Department of Health and Human Services

Part 1. Overview Information

Participating Organization(s)

National Institutes of Health (NIH)

NCI

Components of Participating Organizations

National Cancer Institute (NCI)

Funding Opportunity Title

Modulating Human Microbiome Function to Enhance Immune Responses Against Cancer (R01 Clinical Trial Not Allowed)

Activity Code

R01 Research Project Grant

Announcement Type

Reissue of PAR-19-198

Related Notices

None

Funding Opportunity Announcement (FOA) Number

PAR-22-061

Companion Funding Opportunity

PAR-22-062, R21 Exploratory/Developmental Grants

Number of Applications

See Section III. 3. Additional Information on Eligibility.

Assistance Listing Number(s)

93.393, 93.396

Funding Opportunity Purpose

The purpose of this Funding Opportunity Announcement (FOA) is to support basic research that elucidates mechanisms by which the human microbiome inhibits or enhances anti-tumor immune responses, and to identify potential novel molecular

targets for cancer prevention strategies.

Applications should be focused on delineating how host interactions with specific microbes (or consortia) or their metabolites target immune responses that enhance or prevent inflammation-associated or sporadic tumor formation. Concentration, timing, and duration of administered beneficial microbes may alter its effectiveness and thus those parameters should be rigorously addressed in the application.

Key Dates

Posted Date

November 03, 2021

Open Date (Earliest Submission Date)

January 05, 2022

Letter of Intent Due Date(s)

Not Applicable The following table includes NIH standard due dates marked with an asterisk.

Application Due Dates			Review and Award Cycles		
New	Renewal / Resubmission / Revision (as allowed)	AIDS	Scientific Merit Review	Advisory Council Review	Earliest Start Date
February 05, 2022 *	March 05, 2022 *	Not Applicable	July 2022	October 2022	December 2022
June 05, 2022 *	July 05, 2022 *	Not Applicable	November 2022	January 2023	April 2023
October 05, 2022 *	November 05, 2022 *	Not Applicable	March 2023	May 2023	July 2023
February 05, 2023 *	March 05, 2023 *	Not Applicable	July 2023	October 2023	December 2023
June 05, 2023 *	July 05, 2023 *	Not Applicable	November 2023	January 2024	April 2024
October 05, 2023 *	November 05, 2023 *	Not Applicable	March 2024	May 2024	July 2024
February 05, 2024 *	March 05, 2024 *	Not Applicable	July 2024	October 2024	December 2024
June 05, 2024 *	July 05, 2024 *	Not Applicable	November 2024	January 2025	April 2025
October 05, 2024 *	November 05, 2024 *	Not Applicable	March 2025	May 2025	July 2025

All applications are due by 5:00 PM local time of applicant organization. All types of non-AIDS applications allowed for this funding opportunity announcement are due on the listed date(s).

Applicants are encouraged to apply early to allow adequate time to make any corrections to errors found in the application during the submission process by the due date.

Expiration Date

January 08, 2025

Due Dates for E.O. 12372

Not Applicable

Required Application Instructions

It is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide,except where instructed to do otherwise (in this FOA or in a Notice from NIH Guide for Grants and Contracts).

Conformance to all requirements (both in the Application Guide and the FOA) is required and strictly enforced. Applicants must read and follow all application instructions in the Application Guide as well as any program-specific instructions noted in Section IV. When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions.

Applications that do not comply with these instructions may be delayed or not accepted for review.

There are several options available to submit your application through Grants.gov to NIH and Department of Health and Human Services partners. You **must** use one of these submission options to access the application forms for this opportunity.

1. Use the NIH ASSIST system to prepare, submit and track your application online.
   Apply Online Using ASSIST
2. Use an institutional system-to-system (S2S) solution to prepare and submit your application to Grants.gov and eRA Commons to track your application. Check with your institutional officials regarding availability.
3. Use Grants.gov Workspace to prepare and submit your application and eRA Commons to track your application.

