Development and Application of Ophthalmic Imaging Technologies to Advance Our Understanding of Systemic Diseases Research Opportunity Announcement

Overview Information

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	This Other Transactions Research Opportunity Announcement (OT ROA) is to support the development and application of ophthalmic imaging technologies to advance our understanding of systemic diseases (hereinafter referred to as Oculomics). This research opportunity will be administered by the NIH Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), Office of Strategic Coordination (OSC), also known as the Common Fund.
Research Opportunity Title	Development and Application of Ophthalmic Imaging Technologies to Advance Our Understanding of Systemic Diseases (OT2)
Activity Code	This funding opportunity will use the Other Transactions Authority (OTA) governed by 42 U.S. Code § 282 (n)(1)(b). OT awards are not grants, cooperative agreements or contracts and use an OTA, provided by law. Policies and terms for individual OTs may vary between awards. Each award is therefore issued with a specific agreement, which is negotiated with the recipient and may be expanded, modified, partnered, not supported, or later discontinued based on program needs, changing research landscape, performance and or availability of funds.
Research Opportunity Announcement (ROA) Number	**OTA-24-006**
Related Notices	
Research Opportunity Purpose	The purpose of this announcement is to invite applications from eligible organizations to support the development and application of novel, noninvasive ocular imaging technologies and associated machine learning algorithms, as appropriate, to identify systemic disease biomarkers with high sensitivity and specificity for early disease detection, classification, and monitoring.
Key Dates	**Release Date of this Research Opportunity Announcement:** March 11, 2024 **Letters of Intent (LOI) Due Date:** April 16, 2024, by 5:00 PM local time of applicant organization. ***LOIs are required. Only invited applicants meeting LOI screening criteria will be eligible to submit a full application.*** **Notification of LOI Screening results** will be provided to applicants by April 25, 2024. **Application Due Date:** May 27, 2024, by 5:00 PM local time of applicant organization. Late applications to this ROA will not be accepted. **Award Negotiations:** to begin on or about June 17, 2024. Applicants are expected to respond to written inquiries, attend videoconferences

	or teleconferences as requested. **Earliest Start Date:** August 1, 2024 **Informational Webinar**: Webinar information will be posted on. https://commonfund.nih.gov/venture/oculomics

Agency Contacts

NIH encourages inquiries concerning this announcement and welcomes the opportunity to answer questions from potential applicants.

Scientific Contacts	Tony D. Gover, Ph.D. Program Director National Eye Institute (NEI) Telephone: (301) 529-7370 Email: tony.gover@nih.gov Mary Ann Wu, Ph.D. Other Transactions Program Official Office of Strategic Coordination (OSC), Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI), Office of the Director (OD), NIH Email: maryann.wu@nih.gov
Financial/Agreements Officer Contact	Erna Petrich Other Transactions Agreements Officer Office of Strategic Coordination (OSC), Division of Program Coordination, Planning and Strategic Initiatives (DPCPSI), Office of the Director (OD), NIH Email: DOTM@nih.gov (Subject line must include "OCULOMICS")

Background:

This initiative is part of the Venture Program, a new effort within the Common Fund to support novel, short-term, bold initiatives that have the potential for significant impact in biomedical and behavioral research. Venture initiatives are innovative and nimble, introducing additional flexibility for the Common Fund to tackle a wider variety of research topics. Venture initiatives embrace scientific risk and have strong potential to accelerate science rapidly. These short-term initiatives will be supported for a maximum of 3 years and will include clearly defined goals and milestones to facilitate rigorous measurement of research progress. Each Venture initiative is expected to produce specific deliverables, which can be new knowledge, methods, technologies, or devices.

This OT ROA is to support the NIH Common Fund Venture Initiative for Oculomics. Oculomics will have a significant impact on early biomarker detection of systemic diseases even before the onset of symptoms and will help clinicians with early disease detection, diagnosis, risk assessment, disease progression, and will accelerate therapeutic development by defining endpoints for clinical trials.

Ocular imaging technologies provide a unique opportunity for direct *in-vivo* and noninvasive assessment of systemic diseases, including neurodegenerative, cardiovascular, inflammatory, metabolic, diabetes, hypertension, and renal diseases. Optical Coherence Tomography (OCT), OCT-Angiography (OCTA), and color fundus photography of the retina have demonstrated promise in detecting biomarkers associated with a broad array of diseases. Current research in this area typically utilizes commercial retinal imaging

equipment, large prospective cohorts followed over several years, and machine learning algorithms to identify systemic disease biomarkers. Unfortunately, several of the retinal biomarkers identified for systemic diseases lack specificity and sensitivity, making the clinical utility of these biomarkers unclear.

Numerous advanced imaging techniques have been developed in recent years that provide superior image resolution, signal-to-noise, and image depth compared to classical OCT, OCTA, and fundus imaging. Imaging techniques have also been developed to provide the ability for functional measurements and substance identification. These techniques can further provide information regarding water content, protein, lipid, collagen/elastin, cellular activity, redox state, metabolic rates of oxygen, and blood flow. Example imaging technologies that have been underutilized or not used in the field of oculomics include adaptive optics OCT (AO-OCT), AO two-photon microscopy, scanning laser ophthalmoscope, spectral domain-OCT, super-resolution ultrasound localization microscopy, visible-light OCT, opto-acoustic techniques, terahertz imaging, and retinal hyperspectral imaging. These noninvasive imaging technologies, and several others, when combined with advanced machine learning algorithms, have the potential to provide superior biomarker identification for a broad range of systemic diseases and with the required sensitivity and specificity to have clinical utility.

The anticipated outcome of proposed efforts will be the development, application and initial translation of new imaging technologies and machine learning algorithms for the detection and identification of novel systemic disease biomarkers. By the end of the three-year period of performance, developed technologies should be demonstrated in appropriate animal models of disease or human patients. This ROA is intended to support innovative ophthalmic imaging technology development for advancing our understanding of systemic diseases that can lead to new methods for disease prevention, detection, diagnosis, and treatment. Technologies may include, but are not limited to, novel ophthalmic imaging approaches as well as AI/ML algorithms and computational models.

