support this project.

Implications of Success: Research findings resulting from successful completion of projects under RFA are expected to yield clinically informative predictive biomarkers and/or testable mechanisms for immuno-oncology treatment responses. Success in development of predictive biomarkers and understanding of mechanisms of response and resistance will also ultimately lead to evidence to support clinical trials of novel combination therapies involving checkpoint inhibitors in the future.

B. RFA 2. What are the treatment response predictive factors for Non-Hodgkins Lymphoma (NHL) and how might this information lead to new target discovery or rationale for combination therapies?

Intent: NHLs comprise a very diverse collection of malignancies, and unlike classical Hodgkins lymphoma, do not share a common genetically determined sensitivity to checkpoint inhibitors. Although 9p24.1 alterations and rearrangements have been reported in NHLs, they are rare. Nevertheless, there are other biological mechanisms that support the use of PD-1 blockade in subtypes of NHLs. Optimizing checkpoint blockade in NHL is unlikely to have a uniform answer; however, understanding the biological basis of checkpoint blockade may provide knowledge needed to design clinical trials using combination therapies. One possible approach, for example, is the use of epigenetic drugs to modulate immune responses to checkpoint inhibitors and other immuno-oncology treatments. The intent of this RFA is to invite applications to study biomarkers and pathways in NHLs leading to a greater understanding of the biological basis of immune and target-based therapies and development of a rationale choice of optimal target pathways and strategies for combination therapy. The development of analytic tools with both prognostic and predictive utility to individualize therapy, including being matched to target-based clinical trials, is a priority. Using the ORIEN Avatar and Total Cancer Care protocol, all types of NHL may be studied, but there is an expectation that diffuse large B cell lymphoma (DLBCL) and follicular lymphoma will be the dominant NHL types studied.

This Request for Application invites research applications to address the following questions:

1. What are the molecular subtypes of NHL that determine response to specific chemotherapy platforms and targeted agents? For example, what patient groups are not likely to be cured with standard regimens, such as R-CHOP?
2. What are the predictive biomarkers and biological mechanisms for patient response to immunotherapies, including immune checkpoint inhibitors? What other factors, such as specific tumor genetic mutations and/or the tumor microenvironment, co-expression of checkpoints in TILs, infection of EBV, influence patient response to immuno-therapeutics?
3. What are possible mechanisms of resistance to immunologic agents? What are the approaches that might improve design of next generation of immuno-oncology treatments and/or the use of combination therapies to improve response?
4. Using the ORIEN Avatar system, what evidence can be derived to support rationale combination therapies that would result in improved response rates and improved duration of response?
5. Can physics and mathematical models impact the development of tumor immunotherapy? The emphasis should be proposing practical solutions that could lead to improved treatment responses.

Background: The use of immunotherapeutics over the past decade has been actively pursued in many cancers, including lymphoma. The enhancement of host antitumor immunity may be accomplished by several different approaches including CAR-T, immunization with tumor antigens, enhancing costimulatory signals of immune cells, or disrupting tumors' reliance on checkpoint pathways. Of the various approaches to enhance host antitumor activity, "checkpoint blockade" has made significant progress across many tumor types, of PD-1 ligands. In general, NHLs do not display a high frequency of 9p24.1 alterations and do not share vulnerability to PD-1 blockade. A few NHL types possess genetic or immunologic features that do predict sensitivity to checkpoint blockade and these include PMBL, PCNSL, PTL and GZL. Most patients with DLBCL, the most common type of NHL, do not have 9p24.1 alterations and response to single agent checkpoint inhibitors is low. Studies are in progress to combine checkpoint blockade agents with other treatments including immunomodulatory agents like, lenalidomide and ibrutinib. Other approaches to enhance immune response in NHL have also been reported recently, such as the use epigenetic therapy in combination with immunotherapy. Although there are several FDA-approved agents that target DNA methylation and histone acetylation, the promise of epigenetic therapy for cancer remains to be realized. Therefore, additional treatment strategies are needed to determine the efficacy of epigenetic therapy.