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Part 2. Full Text of Announcement

Section I. Funding Opportunity Description

Purpose

The purpose of this Funding Opportunity Announcement (FOA) is to support basic research that elucidates mechanisms by which the human microbiome inhibits or enhances anti-tumor immune responses, and to identify potential novel molecular targets for cancer prevention strategies. Cancer patients often carry distinct alterations of their gut microbiota that differ from healthy individuals. For example, specific commensals including Bifidobacterium and Lactobacillus are consistently diminished, and a greater abundance of Fusobacterium and Enterobacteriaceae are often found in these patients. But it remains unclear if such shifts in microbial composition play a causal or consequential role in the development of cancer.

Applications should be focused on delineating how host interactions with specific microbes (or consortia) or their metabolites target immune responses to prevent inflammation-associated or sporadic tumor formation. Concentration, timing, and duration of administered beneficial microbes may alter their effectiveness and thus those parameters should be rigorously addressed in the application.

Whereas this FOA is for well-developed projects supported with preliminary data, a companion FOA of identical scientific scope (PAR-22-062) is meant for pilot/exploratory projects.

Specific Areas of Research Interest

Growing evidence supports an important role for the gut microbiome in the etiology and prevention of human cancer through effects on epithelial barrier integrity, suppression/promotion of chronic inflammatory conditions, and modulation of innate and adaptive anti-tumor immune responses in the colon and in distal tissues. These critical host-microbe interactions have been recently termed the "immuno-oncology-microbiome axis". Several studies have demonstrated that altering the commensal microbiota by administration of beneficial microbes or the inhibition of tumor-promoting microbes can modify host lymphoid tissues and immune responses and thereby prevent the development of inflammation-associated and sporadic cancers in susceptible animal models. The efficacy of probiotic microbes is often species- and strain-specific and thus requires an understanding and selection of specifically targeted host-microbe interactions to elicit a desirable outcome. Despite the rapid translation of the immunomodulatory effects of host-microbe interactions in immune checkpoint cancer therapy, our current level of understanding of the molecular mechanisms and signaling pathways that mediate these protective effects is very limited and there is still a critical need for basic research that promotes our mechanistic understanding of these interactions, and the application of this new knowledge to cancer prevention and etiology. Therefore, the goal of this concept is to support basic and applied research approaches that identify and validate effective strategies that alter host-microbe interactions that enhance anti-tumor immune responses in the host.

The intestine is densely populated by commensal bacteria that produce a vast array of metabolic products that influence host immune system development and function. Sophisticated and novel techniques have been developed to characterize the immune-modulating properties of human-colonizing microbes. Animal models with genetic modifications in inflammatory response genes have been used to analyze key molecular events of immune cell response to the presence or absence of specific microbes of interest. In addition, several microbially-derived metabolites have been demonstrated to directly modulate anti-tumor immune responses through their interactions with immune cell membrane and cytoplasmic receptors. Microbial metabolism can also have indirect effects on tumor immune responses, for example by producing secondary bile acids that inhibit hepatocyte production of chemokines that direct a protective NKT cell response against developing liver tumors.

Thus, state-of-the-art metabolomic, molecular immunology and bioinformatic techniques may now be combined with cancer models to establish a physiological role for commensal microbes in tumor immunology. Bioinformatic analysis of metagenomic databases can infer the metabolic capacity of microbial communities and expedite identification of affected host immune cell populations and pathways to facilitate approaches that test predictions of microbial interactions that control host immune responses. Computational approaches may also be used to identify patterns of microbial and immunological changes that can generate molecular fingerprints of cancer risk.

Appropriate topics for this FOA include but are not limited to projects that:

- Determine how Lactobacilli species inhibit colon cancer and if its anti-tumor activity requires the induction of T-cell-dependent IgAs;
- Examine how commensal microbiota affect differentiation of naïve T cells to distinct Th17 subsets that may suppress or enhance tumor formation;
- Evaluate the role of colonic Foxp3+RORγt+ Treg cells in mediating the anti-inflammatory effects of commensal microbes to prevent colon cancer;
- Determine how modulation of commensal H2S production affects host immunosurveillance;
- Examine how SCFA production may affect anti-tumor immune functions of tumor associated macrophage;
- Examine how microbial bile acid metabolism affects immune responses in liver and colon tumors.

Non-Responsive Applications

Applications that propose the following will be deemed non-responsive to the goals of this FOA and will not be reviewed:

- Establish an association between microbial species and altered tumor immunity without defining and testing a mechanism of action;

- Focus on microbial modulation of non-immune tumor stroma signaling;
- Focus on microbial mechanisms that do no effect modulation of tumor immunity.