This ROA strongly encourages applicants to form multidisciplinary teams that consist of academic/industry experts relevant to the research plan (i.e., device developers, imaging bioengineers, vision scientist and clinicians, and biomedical scientist and clinicians with expertise in specific systemic disease areas).

The Oculomics initiative will utilize Other Transaction Awards. OT awards provide budgetary flexibility and accountability that are crucial to the multidisciplinary, milestone-driven projects that are anticipated for funding. NIH will provide funds on a milestone-driven basis assessed at least annually, and as agreed upon and included in the Terms and Conditions of Award. Funds may be increased, extended, reallocated, recovered or terminated in cases where unexpected findings, bottlenecks or roadblocks may modify plans or prevent completion of a project attempting to develop innovative oculomics technologies. Certain milestones may be designated as “go/no-go” milestones and must be successfully achieved by the specified timepoint for project continuation; failure to meet “go/no-go” milestones will be basis for project termination. See Section 9 about special award terms and additional information.

Plan for Enhancing Diverse Perspectives:

The Oculomics initiative recognizes that diverse teams working together and capitalizing on innovative ideas and distinct perspectives outperform homogeneous teams. There are many benefits that flow from a diverse scientific workforce, including fostering scientific innovation, enhancing global competitiveness, contributing to robust learning environments, improving the quality of the research, advancing the likelihood that underserved populations participate in, and benefit from, research and enhancing public trust (see, e.g., Notice of NIH's Interest in Diversity, NOT-OD-20-031). To support the best science, this initiative encourages inclusivity in research. Examples of structures that promote diverse perspectives include but are not limited to:

- Participation of investigators from diverse backgrounds, including groups historically

underrepresented in the biomedical, behavioral, and clinical research workforce (see NOT-OD-20-031), such as underrepresented racial and ethnic groups, those with disabilities, those from disadvantaged backgrounds, and women.

- Engagement with different types of institutions and organizations (e.g., research-intensive and research active, undergraduate-focused, minority-serving, community-based).
- Partnerships that may enhance geographic and regional diversity.
- Use of the project infrastructure (i.e., research and structure) to support career-enhancing research opportunities for diverse junior, early-, and mid-career researchers.
- Training and mentoring opportunities encouraging participation of students, postdoctoral researchers, and co-investigators from diverse backgrounds.
- Transdisciplinary collaborations that require unique expertise and/or solicit diverse perspectives to address research questions.
- Inclusion of community-based partners to ensure alignment of research goals and activities with community values.

Objective Review: NIH will convene an appropriate review group to evaluate applications. See the Objective Review section of this opportunity for further details.

Eligibility: See the Eligibility section of this opportunity.

Application budget: The Common Fund may allocate up to $4,800,000 total (direct + F&A) costs per year for up to three years for the Venture Oculomics Initiative. The maximum total costs anticipated per year for each award is $1,600,000. These awards are contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications.

The application budget should reflect the proposed activities and personnel. The OT mechanism allows for significant flexibility to make budget adjustments as needed to meet NIH's programmatic priorities. Award levels may increase or decrease over time based on funding availability, establishment or termination of sub-awards, recipient performance, and other programmatic priorities. It is anticipated that funds will be allocated on a yearly basis.

Cost share is not required but may be proposed. However, including a cost share will not impact an applicant's chances of selection.

Anticipated number of Awards: The Common Fund Venture Oculomics Initiative anticipates making three awards.

Award Project Duration: Project duration is anticipated to be up to three (3) years, subject to program needs and availability of funds. Research activities and the associated milestones may be shortened or extended as needed within that period. Workplans for research activities and the associated milestones will be negotiated with the NIH staff annually at a minimum.

Authority: Other Transactions awards will be made pursuant to current authorizing legislation, including Section 402(n) of the Public Health Service Act, 42 U.S.C. 282(n), as amended.

Outline of this Opportunity

1. Requirements – Oculomics Initiative
2. Eligible Organizations
3. Eligibility Requirements
4. Multiple Principal Investigators and Partnerships among Applicant's Institutions
5. Financial and Risk Assessment
6. Cost Sharing
7. Developing Applications
8. Objective Review
9. Special Award Terms and Information

1. Requirements – Oculomics Initiative

The outcome of proposed efforts will be the development and application of new imaging technologies for the detection and identification of novel systemic disease biomarker(s). This initiative encourages but does not require the development of machine learning algorithms to support the application of novel imaging technologies. By the end of the three-year period of performance, developed technologies should be demonstrated in appropriate animal models of disease or human patients. Products from this initiative are expected to be matured for future clinical validation. Applicants must address at least one systemic disease in neurology, cardiovascular, or metabolic diseases/disorders. Applications that focus on more than one systemic disease/disorder, more than one area of disease/disorder or utilize multiple imaging modalities are encouraged. This ROA is not intended to support expansion of previous or ongoing efforts that currently utilize OCT, OCTA or fundus photography for detection of systemic diseases. However, applications proposing new efforts that utilize OCT, OCTA, or fundus photography and can demonstrate a novel approach and/or clear technological advancement over existing technology may apply.

2. Eligible Organizations

Non-domestic (non-U.S.) Entities (Foreign applicants) **are not** eligible to apply.

Non-domestic components of domestic organizations **are not** eligible.

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

Any public or private non-domestic entity is ineligible to apply for this program as a primary applicant. Additionally, any non-domestic components of U.S. Organizations are ineligible to apply for this program as a primary applicant. Public or private non-domestic entities and non-domestic components of U.S. Organizations are eligible to be listed as sub-contractors/recipients, so long as, they are not excluded from applying for Federal programs throughout the U.S. Government (unless otherwise noted) and from receiving certain types of Federal financial and nonfinancial assistance and benefits.