Feasibility: In response to this RFA, multidisciplinary teams of investigators from multiple ORIEN institutions are invited to submit research proposals toward the intent of this RFA. We especially encourage researchers to enrich and utilize the ORIEN Avatar for this project. The NHL patients included in this RFA should be enrolled in the ORIEN Avatar program that covers the cost of generating molecular data (WES for tumor and matched normal, RNAseq for tumor) and collecting clinical data from patients assigned to the Avatar program. In addition to the current Avatar data, applicants who possess enough patient specimens (as demonstrated by power calculation) may propose and request funding for the following:

- Immunophenotyping of tumor and blood
- Circulating tumor DNA sequencing from blood
- T-cell receptor repertoires, from tumor and blood
- Microbiome sequencing/profiling
- Epigenetic analysis including Methylation and Acetylation
- Proteomics
- Refractory/relapse tumor/blood samples for additional sequencing

Applicants are also encouraged to discuss with M2GEN about defining and collecting additional clinical data that may be relevant to this RFA.

Implications of Success: Research findings resulting from successful completion of projects under RFA are expected to yield clinically informative predictive biomarkers and/or testable mechanisms for treatment responses. Success in development of predictive biomarkers and understanding mechanisms of response and resistance should ultimately lead to evidence to support clinical trials of novel combination therapies in the future.

- **Category II. Investigator Initiated Proposals**

ORIEN members may propose a wide range of investigations including, basic, translational, clinical, and population science studies; and/or development of novel approaches to facilitate data aggregation and analysis. The proposals should expand the volume and use of data created through the ORIEN Avatar Research Program and/or data collected from the TCC Protocol. Funding for clinical trials is not anticipated; however, correlative science to enhance clinical trial design and accrual will be considered.

Applicants are encouraged to include tenure-track Junior Faculty in their proposals.

Terms of Award

Funding for all projects will be for a two year award period. M2Gen will award the following through this program:

- Two (2) proposals in Category 1 (ORIEN Avatar Question) for up to \$500,000 total costs per year for up to two years;
- Four (4) proposals in Category 2 (Investigator initiated) for up to \$125,000 total costs per year for up to two years.

Anticipated start date for the awards will be September 1, 2018 for a two year period. Separate budgets should be provided for costs at each involved ORIEN site in lieu of having a primary institution and subcontracts. M2Gen will pay each site participating in the team science project directly on a monthly cost reimbursement basis based on ORIEN member invoicing, consistent with the approved project budget.

Indirect cost rate (F&A) will be 20% of the direct costs of the award and must be included within the proposed budget, if applicable. An interim report demonstrating progress to-date, plans for year two and activities/plans to seek extramural funding will be required at the end of the first award year. Interim reports should include a description of results and how the work will be carried forward in the coming year. It is expected that the proposal will result in peer-reviewed publication(s) and a plan for extramural funding by the end of the award period. Any publications or presentations of work resulting from this award should acknowledge support from M2Gen and membership in ORIEN.

Proposal Requirements

Applications for either the ORIEN Avatar Question or the Investigator-initiated Proposals should be submitted on-line at <http://www.oriencancer.org/nova-award.php>. Multiple Co-Principal Investigators are allowed, however, only one application may be submitted for each project by the ORIEN team applying.

Applications should include the following:

- I. Face page
- II. Abstract (limited to 300 words). Abstract should include rationale explaining why this project should be considered as an ORIEN Nova Award. If in response to an ORIEN Avatar Question, please provide rationale for how the proposal addresses the research challenge outlined in RFA and how ORIEN Avatar will be integrated into the project.
- III. Role of the Co-PI's and Overview of the Collaboration (describe the contribution of the Co-PI's and how the Co-PI's compliment each other in performance of research). Limited to one (1) page.
- IV. Research Plan – Maximum of five (5) pages in total to include the following:
 - a. **Goals/Specific Aims:** Discuss the question or problem to be addressed, barriers to conducting such work outside of a Team Science setting and the long-term objectives that the research proposal is intended to accomplish. Clearly state the short-term objectives of this application and the hypotheses to be tested.
 - b. **Background and Significance:** Briefly present the background leading to the present research proposal, critically evaluating existing knowledge and identifying the gaps that the project is intending to fill.
 - c. **Preliminary Data:** Provide an account of any relevant preliminary studies to establish the experience of the investigators or support the proposed science.
 - d. **Research Design and Methods:** Summarize the study design and experiments/analyses that the project will conduct.
 - e. **TCC/Avatar Cases Needed:** Describe the expected number of TCC and/or Avatar cases that will be needed to conduct the proposal and whether the cases will be prospectively consented patients or existing patients and/or data.
 - f. **Future Plans and Timeline for Extramural Grants Submission:** It is expected that the proposal will result in peer-reviewed publication(s) and a plan for extramural funding by the end of the award period. A description of the plans for publication(s) and extramural grant submissions should be provided.
- V. References
- VI. Budget and Budget Justification. Budget should include a summary budget for all participating sites as well as a budget per ORIEN Member institution. Please use PHS 398 budget form page 5 found at <https://grants.nih.gov/grants/funding/phs398/fp5.pdf> . A budget form is required for:
 - a. Each project year (2 years max)
 - b. Each ORIEN Member site
 - c. A summary budget per year, including budget for all participating ORIEN Member sites
- VII. Key Personnel List and NIH Biosketches