See Section VIII. Other Information for award authorities and regulations.

Section II. Award Information

Funding Instrument

Grant: A support mechanism providing money, property, or both to an eligible entity to carry out an approved project or activity.

Application Types Allowed

New
Renewal
Resubmission

The OER Glossary and the SF424 (R&R) Application Guide provide details on these application types. Only those application types listed here are allowed for this FOA.

Clinical Trial?

Not Allowed: Only accepting applications that do not propose clinical trials.

Need help determining whether you are doing a clinical trial?

Funds Available and Anticipated Number of Awards

The number of awards is contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications.

Award Budget

Application budgets are not limited but need to reflect the actual needs of the proposed project.

Award Project Period

The maximum project period is 5 years.

NIH grants policies as described in the NIH Grants Policy Statement will apply to the applications submitted and awards made from this FOA.

ection III. Eligibility Information

Eligible Applicants

ligible Organizations

gher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

The following types of Higher Education Institutions are always encouraged to apply for NIH support as Public or Private Institutions of Higher Education:

- Hispanic-serving Institutions
- Historically Black Colleges and Universities (HBCUs)
- Tribally Controlled Colleges and Universities (TCCUs)
- Alaska Native and Native Hawaiian Serving Institutions
- Asian American Native American Pacific Islander Serving Institutions (AANAPISIs)

ɔnprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)

ɔr-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

ɔcal Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribal Governments (Other than Federally Recognized)

ɛderal Government

- Eligible Agencies of the Federal Government
- U.S. Territory or Possession

ɔher

- Independent School Districts
- Public Housing Authorities/Indian Housing Authorities
- Native American Tribal Organizations (other than Federally recognized tribal governments)
- Faith-based or Community-based Organizations
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Institutions)

ɔreign Institutions

ɔn-domestic (non-U.S.) Entities (Foreign Institutions) **are** eligible to apply.

ɔn-domestic (non-U.S.) components of U.S. Organizations **are** eligible to apply.

ɔreign components, as defined in the *NIH Grants Policy Statement*, **are** allowed.

ɛquired Registrations

ɔplicant organizations

ɔplicant organizations must complete and maintain the following registrations as described in the SF 424 (R&R) Application Guide to be eligible apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or ɔre, so applicants should begin the registration process as soon as possible. The NIH Policy on Late Submission of Grant Applications states at failure to complete registrations in advance of a due date is not a valid reason for a late submission.

- Dun and Bradstreet Universal Numbering System (DUNS) - All registrations require that applicants be issued a DUNS number. After obtaining a DUNS number, applicants can begin both SAM and eRA Commons registrations. The same DUNS number must be used for all registrations, as well as on the grant application.
- System for Award Management (SAM) – Applicants must complete and maintain an active registration, which requires renewal at least annually. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.
    - NATO Commercial and Government Entity (NCAGE) Code – Foreign organizations must obtain an NCAGE code (in lieu of a CAGE code) in order to register in SAM.
- eRA Commons - Applicants must have an active DUNS number to register in eRA Commons. Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration, but all registrations must be in place by time of submission. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.

- Grants.gov – Applicants must have an active DUNS number and SAM registration in order to complete the Grants.gov registration.

ogram Directors/Principal Investigators (PD(s)/PI(s))

l PD(s)/PI(s) must have an eRA Commons account. PD(s)/PI(s) should work with their organizational officials to either create a new account or affiliate their existing account with the applicant organization in eRA Commons. If the PD/PI is also the organizational Signing Official, they must ıve two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

ligible Individuals (Program Director/Principal Investigator)

ıy individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Program rector(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with his/her organization to develop an application for support. dividuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for H support.

ɔr institutions/organizations proposing multiple PDs/PIs, visit the Multiple Program Director/Principal Investigator Policy and ıbmission details in the Senior/Key Person Profile (Expanded) Component of the SF424 (R&R) Application Guide.

Cost Sharing

ıis FOA does not require cost sharing as defined in the NIH Grants Policy Statement.

Additional Information on Eligibility

umber of Applications

ɔplicant organizations may submit more than one application, provided that each application is scientifically distinct.