A Letter of Intent (LOI) is required for this initiative (see Section 7.2). Only applicant organizations that have submitted a LOI and have been invited to submit a full application are eligible to apply. Applicant organizations may submit more than one LOI and subsequently may be invited to submit more than one application, provided that each project is scientifically distinct. Individuals not affiliated with an organization, or those who want to submit an application independent of their current organization, **may not** apply.

The following entities are eligible to apply under this ROA:

Higher 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)

Nonprofits 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)
- Faith-based or Community-based Organizations
- Regional Organizations

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

Governments
- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- American Indian/Native American Tribal Governments (Federally Recognized)
- American Indian/Native American Tribal Governments (Other than Federally Recognized)
- Eligible Agencies of the Federal Government
- U.S. Territory or Possession

Other
- Independent School Districts
- Native American Tribal Organizations (other than Federally recognized tribal governments)

3. Eligibility Requirements

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the Principal Investigator(s) (PI(s)) is invited to work with their organization to develop an application for support. Individuals from diverse backgrounds, including those from underrepresented racial and ethnic groups, individuals with disabilities, and women are always encouraged to apply for NIH support. See “Reminder: Notice of NIH's Encouragement of Applications Supporting Individuals from Underrepresented Ethnic and Racial Groups as well as

Individuals with Disabilities", NOT-OD-22-019.

This ROA strongly encourages applicants to form multidisciplinary teams that consist of academic/industry experts relevant to the research plan (i.e., device developers, imaging bioengineers, vision scientist and clinicians, and biomedical scientist and clinicians with expertise in specific systemic disease areas).

4. Multiple Principal Investigators and Partnerships among Applicants' Institutions

More than one individual may be named as Principal Investigator (PI) in the application. One individual must be identified as the contact Principal Investigator. The contact PI and all other individual PIs must each commit at least 10% level of effort to the proposed project. The contact Principal Investigator must be employed by or affiliated with the applicant organization. ***If a multiple Principal Investigator (MPI) application is submitted, an MPI Leadership plan is required.***

Partnerships among institutions with investigators having complementary skills and expertise to meet the requirements of this ROA are not required but are allowed.

5. Financial and Risk Assessment

Applicants may be subject to financial analysis and risk assessment conducted by NIH staff.

6. Cost Sharing

Cost Sharing is not required but may be proposed. Those proposing to develop commercial applications or who are using other state or government resources may consider identifying a cost share percentage. Applicants may voluntarily choose to propose a financial plan that includes non-federal resources. The budget submission must clearly identify and justify the use of these resources. Any voluntary cost share must be supported in the application by including a letter of support from the providing organization(s)/individual(s). Inclusion of cost sharing will have no influence in application selection.

7. Developing Applications

7.1 Application Submission Instructions

Complete applications must be submitted under **OTA-24-006** via NIH eRA Commons ASSIST no later than the "***Application Due Date***" shown at the top of this notice, by 5 PM local time of applicant organization.

Late applications submitted to this ROA will not be accepted.

For further information, please consult the FAQ page: https://commonfund.nih.gov/venture/oculomics/faqs

Questions about the scientific scope of this announcement should be addressed to: oculomics@od.nih.gov

Letters of Intent (LOIs), due by the "***Letters of Intent Due Date***" shown at the top of this notice, **are required.**

7.2 Letter of Intent

Interested applicants **must** submit a Letter of Intent (LOI) and supporting documentation. LOIs will only be accepted from entities listed in the Eligible Organizations section of this Announcement, who meet the criteria listed in the Eligibility Requirements. LOIs submitted from organizations not included in the Eligibility section will not be reviewed. LOIs will undergo an administrative review by NIH staff. Applications that are deemed non-responsive or incomplete will not be reviewed. LOIs deemed responsive will undergo review as described below.

The LOI and supporting documentation must be submitted as two separate PDFs. The LOI must be no more than 5 pages with sections outlining the following:

- **Project Narrative** (five-page limit): The Project Narrative page limit applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings) used to describe the project. Inclusion of URLs in the Project Narrative are prohibited and may result in administrative withdrawal of the LOI. The Project Narrative should include the following:
    - **Research Idea:** Describe how the proposed project relates to the Oculomics Venture Initiative and which biomarkers and systemic disease(s) will be investigated. Describe the ideas and scientific rationale for the proposed ocular imaging technologies and computational algorithms for the specific disease(s) of study; include relevant literature citations.
    - **Research Strategy:** Concisely state the project's specific aims, objectives, and major milestones. Briefly describe the experimental approach, including study design and endpoints/outcome measures.
    - **Personnel:** Briefly state the qualifications of the PI, PM/PD and other key personnel to perform the research and development of non-invasive imaging technologies and machine learning algorithms for identification of novel and clinically relevant biomarkers. Note any special expertise in ophthalmology/vision science, the systemic disease(s) of focus, engineering, and computational scientists.
    - **Impact:** Describe how the proposed work will have an impact on improving screening, diagnosis, and monitoring of systemic disease(s).

- **Supporting Documentation:** The items to be included as supporting documentation are limited to the following:
    - **Personnel:** List of Key Personnel, their email address, their institutional affiliation and role in the project.
    - **References Cited:** List the references cited (including URLs if available) in the Project Narrative using a standard reference format that includes the full citation (i.e., author[s], year published, reference title, and reference source, including volume, chapter, page numbers, and publisher, as appropriate).
    - **Key Personnel Biographical Sketches** (two-page limit per individual): All biographical sketches should be uploaded as a single combined file. Biographical sketches should be used to demonstrate background and expertise through education, positions, publications, and previous work accomplished in the previous ten years.