Applications should be formatted using Arial 11 black font, single spaced with all text showing and 0.5 inch margins (all sides). The Project Title and Principal Investigator's name should be shown in the header of all application pages.

Allowable and Unallowable Costs

Investigators are strongly encouraged to review the matrix provided in Appendix I when initiating budgets for their proposals to ensure applications adhere to the financial/budgeting policies of the funding mechanism.

Application Submission Key Dates and Process

April 4, 2018	Funding Opportunity Announcement Issued
↓ (5 weeks)	
May 9, 2018	Letter of Intent Due by 5:00 pm ET
↓ (3 weeks)	
May 30, 2018	Invitation to Apply Notification Sent to LOI Submitters
↓ (7 weeks)	
July 18, 2018	ORIEN NOVA Award Applications Due by 5:00 pm ET
↓ (6 weeks)	
August 29, 2018	ORIEN NOVA Award Peer Review Subcommittee Concludes Review & Selection
August 31, 2018	ORIEN NOVA Awardees Notified & Announced
September 1, 2018	ORIEN NOVA Funding Award Period Begins

Applications should be submitted on-line at <http://www.oriencancer.org/nova-award.php>. Any questions can also be directed to ORIENprojects@m2gen.com.

Awardee Obligations

- ORIEN NOVA Award teams will be required to present a progress report at the ORIEN Annual Meeting (Spring).
- Awardees will complete a Progress Report annually. These reports are completed via email, average 2-3 pages, and describe: 1) project progress and results; 2) all poster presentations/publications and funding resulting from the funded project; 3) any patents & licenses granted or applied for.
- Awardees must acknowledge the funding mechanism in any publications or presentations related to their institutional award funding by including the statement *"This publication is supported by ORIEN and M2GEN"*



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- Progress reports will be reviewed by the ORIEN NOVA Award Peer Review Subcommittee prior to funding for year two of the award to ensure scientific progress has been made.
- Finally, awardees are expected to complete their pilot projects within their approved project period and budget, unless an extension is requested and approved in writing. No-cost extensions are not automatically granted. Any funds not expended and invoiced within the project period and justified as outlined in the project budget will become unavailable at the end of the award period. Exceptions may be made if proper rationale is provided and approved by M2Gen.

APPENDIX I.

Common Research Expenses	
<p><u>Allowable</u></p> <ul style="list-style-type: none"> • PI effort should be proportional to effort on the project and is capped at 5% of up to the NIH salary cap. • Co-investigators and research staff needed to perform the milestones • Research supplies, sample assays, sample access fees, • Technical assistance • Publication costs, including reprints • Shared resources costs • Special fees (pathology, photography, flow cytometry, bioinformatics or biostatistics fees, etc.) • Lab supplies • Travel cost associated with attendance at required ORIEN Spring Retreat, capped at \$3000 per institution 	<p><u>Unallowable</u></p> <ul style="list-style-type: none"> • Secretarial/administrative salaries • Tuition • Books and periodicals • Membership dues • Computers and/or tablets/e-readers • Office and laboratory furniture • Office equipment and supplies • Rental of office or laboratory space • Recruiting and relocation expenses • Non-medical services to patients • Per-diem charges for hospital beds • Construction, renovation, or maintenance of buildings/laboratories • Conference registrations and meeting costs • Stipends for graduate students and post doctoral assistants