ıe NIH will not accept duplicate or highly overlapping applications under review at the same time, per 2.3.7.4 Submission of Resubmission ɔplication. This means that the NIH will not accept:

- A new (A0) application that is submitted before issuance of the summary statement from the review of an overlapping new (A0) or resubmission (A1) application.
- A resubmission (A1) application that is submitted before issuance of the summary statement from the review of the previous new (A0) application.
- An application that has substantial overlap with another application pending appeal of initial peer review (see 2.3.9.4 Similar, Essentially Identical, or Identical Applications)

ection IV. Application and Submission Information

Requesting an Application Package

ıe application forms package specific to this opportunity must be accessed through ASSIST, Grants.gov Workspace or an institutional stem-to-system solution. Links to apply using ASSIST or Grants.gov Workspace are available in Part 1 of this FOA. See your dministrative office for instructions if you plan to use an institutional system-to-system solution.

Content and Form of Application Submission

is critical that applicants follow the instructions in the Research (R) Instructions in the SF424 (R&R) Application Guide except where structed in this funding opportunity announcement to do otherwise. Conformance to the requirements in the Application Guide is quired and strictly enforced. Applications that are out of compliance with these instructions may be delayed or not accepted for view.

etter of Intent

though a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it ıntains allows IC staff to estimate the potential review workload and plan the review.

/ the date listed in Part 1. Overview Information, prospective applicants are asked to submit a letter of intent that includes the following

ormation:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity

ıe letter of intent should be sent to:

illip J. Daschner, M.Sc.
ational Cancer Institute (NCI)
elephone: 240-276-6227
ax: 240-276-7867
nail: PD93u@nih.gov

age Limitations

l page limitations described in the SF424 Application Guide and the Table of Page Limits must be followed.

structions for Application Submission

ıe following section supplements the instructions found in the SF424 (R&R) Application Guide and should be used for preparing an application this FOA.

F424(R&R) Cover

l instructions in the SF424 (R&R) Application Guide must be followed.

F424(R&R) Project/Performance Site Locations

l instructions in the SF424 (R&R) Application Guide must be followed.

F424(R&R) Other Project Information

l instructions in the SF424 (R&R) Application Guide must be followed.

F424(R&R) Senior/Key Person Profile

l instructions in the SF424 (R&R) Application Guide must be followed.

&R or Modular Budget

l instructions in the SF424 (R&R) Application Guide must be followed.

&R Subaward Budget

l instructions in the SF424 (R&R) Application Guide must be followed.

HS 398 Cover Page Supplement

l instructions in the SF424 (R&R) Application Guide must be followed.

HS 398 Research Plan

l instructions in the SF424 (R&R) Application Guide must be followed, with the following additional instructions:

esource Sharing Plan: Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) plication Guide.

- All applications, regardless of the amount of direct costs requested for any one year, should address a Data Sharing Plan.

ppendix:

nly limited Appendix materials are allowed. Follow all instructions for the Appendix as described in the SF424 (R&R) Application uide.

HS Human Subjects and Clinical Trials Information

hen involving human subjects research, clinical research, and/or NIH-defined clinical trials (and when applicable, clinical trials research perience) follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the lowing additional instructions:

you answered “Yes” to the question “Are Human Subjects Involved?” on the R&R Other Project Information form, you must include at least one uman subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study** cord.

udy Record: PHS Human Subjects and Clinical Trials Information

l instructions in the SF424 (R&R) Application Guide must be followed.

elayed Onset Study

ote: Delayed onset does NOT apply to a study that can be described but will not start immediately (i.e., delayed start).All instructions in the F424 (R&R) Application Guide must be followed.

HS Assignment Request Form

l instructions in the SF424 (R&R) Application Guide must be followed.

oreign Institutions

oreign (non-U.S.) institutions must follow policies described in the NIH Grants Policy Statement, and procedures for foreign institutions described roughout the SF424 (R&R) Application Guide.