Letter of Intent Screening:

- To determine the technical merits of the Project Narrative and the relevance to the purpose of the Oculomics Venture Initiative, Project Narratives will be screened by NIH staff based on the following criteria:
    - **Research Idea:** The degree to which the project addresses the goal of the Oculomics Venture

Initiative. The degree to which the proposed imaging technology demonstrates a clear technological advancement from previous efforts. How well the scientific rationale is supported.
    - **Research Strategy:** How well the specific aims, objectives, and milestones are likely to accomplish the goals stated in the LOI.
    - **Personnel:** How the background and experience of the PI and other key personnel are appropriate to successfully complete the proposed development effort.
    - **Impact:** The degree to which the proposed development effort, if successful, will have an impact on accelerating the movement of promising diagnostic technologies into clinical application and the impact these new technologies will have on disease screening, diagnosis, and monitoring.

- **Notification of Letter of Intent Screening Results:**
    - Following the Letter of Intent screening, PIs will be notified by the "Notification of LOI Screening results" date shown at the top of this notice as to whether they are invited to submit full applications or not; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their Project Narrative.

Letters of intent must be submitted by email as two PDF attachments to oculomics@od.nih.gov. LOIs submitted by other means will not be considered.

7.3 Full Application

Only applicants that have submitted an LOI and have been invited to submit a full application are eligible to apply. Applications will only be accepted from entities listed in the Eligible Organizations section of this Announcement, who meet the criteria listed in the Eligibility Requirements. Applications submitted from organizations not included in the Eligibility section will not be reviewed. Applications must be prepared and submitted using NIH's eRA ASSIST. Complete applications must be submitted by the Recipient Business Official (RBO). The organization must be registered in eRA Commons with one person designated as the contact Principal Investigator (PI) and one person designated as the RBO. Registration process can take a long time, so applicants should begin the registration process as soon as possible.

Failure to complete registrations in advance of the due date is not a valid reason for a late submission. The RBO's signature certifies that the applicant has the ability to provide appropriate administrative and scientific oversight of the project and agrees to be fully accountable for the appropriate use of any funds awarded and for the performance of the OT award-supported project or activities resulting from the application.

Application Format
Applications must be prepared using 11-point font with 1" margins and be single- spaced. Use of graphics and images is allowed, although applications deemed to be using images to bypass the font and margin requirements may be administratively withdrawn. The use of hyperlinks (outside of published literature citations, USPTO links or biosketch publication list sites) is strictly prohibited.

Full applications must include the following components. Do not include additional project data, images, graphics, etc. in sections other than Research Strategy to circumvent page limits. (Page limits in parentheses):

- **Abstract** (1 page)**:** Provide a summary of the planned activities and approaches and key achievable goals.

- **Specific Aims** (1 page)**:** Describe the specific aims and objectives the application proposes to achieve.

- **Project Information Summary** (3 pages): Provide the information about (note: do not upload this into the "Cover Letter Attachment" field in the ASSIST form but provide it as part of the Attachments section in the form):
  - Project Title
  - Number and title of this Research Opportunity Announcement
  - Principal Investigator(s) first and last name, title, institution, mailing address, email address, and phone number. If multiple Principal Investigators are named, the Contact Principal Investigator must be clearly identified.
  - Name and address of the submitting organization and department, if any, with the organizational Unique Entity Identifier (UEI) number and employment identification number (EIN) provided.
  - Recipient Business Official/Signing Official first and last name, title, institution, mailing address, email address and phone number.
  - Proposed budgets per year for 3 years (direct, indirect and total costs).
  - Proposed project period dates.
  - Full names (last name, first name) of all key personnel, email address, institutional affiliation, title, and percent effort.
  - Identify if the work involves human subjects and/or vertebrate animals.
  - Copy of the "Invitation to Submit" email

- **Research Strategy** (12 pages)**:** Describe how the project will lead to the development and application of new noninvasive ocular imaging technologies and associated machine learning algorithms (if applicable) to identify systemic disease biomarkers with high sensitivity and specificity. The research strategy must include:
  - Rationale and detailed description of the imaging technology being developed.
  - Scientific rationale for the type of imaging or biomarker being studied.
  - Preliminary data that supports the proposed effort (cite relevant literature).
  - Describe the experimental design, methods, and expected outcome measures.
  - Provide detailed description and rational for any animal models of disease utilized in the application.
  - Address potential pitfalls and present alternative methods and approaches.
  - Advantages and strengths of the proposed approaches.
  - Describe how the proposed work will have an impact on improving screening, diagnosis, and monitoring of systemic disease(s) and how the work will produce an innovative product.

- **Intellectual Property (IP) Strategy** (1 pages): Applicants should describe the IP landscape surrounding their diagnostic. This should include any known constraints that could impede the development of their diagnostic (e.g., certain restrictions under transfer or sharing agreements, applicants' previous or present IP filings and publications, similar technologies that are under patent and/or on the market, etc.) and how these issues could be addressed as appropriate and consistent with achieving the goals of the program. If patents pertinent to the diagnostic being developed under this application have been filed, the applicants should indicate the details of filing dates, what types of patents are filed, application status, and associated United States Patent Office (USPTO) links, if applicable. Applicants should also discuss future IP filing plans.

- **Leadership Plan** (3 pages):
  - Organizational and reporting structure, and personnel responsibilities.
  - Relevant past performance for the team working in and leading large projects and across teams (labs, companies, consortia) and any prior experience of the team working together.
  - Describe how the proposed team meets the eligibility requirements stated above.

- Multiple Principal Investigator (MPI) Leadership Plan, if applicable.

- **Milestones and Deliverables** (2 pages): All applications should provide detailed milestone and deliverables information for planned activities and partnerships, as further described below in section 7.5.

- **Key Personnel List** Provide a list of each named key individual (PI(s), PM/PD, Key Personnel, other significant contributors) along with their intuitional affiliation, their role in the project and their proposed level of effort.

- **Biosketches** (5 pages per individual): Provide a biosketch of each named key individual. The information in the biosketch should include the name and position title, education/training including institution, degree, date (or expected date), and field; list of positions and employment in chronological order (including dates); list of relevant publications, proposed level of effort and a personal statement that briefly describes the individual's role in the project and why they are well-suited for this role. Providing successful examples from past work on similar infrastructure building projects as appropriate to illustrate the relevant experience is desired. The format used for an NIH grant application is acceptable: https://grants.nih.gov/grants/forms/biosketch.htm.