Unique Entity Identifier and System for Award Management (SAM)

ee Part 1. Section III.1 for information regarding the requirement for obtaining a unique entity identifier and for completing and maintaining active gistrations in System for Award Management (SAM), NATO Commercial and Government Entity (NCAGE) Code (if applicable), eRA Commons, id Grants.gov

Submission Dates and Times

art I. Overview Information contains information about Key Dates and times. Applicants are encouraged to submit applications before the due ite to ensure they have time to make any application corrections that might be necessary for successful submission. When a submission date ls on a weekend or Federal holiday, the application deadline is automatically extended to the next business day.

rganizations must submit applications to Grants.gov (the online portal to find and apply for grants across all Federal agencies). Applicants must en complete the submission process by tracking the status of the application in the eRA Commons, NIH’s electronic system for grants lministration. NIH and Grants.gov systems check the application against many of the application instructions upon submission. Errors must be rrected and a changed/corrected application must be submitted to Grants.gov on or before the application due date and time. If a anged/Corrected application is submitted after the deadline, the application will be considered late. Applications that miss the due date and ne are subjected to the NIH Policy on Late Application Submission.

oplicants are responsible for viewing their application before the due date in the eRA Commons to ensure accurate and successful submission.

formation on the submission process and a definition of on-time submission are provided in the SF424 (R&R) Application Guide.

Intergovernmental Review (E.O. 12372)

is initiative is not subject to intergovernmental review.

Funding Restrictions

l NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement.

e-award costs are allowable only as described in the NIH Grants Policy Statement.

Other Submission Requirements and Information

oplications must be submitted electronically following the instructions described in the SF424 (R&R) Application Guide. Paper applications will t be accepted.

oplicants must complete all required registrations before the application due date. Section III. Eligibility Information contains information about gistration.

r assistance with your electronic application or for more information on the electronic submission process, visit How to Apply – Application uide. If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must low the Dealing with System Issues guidance. For assistance with application submission, contact the Application Submission Contacts in ection VII.

Important reminders:

All PD(s)/PI(s) must include their eRA Commons ID in the Credential field of the Senior/Key Person Profile Component of the SF424(R&R) Application Package. Failure to register in the Commons and to include a valid PD/PI Commons ID in the credential field will prevent the successful submission of an electronic application to NIH. See Section III of this FOA for information on registration requirements.

The applicant organization must ensure that the DUNS number it provides on the application is the same number used in the organization's profile in the eRA Commons and for the System for Award Management. Additional information may be found in the SF424 (R&R) Application Guide.

See more tips for avoiding common errors.

oon receipt, applications will be evaluated for completeness and compliance with application instructions by the Center for Scientific Review and sponsiveness by components of participating organizations, NIH. Applications that are incomplete, non-compliant and/or nonresponsive will not e reviewed.

equests of $500,000 or more for direct costs in any year

oplicants requesting $500,000 or more in direct costs in any year (excluding consortium F&A) must contact a Scientific/ Research Contact at ast 6 weeks before submitting the application and follow the Policy on the Acceptance for Review of Unsolicited Applications that Request 00,000 or More in Direct Costs as described in the SF424 (R&R) Application Guide.

ost Submission Materials

oplicants are required to follow the instructions for post-submission materials, as described in the policy. Any instructions provided here are in ldition to the instructions in the policy.

ection V. Application Review Information

Criteria

nly the review criteria described below will be considered in the review process. Applications submitted to the NIH in support of the NIH mission e evaluated for scientific and technical merit through the NIH peer review system.

verall Impact

eviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence the research field(s) involved, in consideration of the following review criteria and additional review criteria (as applicable for the project oposed).

cored Review Criteria

eviewers will consider each of the review criteria below in the determination of scientific merit, and give a separate score for each. An application es not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not novative may be essential to advance a field.

Significance

Does the project address an important problem or a critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

ecific for this FOA: How well does the project target and explore critical host-microbe interactions that modulate tumor immunity? How well es the project employ and test novel methods and approaches for developing probiotic organisms or their products to enhance anti-tumor munity? How well are adequate resources and scientific expertise demonstrated to rigorously identify and test host-microbe signaling pathways portant for modulating anti-tumor immunity?

Investigator(s)

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

Innovation

Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

pecific for this FOA: How well does the project identify novel tumor-promoting or probiotic organisms, or their molecular products? How likely e novel host-microbe signaling pathways to be identified and their molecular components characterized? Are novel models developed and nployed to identify immune-modulating microbial interactions?