- **Other Support**: Provide Other Support for all key personnel using NIH grant application format as found here: https://grants.nih.gov/grants/forms/othersupport.htm

- **Equipment and Facilities** (2 pages): Provide the information about the equipment and other physical resources available to the project team to adequately complete the project milestones.

- **Institutional Letter of Support** (2 pages): Provide a letter of support from the applicant's organization indicating institutional commitment for the project (e.g., relaying support for contributions, including, but not limited to, support for training activities, licenses, and other resources) and preparations to enter into a negotiated Other Transaction Agreement.

- **Additional letters of support:** Letters of support will be reviewed. Only include letters from persons who have an assigned role in the project.

- **Budget and Budget Justification** (no page limitation): All applications should provide detailed budget information for planned activities and partnerships, as further described below In section 7.5.

- **Bibliography** (no page limitation).

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

- **Data Management and Sharing Plan** (2 pages)**:** All applications, regardless of the amount of direct costs requested for any one year, must address a Data Management and Sharing Plan.

- **Plan for Enhancing Diverse Perspectives (PEDP)** (1 page): All applicants must include a summary of strategies to advance the scientific and technical merit of the proposed project through expanded inclusivity. Broadly, diverse perspectives can refer to the people who do the research and the places where the research is done, as well as who participates in the research as part of the study population. The PEDP should provide a holistic and integrated view of how enhancing diverse perspectives is viewed

and supported throughout the application and can incorporate elements with relevance to any review criteria as appropriate. The PEDP will be considered a part of the scientific and technical merit of the proposed project and assessed as part of the scientific evaluation in making funding decisions consistent with applicable law.

The PEDP will vary depending on the scientific aims, expertise required, the environment and performance site(s), as well as how the project aims are structured. Where possible, applicant(s) should align their description with the required elements within the research strategy section. The PEDP should include a timeline and milestones for relevant components. Examples of items that advance inclusivity in research and may be part of the PEDP can include, but are not limited to:

- Discussion of engagement with different types of institutions and organizations (e.g., research-intensive, undergraduate-focused, minority-serving, community-based).
- Description of any planned partnerships that may enhance geographic and regional diversity.
- Plan to develop transdisciplinary collaboration(s) that require unique expertise and/or solicit diverse perspectives to address research question(s).
- Outreach and planned engagement activities to enhance recruitment of individuals from diverse groups as participants including those from under-represented backgrounds.
- Plan to ensure equitable dissemination of data, tools, and products to all end users.

The PEDP must include the following:

- Description of defined activities and actionable strategies for the inclusion of diverse perspectives in the project.
- Description of how the PEDP will bring unique advantages or capabilities to the project.
- Milestones or other metrics for the evaluation of PEDP activity progress and success.
- Proposed monitoring activities to identify and measure PEDP progress benchmarks.
- Anticipated timeline of proposed PEDP activities.

While applicants may discuss prior activities, the PEDP should emphasize efforts and contributions that directly relate to the proposed project. Additional information and FAQs about the PEDP are available on the program website at https://commonfund.nih.gov/venture/oculomics/faqs.

- **PHS Human Subjects and Clinical Trials Information**
  - When involving human subjects research, clinical research, and/or NIH-defined clinical trials follow all instructions for the PHS Human Subjects and Clinical Trials Information form in the SF424 (R&R) Application Guide, with the following additional instructions:
  - If human subjects are involved, you must include at least one human subjects study record using the **Study Record: PHS Human Subjects and Clinical Trials Information** form or **Delayed Onset Study record.**
  - **Study Record: PHS Human Subjects and Clinical Trials Information**
    All instructions in the SF424 (R&R) Application Guide must be followed. Additional information can be found here: Study Record - Section 1 Basic Information (nih.gov)
  - **Delayed Onset Study**
    Projects proposing Delayed Onset Studies will **not** be accepted under this ROA.
    Note: 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 SF424 (R&R) Application Guide must be followed.

7.4 Budget details

The Common Fund Venture Initiative may allocate up to $1,600,000 total (direct + F&A) costs per year for up to three years per award. Support of three projects is anticipated. The funding will depend on (1) the objectives for the project proposed by the applicants and how well they fit with the goals of Oculomics Initiative, (2) the quality of the applications received, (3) availability of funds and (4) programmatic priorities. The NIH may elect to negotiate any or all elements of the proposed budget. Institutions with an established Facilities and Administrative (F&A) rate should use their federally approved rate to calculate indirect costs for non-compute expenses.

F&A costs on foreign component will be reimbursed at a rate of eight (8) percent of modified total direct costs, exclusive of tuition and related fees, direct expenditures for equipment, and subawards in excess of $25,000.

In ASSIST Core tab, applicants should enter the total dollar number in the field of **Total Requested Funds.** For budget details, applicants shall download the form from https://commonfund.nih.gov/OTforms and then complete SF424 budget forms on their own computers instead of in internet browsers. The prime applicant is responsible for including all third parties' budget and budget justification. In order to successfully upload budget forms as an attachment into ASSIST, the applicant should flatten the fillable PDF. There are a number of methods to flatten a PDF, the easiest of which is to print it as a PDF.

The detailed budget request should provide the overall expected cost for each of the following categories and for each of the three years: personnel, equipment, travel, funds for third parties (i.e., subrecipients), if applicable, other direct costs, and total cost (with indirect costs included).

Budget justification must be provided for all budget items and budget years. Detailed quotations are required for equipment items exceeding $5,000.

Budgets must adhere to latest NIH salary limitation notice (See Salary Cap Summary/Guidance on Salary Limitation for Grants and Cooperative Agreements). https://grants.nih.gov/grants/guide/notice-files/NOT-OD-23-056.html.

Subrecipients are required to provide details of cost breakdown. Prime recipient should follow their internal policies and procedures to calculate subrecipient's budget.

7.5 Milestones and Deliverables

The expected project duration is 3 years. Provide a table of milestones and deliverables for each year of the three-year application. Milestones must be specific, quantifiable, and scientifically justified. Milestones, due dates, and estimated costs should be provided in the table. An example table template is provided below for reference.

Example table of milestones and deliverables:

Note 1: Applicants must ensure that the total budget request is consistent with the sum of item budget estimates in Milestones and Deliverables table for the project.

Note 2: Provided costs for the task should include all the costs for personnel, equipment, facilities, other resources, travel, and other associated costs.

Note 3: Total cost (direct and indirect) for the tasks should be provided.

Milestone	Tasks/ Subtasks	Due Date (Months after award)	Milestone Definition	Estimated total cost (direct plus indirect cost) for the task
1	1.1	3	Milestone Name/Description • Bulleted list of tasks completed • Bulleted list of deliverables (including data sharing) • Completion criteria for the task • Potential risk factors and decision points	$10,000
1	1.2	3	Milestone Name/Description a. Bulleted list of tasks completed b. Bulleted list of deliverables (including data sharing) c. Completion criteria for the task d. Potential risk factors and decision points	$10,000
2	2.1	6	Milestone Name/Description 1. Bulleted list of tasks completed 2. Bulleted list of deliverables (including data sharing) 3. Completion criteria for the task 4. Potential risk factors and decision points	$10,000

7.6 Systems Registration

Applicants invited to submit a full application must submit via the NIH eRA Commons ASSIST system no later than the "Application Due Date" shown at the top of this notice, by 5 PM local time of applicant organization. Use OTA-24-006 in the Funding Opportunity Announcement field. Here are instructions for submitting via the NIH eRA ASSIST system. Technical assistance is available from the eRA Service Desk.

To submit a full application via ASSIST, the applicant organization must be registered in eRA Commons (See Submission Instructions). If you are invited to submit a full application, you must be registered in eRA Commons, which may take six (6) weeks or more to complete, applicants should therefore begin the registration process as soon as possible.

On the eRA Commons home page, select the "Register Organization" link for more details.

To complete registration, if you have not done so already, you may need to register for the following:

- 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.
- Unique Entity Identifier (UEI)- A UEI is issued as part of the SAM.gov registration process. SAM registrations prior to fall 2021 were updated to include a UEI. The same UEI must be used for all registrations, as well as on the other transactions application.
- eRA Commons - Once the unique organization identifier (UEI after April 2022) is established,

organizations can register with eRA Commons in tandem with completing their full SAM and Grants.gov registrations; all registrations must be in place by time of submission of the full application. eRA Commons requires organizations to identify at least one RBO and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.

If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Dealing with System Issues guidance.

8. Objective Review

Applications to Other Transactions Research Opportunity announcements such as this one, are not reviewed by the standard NIH peer review process, but using custom processes referred to as Objective Review. Responsive full applications submitted in response to the solicitation, will be reviewed by subject matter experts (SMEs) via an objective review process. Objective review will involve the submission of written critiques by SMEs against the Review Criteria described below, and interactive individual discussions between those experts and NIH program staff. The SMEs may include NIH staff, other federal staff, and individuals external to federal government. Components of the full applications may be accepted into the final plan in whole, in part, or may be omitted. The outcome of each review could result in a modified work plan for each application based on reviewers' comments and recommendations. The modified workplan, as shaped by the review process, will serve as a blueprint for the final negotiated terms and milestones for the resulting awards.

NIH will NOT provide feedback on applications, except as a part of follow-up on an as-needed basis.

NIH will not accept an appeal of the objective review or funding decision outcomes.

8.1 Review of Full Applications

Full applications will undergo an administrative review by NIH staff. Applications that are deemed non-responsive or incomplete will not move forward to objective review. Full applications deemed responsive will undergo an objective review by a panel of SMEs which may include NIH federal employees, federal employees of other agencies, and outside experts, as needed.

The Overall Impact will be assessed by Review Criteria outlined below in decreasing order of importance:

- Reasonableness and merit of the proposed plans and approaches
  - To what extent are the planned activities likely to advance the goals of the Oculomics program and successfully address the Research Strategy as defined in Sections 7.3 above?
  - Is the overall approach well-reasoned, feasible, and appropriate to accomplish the study specific aims?
  - Is the proposed research, including the scientific rationale, well-supported by preliminary data, published literature, and known biological mechanisms?
  - Adequacy of the milestones and deliverables, and their timeline for fulfilling the planned goals of the project.
  - Ability to identify and mitigate technical and management risks.
  - Adequacy of the Intellectual Property.
  - Adequacy of the PEDP.

- Appropriateness of the key personnel
  - Is the expertise, demonstrated capabilities, and past performance of the PI(s), PM/PDs, and key personnel appropriate for the proposed activities and successful execution of the proposed complex program? Is the necessary expertise illustrated, documented, and shown adequately with relevant examples from past work?
  - Are the leadership plan and the multiple PI plan (if applicable) appropriate? Is the organizational and reporting structure appropriate? What expertise, if any, is missing from the team?
  - Is there adequate Project Management and administrative support to ensure effective execution and monitoring of activities necessary to complete the project milestones?

- Appropriateness of the equipment and facilities, and other resources
  - Are the proposed facilities, computing infrastructure, backup plans, physical security of any data, communication networks, relevant other equipment, and project management tools adequate to support the successful execution of the proposed program?
  - Are the plans for replacing, maintaining, and repairing equipment appropriate?

- Appropriateness of the proposed budget
  - Is the proposed budget reasonable and commensurate with the proposed work?
  - Are there any areas where less funding is needed or where more funding would improve the overall impact?