Approach

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

If the project involves human subjects and/or NIH-defined clinical research, are the plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion or exclusion of individuals of all ages (including children and older adults), justified in terms of the scientific goals and research strategy proposed?

pecific for this FOA: How well does the project employ relevant models to identify and characterize microbial signaling pathways that alter mor immunity? How well are state of the art bioinformatic analyses used to integrate host and microbe metabolomics, proteomics, and olecular immunology data sets to establish an immunomodulatory role for tumor-associated microbes? How well are human samples used to amine and validate findings and increase clinical relevance?

Environment

Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

dditional Review Criteria

s applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in oviding an overall impact score, but will not give separate scores for these items.

Protections for Human Subjects

For research that involves human subjects but does not involve one of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials. For additional information on review of the Human Subjects section, please refer to the Guidelines for the Review of Human Subjects.

Inclusion of Women, Minorities, and Individuals Across the Lifespan

When the proposed project involves human subjects and/or NIH-defined clinical research, the committee will evaluate the proposed plans for the inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion (or exclusion) of individuals of all ages (including children and older adults) to determine if it is justified in terms of the scientific goals and research strategy proposed. For additional information on review of the Inclusion section, please refer to the Guidelines for the Review of Inclusion in Clinical Research.

Vertebrate Animals

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following criteria: (1) description of proposed procedures involving animals, including species, strains, ages, sex, and total number to be used; (2) justifications for the use of animals versus alternative models and for the appropriateness of the species proposed; (3) interventions to minimize discomfort, distress, pain and injury; and (4) justification for euthanasia method if NOT consistent with the AVMA Guidelines for the Euthanasia of Animals. Reviewers will assess the use of chimpanzees as they would any other application proposing the use of vertebrate animals. For additional information on review of the Vertebrate Animals section, please refer to the Worksheet for Review of the Vertebrate Animal Section.

Biohazards

Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Resubmissions

›r Resubmissions, the committee will evaluate the application as now presented, taking into consideration the responses to comments from the evious scientific review group and changes made to the project.

Renewals

›r Renewals, the committee will consider the progress made in the last funding period.

Revisions

›t Applicable

dditional Review Considerations

› applicable for the project proposed, reviewers will consider each of the following items, but will not give scores for these items, and should not nsider them in providing an overall impact score.

Applications from Foreign Organizations

Reviewers will assess whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions that exist in other countries and either are not readily available in the United States or augment existing U.S. resources.

Select Agent Research

Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans

eviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are asonable: (1) Data Sharing Plan; (2) Sharing Model Organisms; and (3) Genomic Data Sharing Plan (GDS).

Authentication of Key Biological and/or Chemical Resources:

For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.

Budget and Period of Support

Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

Review and Selection Process

›plications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) convened by Center for Scientific eview (CSR), in accordance with NIH peer review policy and procedures, using the stated review criteria. Assignment to a Scientific Review roup will be shown in the eRA Commons.

› part of the scientific peer review, all applications will receive a written critique.

pplications may undergo a selection process in which only those applications deemed to have the highest scientific and technical merit enerally the top half of applications under review) will be discussed and assigned an overall impact score.

pplications will be assigned on the basis of established PHS referral guidelines to the appropriate NIH Institute or Center. Applications ll compete for available funds with all other recommended applications submitted in response to this FOA. Following initial peer view, recommended applications will receive a second level of review by the appropriate national Advisory Council or Board. The llowing will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.

Anticipated Announcement and Award Dates

ter the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the eRA ommons. Refer to Part 1 for dates for peer review, advisory council review, and earliest start date.

formation regarding the disposition of applications is available in the NIH Grants Policy Statement.

ection VI. Award Administration Information

Award Notices

the application is under consideration for funding, NIH will request "just-in-time" information from the applicant as described in the NIH Grants olicy Statement.

formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization for successful applications. The NoA gned by the grants management officer is the authorizing document and will be sent via email to the recipient's business official.

ecipients must comply with any funding restrictions described in Section IV.5. Funding Restrictions. Selection of an application for award is not authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed ly to the extent considered allowable pre-award costs.

y application awarded in response to this FOA will be subject to terms and conditions found on the Award Conditions and Information for NIH rants website. This includes any recent legislation and policy applicable to awards that is highlighted on this website.

stitutional Review Board or Independent Ethics Committee Approval: Recipient institutions must ensure that protocols are reviewed by their IRB IEC. To help ensure the safety of participants enrolled in NIH-funded studies, the recipient must provide NIH copies of documents related to all ajor changes in the status of ongoing protocols.

Administrative and National Policy Requirements

l NIH grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the NoA. For these terms of award, see the H Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General and Part II: Terms and Conditions of NIH rant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Recipients, and Activities, including of note, but not limited to:

- Federalwide Research Terms and Conditions
- Prohibition on Certain Telecommunications and Video Surveillance Services or Equipment
- Acknowledgment of Federal Funding

a recipient is successful and receives a Notice of Award, in accepting the award, the recipient agrees that any activities under the award are bject to all provisions currently in effect or implemented during the period of the award, other Department regulations and policies in effect at the ne of the award, and applicable statutory provisions.

ecipients of federal financial assistance (FFA) from HHS must administer their programs in compliance with federal civil rights laws that prohibit scrimination on the basis of race, color, national origin, disability, age and, in some circumstances, religion, conscience, and sex. This includes suring programs are accessible to persons with limited English proficiency. The HHS Office for Civil Rights provides guidance on complying th civil rights laws enforced by HHS. Please see https://www.hhs.gov/civil-rights/for-providers/provider-obligations/index.html and tp://www.hhs.gov/ocr/civilrights/understanding/section1557/index.html.

HS recognizes that research projects are often limited in scope for many reasons that are nondiscriminatory, such as the principal investigator's ientific interest, funding limitations, recruitment requirements, and other considerations. Thus, criteria in research protocols that target or

clude certain populations are warranted where nondiscriminatory justifications establish that such criteria are appropriate with respect to the alth or safety of the subjects, the scientific study design, or the purpose of the research. For additional guidance regarding how the provisions ply to NIH grant programs, please contact the Scientific/Research Contact that is identified in Section VII under Agency Contacts of this FOA.

- Recipients of FFA must ensure that their programs are accessible to persons with limited English proficiency. HHS provides guidance to recipients of FFA on meeting their legal obligation to take reasonable steps to provide meaningful access to their programs by persons with limited English proficiency. Please see https://www.hhs.gov/civil-rights/for-individuals/special-topics/limited-english-proficiency/fact-sheet-guidance/index.html and https://www.lep.gov. For further guidance on providing culturally and linguistically appropriate services, recipients should review the National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care at https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=53.
- Recipients of FFA also have specific legal obligations for serving qualified individuals with disabilities. Please see http://www.hhs.gov/ocr/civilrights/understanding/disability/index.html.
- HHS funded health and education programs must be administered in an environment free of sexual harassment. Please see https://www.hhs.gov/civil-rights/for-individuals/sex-discrimination/index.html; https://www2.ed.gov/about/offices/list/ocr/docs/shguide.html; and https://www.eeoc.gov/eeoc/publications/upload/fs-sex.pdf. For information about NIH's commitment to supporting a safe and respectful work environment, who to contact with questions or concerns, and what NIH's expectations are for institutions and the individuals supported on NIH-funded awards, please see https://grants.nih.gov/grants/policy/harassment.htm.
- Recipients of FFA must also administer their programs in compliance with applicable federal religious nondiscrimination laws and applicable federal conscience protection and associated anti-discrimination laws. Collectively, these laws prohibit exclusion, adverse treatment, coercion, or other discrimination against persons or entities on the basis of their consciences, religious beliefs, or moral convictions. Please see https://www.hhs.gov/conscience/conscience-protections/index.html and https://www.hhs.gov/conscience/religious-freedom/index.html.

ease contact the HHS Office for Civil Rights for more information about obligations and prohibitions under federal civil rights laws at tps://www.hhs.gov/ocr/about-us/contact-us/index.html or call 1-800-368-1019 or TDD 1-800-537-7697.