- 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 panel of SMEs 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 panel of SMEs 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 panel of SMEs 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 panel of SMEs will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following three points: (1) a complete description of all proposed procedures including the species, strains, ages, sex, and total numbers of animals to be used; (2) justifications that the species is appropriate for the proposed research and why the research goals

cannot be accomplished using an alternative non-animal model; and (3) interventions including analgesia, anesthesia, sedation, palliative care, and humane endpoints that will be used to limit any unavoidable discomfort, distress, pain and injury in the conduct of scientifically valuable research. Methods of euthanasia and justification for selected methods, if NOT consistent with the AVMA Guidelines for the Euthanasia of Animals, is also required but is found in a separate section of the application. For additional information on review of the Vertebrate Animals Section, please refer to the Worksheet for Review of the Vertebrate Animals Section.

NIH will NOT provide feedback on applications, except as a part of follow-up on an as-needed basis.

8.2 Post-review Funding Plan

NIH intends to fund three awards. However, the actual number of awards will depend in on the availability of funds and on how the objectives proposed by the applicants fit the goals of the Oculomics Program.

The level of funding for awards made under this solicitation will depend on (1) the objectives proposed by the applicants and how well they fit with the goals of the Oculomics initiative, (2) the quality of the applications received, (3) availability of funds and (4) programmatic priorities. The OT mechanism allows for significant flexibility to make budget adjustments as needed to meet NIH's programmatic priorities. Award levels may increase or decrease over time based on funding availability, establishment or termination of subcontracts, recipient performance, and other program priorities.

At any relevant point in the process, including the objective review, NIH reserves the right to:

1) Select for negotiation all, some, one, or none of the applications received in response to this solicitation.
2) Accept applications in their entirety or to select only portions of the application for award.

Appeals of the objective review will not be accepted for applications submitted in response to this ROA.

9. Special Award Terms and Information

9.1 NIH Discretion

The OT award mechanism allows significant ongoing involvement from NIH Program and Project Managers and OT Agreements Officer and Agreements Staff and provides the NIH the flexibility to alter the course of the project in real-time to meet the overarching goals. This may mean an awarded activity could be expanded, modified, partnered, not supported, or discontinued based on program needs, emerging methods or approaches, performance, or availability of funds.

Performance during the award period will be reviewed on an ongoing basis and course corrections will be made, as necessary. As a result, the NIH reserves the right to:

1. Fund projects in increments and/or with options for continued work depending on agreed upon milestones;
2. Specify "go/no-go" milestones that either result in project continuation if achieved, or termination if not achieved, by the specified milestone timepoint.
3. Fund projects of two or more entities (potentially across different applications) as part of a

reorganized collaboration, teaming arrangement, or other means acceptable to the government;
4. Request additional documentation (certifications, etc.), and;
5. Remove participants from award consideration should the parties fail to reach a finalized agreement by addressing the concerns identified in the objective review, and any additional concerns identified by NIH program staff, or the proposer fails to provide requested additional information in a timely manner.

Applications selected for award negotiation may result in the issuance of an OT award based on the nature of the work proposed, the required degree of interaction between parties, and other factors. The NIH reserves the right and sole discretion to engage in negotiation with the selectees submitting a full application under this solicitation.

9.2 Award Governance

The NIH will actively engage with awardee(s) to establish a vision and capabilities for the Oculomics program and to oversee the effort of the awardees to achieve the vision.

NIH Roles and Responsibilities:

- Other Transactions Agreements Officer (OTAO): NIH representative responsible for legally committing the government to an OT award and to the agreement through which terms and conditions are established, and for the administrative and financial aspects of the award. The OTAO is the focal point for receiving and acting on requests for NIH prior approval and is the only NIH official authorized to change the funding, duration, or other terms and conditions of award.
- Other Transactions Agreements Specialist (OTAS): A designee of the OTAO for administrative and financial aspects of the award.
- Other Transactions Program Official (OTPO): Individual within NIH who provides day-to-day programmatic oversight of individual awards, working closely with the OTAO. The OTPO ensures the successful implementation of the program by integrating input from the OSC leadership, Oculomics Initiative Working Group, Project Scientists and other collaborators to create, adjust, or remove milestones. The OTPO evaluates and reviews strategic planning activities and award performance, and recommends approval and acceptance of deliverables to the OTAO.

9.3 OT Agreement Governance

Other Transactions (OT) are a special type of legal instruments other than contracts, grants or cooperative agreements. Generally, these awarding instruments are not subject to the Federal Acquisitions Regulations (FAR), nor grant regulations unless otherwise noted for certain provisions in the terms and conditions of award. They are, however, subject to the OT authorities that govern the initiative and/or programs as well as applicable legislative mandates. The NIH and its components, including OSC, have been authorized by Congress to use them. They provide considerable flexibility to the government to establish policies for the awards, so the policies and terms for individual OT awards may vary between awards. Each award is therefore issued with a specific Agreement, which is negotiated with the recipient and details terms and conditions for that specific award. Program and administrative policies and the terms and conditions of individual awards are intended to supplement, rather than substitute for, governing statutory and regulatory requirements. Awards or a specified subset of awards also may be subject to additional requirements, such as those included in executive orders and appropriations acts (including the other transaction legislation cited in the Agreement), as well as all terms and conditions cited in the Agreement and its attachments, conditions on activities and expenditure of funds in other statutory or regulatory requirements, including any revisions in effect as of the beginning date of the next funding segment. The

terms and conditions of the resulting OT awards are intended to be compliant with governing statutes.

For the awards funded under this ROA, the NIH will engage in negotiations and all agreed upon terms and conditions will be incorporated into the Agreement. Either a bilateral agreement or a Notice of Award (NoA) will be used as the official Agreement. The signature of the RBO certifies that the organization complies, or intends to comply, with all applicable terms and conditions, policies, and certifications and assurances referenced (and, in some cases, included) in the application instructions.

9.4 Reporting and Project Meetings

The terms and conditions of award will address this criterion as appropriate based upon the final negotiated terms and agreed upon budget.

The recipient and key project team members will be required to:

- Participate in an initial virtual kick off meeting with NIH staff and Oculomics stakeholders.
- Participate in site visits or reverse site visits as deemed necessary by the OTPO.
- Participate in bi-weekly virtual progress meetings with NIH staff to ensure program continues to achieve objectives and to discuss progress and strategies. The meeting frequency may be adjusted at the discretion of the NIH program staff to maximize the probability of successfully meeting milestones.
- Submit written budget and milestone reports (quarterly or more frequently as stated in the OT Agreement).
- i-Edison: Agreement terms and conditions will contain a requirement for patent reports and notifications to be submitted electronically through the i-Edison Federal patent reporting system at https://www.nist.gov/iedison.

Costs associated with these activities must be appropriately reflected in the proposed budget.

9.5 Indirect Costs

Institutions with an established Facilities and Administrative (F&A) rate should use up to their Federally approved indirect rate to calculate indirect costs for non-compute expenses.

Indirect costs for compute expenses in any application funded under this OT mechanism will be capped at a rate of ten (10) percent.

F&A costs on foreign components will be reimbursed at a rate of eight (8) percent of modified total direct costs, exclusive of tuition and related fees, direct expenditures for equipment, and subawards in excess of $25,000.

9.6 Management Systems and Procedures

Recipient organizations are expected to have systems, policies, and procedures in place by which they manage funds and activities. Recipients may use their existing systems to manage OT award funds and activities as long as they are consistently applied regardless of the source of funds and across their business functions. To ensure that an organization is committed to compliance, recipient organizations are expected to have in use clearly delineated roles and responsibilities for their organization's staff, both programmatic and administrative; written policies and procedures; training; management controls and other internal

controls; performance assessment; administrative simplifications; and information sharing

9.7 Financial Management System Standards

Recipients must have in place accounting and internal control systems that provide for appropriate monitoring of other transaction accounts to ensure that obligations and expenditures are congruent with programmatic needs and are reasonable, allocable, and allowable. A list of unallowable costs will be included in the terms and conditions of the award. In addition, the systems must be able to identify unobligated balances, accelerated expenditures, inappropriate cost transfers, and other inappropriate obligation and expenditure of funds, and recipients must notify NIH when problems are identified. A recipient's failure to establish adequate control systems constitutes a material violation of the terms of the award.

9.8 Property Management System Standards

Recipients may use their own property management policies and procedures for property purchased, constructed, or fabricated as a direct cost using NIH OT award funds. The terms and conditions of award will address this criterion as appropriate based upon the final negotiated and agreed upon budget. Procurement System Standards and Requirements Recipients may acquire a variety of goods or services in connection with an OT award-supported project, ranging from those that are routinely purchased goods or services to those that involve substantive programmatic work. Recipients must acquire goods and services under OT awards in compliance with the organizations established policies and procedures. The terms and Conditions of award will address this criterion as appropriate based on the final negotiated and agreed upon budget.

9.9 Organizational Conflicts of Interest (OCIs)

Applicants are required to identify and disclose all facts relevant to potential OCIs involving subrecipients, consultants, etc. Under this section, the proposer is responsible for providing this disclosure with each Detailed Plan. The disclosure must include the PI/Collaborators', and as applicable, proposed member's OCI mitigation plan. The OCI mitigation plan must include a description of the actions the proposer has taken, or intends to take, to prevent the existence of conflicting roles that might bias the proposer's judgment and to prevent the proposer from having an unfair competitive advantage.

The government will evaluate OCI mitigation plans to avoid, neutralize, or mitigate potential OCI issues before award issuance and to determine whether it is in the government's interest to grant a waiver. The government will only evaluate OCI mitigation plans for applications that are determined selectable. The government may require applicants to provide additional information to assist the government in evaluating the proposer's OCI mitigation plan. If the government determines that a proposer failed to fully disclose an OCI or failed to reasonably provide additional information requested by the government to assist in evaluating the proposer's OCI mitigation plan, the government may reject the Detailed Plan and withdraw it from consideration for award.

9.10 Monitoring

Recipients are responsible for managing the day-to-day operations of OT award-supported activities using their established controls and policies. However, to fulfill their role in regard to the stewardship of federal funds, the program team will monitor their OT awards to identify potential problems and areas where technical assistance might be necessary. This active monitoring is accomplished through review of reports and correspondence, audit reports, site visits and other information, which may be requested of the recipient. The names and contact information of the individuals responsible for monitoring the programmatic and business management aspects of awards will be provided to the recipient at the time of award.

Monitoring of a project or activity will continue for as long as NIH retains a financial interest in the project or activity as a result of property accountability, audit, and other requirements that may continue for a period of time after the OT award is administratively closed out and NIH is no longer providing active OT award support.

9.11 Audit

NIH OT recipients for the Program are subject to the audit requirements of OMB 2 CFR 200, Subpart F- Audit Requirements, as implemented by DHHS 45 CFR Subpart F. In general, 45 CFR 75, Subpart F-Audit Requirements requires a state government, local government, or non-profit organization (including institutions of higher education). Please consult the provisions within Subpart F to determine requirements for the program specific audit requirements.

For-profit organizations have two options regarding the type of audit that will satisfy the audit requirements. The recipient either may have (1) a financial-related audit (as defined in, and in accordance with, the Government Auditing Standards (commonly known as the “Yellow Book”), GPO stock 020-000-00-265-4, of a particular award in accordance with Government Auditing Standards, in those cases where the recipient receives awards under only one DHHS program, or (2) an audit that meets the requirements of 45 CFR 75, Subpart F-Audit Requirements.

9.12 Public Policy Requirements and Objectives

NIH intends to uphold high ethical, health, and safety standards in both the conduct of the research it funds and the expenditure of public funds by its recipients. The signature of the RBO on the application certifies that the organization complies, or intends to comply, with all applicable policies, certifications, and assurances.