accordance with the statutory provisions contained in Section 872 of the Duncan Hunter National Defense Authorization Act of Fiscal Year 2009 ublic Law 110-417), NIH awards will be subject to the Federal Awardee Performance and Integrity Information System (FAPIIS) requirements. APIIS requires Federal award making officials to review and consider information about an applicant in the designated integrity and performance stem (currently FAPIIS) prior to making an award. An applicant, at its option, may review information in the designated integrity and rformance systems accessible through FAPIIS and comment on any information about itself that a Federal agency previously entered and is rrently in FAPIIS. The Federal awarding agency will consider any comments by the applicant, in addition to other information in FAPIIS, in aking a judgement about the applicant's integrity, business ethics, and record of performance under Federal awards when completing the review risk posed by applicants as described in 45 CFR Part 75.205 and 2 CFR Part 200.206 "Federal awarding agency review of risk posed by plicants." This provision will apply to all NIH grants and cooperative agreements except fellowships.

ooperative Agreement Terms and Conditions of Award

ot Applicable

Reporting

hen multiple years are involved, recipients will be required to submit the Research Performance Progress Report (RPPR) annually and financial atements as required in the NIH Grants Policy Statement.

final RPPR, invention statement, and the expenditure data portion of the Federal Financial Report are required for closeout of an award, as scribed in the NIH Grants Policy Statement. NIH FOAs outline intended research goals and objectives. Post award, NIH will review and easure performance based on the details and outcomes that are shared within the RPPR, as described at 45 CFR Part 75.301 and 2 CFR Part 0.301.

ne Federal Funding Accountability and Transparency Act of 2006 (Transparency Act), includes a requirement for recipients of Federal grants to port information about first-tier subawards and executive compensation under Federal assistance awards issued in FY2011 or later. All cipients of applicable NIH grants and cooperative agreements are required to report to the Federal Subaward Reporting System (FSRS) ailable at www.fsrs.gov on all subawards over $25,000. See the NIH Grants Policy Statement for additional information on this reporting quirement.

accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently tive Federal grants, cooperative agreements, and procurement contracts from all Federal awarding agencies with a cumulative total value eater than $10,000,000 for any period of time during the period of performance of a Federal award, must report and maintain the currency of

formation reported in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the ward or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make miannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and rformance system (currently FAPIIS). This is a statutory requirement under section 872 of Public Law 110-417, as amended (41 U.S.C. 2313). s required by section 3010 of Public Law 111-212, all information posted in the designated integrity and performance system on or after April 15, 011, except past performance reviews required for Federal procurement contracts, will be publicly available. Full reporting requirements and ocedures are found in Appendix XII to 45 CFR Part 75 – Award Term and Conditions for Recipient Integrity and Performance Matters.

ection VII. Agency Contacts

e encourage inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants.

pplication Submission Contacts

RA Service Desk (Questions regarding ASSIST, eRA Commons, application errors and warnings, documenting system problems that reaten submission by the due date, and post-submission issues)

nding Help Online: http://grants.nih.gov/support/ (preferred method of contact)
elephone: 301-402-7469 or 866-504-9552 (Toll Free)

eneral Grants Information (Questions regarding application instructions, application processes, and NIH grant resources)
nail: GrantsInfo@nih.gov (preferred method of contact)
elephone: 301-945-7573

rants.gov Customer Support (Questions regarding Grants.gov registration and Workspace)
ontact Center Telephone: 800-518-4726
nail: support@grants.gov

cientific/Research Contact(s)

illip J. Daschner, M.Sc.
ational Cancer Institute
elephone: 240-276-6227
nail: PD93u@nih.gov

oung S. Kim, Ph.D.
ational Cancer Institute
elephone: 240-276-7115
nail: yk47s@nih.gov

eer Review Contact(s)

xamine your eRA Commons account for review assignment and contact information (information appears two weeks after the submission due ate).

inancial/Grants Management Contact(s)

utema Nyankale
ational Cancer Institute
elephone: 240-276-5987
nail: mutema.nyankale@nih.gov

ection VIII. Other Information

ecently issued trans-NIH policy notices may affect your application submission. A full list of policy notices published by NIH is provided in the H Guide for Grants and Contracts. All awards are subject to the terms and conditions, cost principles, and other considerations described in the H Grants Policy Statement.

uthority and Regulations

wards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under ederal Regulations 42 CFR Part 52 and 45 CFR Part 75.

Weekly TOC for this Announcement
NIH Funding Opportunities and Notices

National Institutes of Health
Office of Extramural Research

Department of Health
and Human Services (HHS)

USA.gov
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Note: For help accessing PDF, RTF, MS Word, Excel, PowerPoint, Audio or Video files, see Help Downloading Files.