

## Part 1. Overview Information

<b>Participating Organization(s)</b>	National Institutes of Health (NIH), University of Nevada Las Vegas
<b>Components of Participating Organizations</b>	National Institute of General Medical Sciences (NIGMS), Nevada Institute of Personalized Medicine
<b>Funding Opportunity Title</b>	Pilot Projects in Personalized Medicine
<b>Activity Code</b>	P20 Pilot Research Project
<b>Announcement Type</b>	Pilot grants for COBRE award number P20 GM121325
<b>Related Notices</b>	Funding Opportunity Announcement (FOA) Number PMIN-COBRE-001
<b>Companion Funding Opportunity</b>	None
<b>Number of Applications</b>	See Section III. 3. Additional Information on PI and Organization Eligibility.
<b>Amount of Award</b>	Up to \$75,000 in Direct Costs and awardee may apply for a competitive renewal for an additional year of funding.
<b>Catalog of Federal Domestic Assistance (CFDA) Number(s)</b>	93.172
<b>Funding Opportunity Purpose</b>	The purpose of this funding opportunity announcement (FOA) is to support basic and translational pilot projects in personalized medicine designed to utilize our research cores, enable acquisition of preliminary data for a federal grant application, and cultivate a team of new investigators as project PIs for our COBRE Phase II continuation grant.

### Key Dates

<b>Posted Date</b>	July 13, 2018
<b>Open Date (Earliest Submission Date)</b>	August 15, 2018
<b>Letter of Intent Due Date(s)</b>	August 15, 2018 ( <i>Letters of Intent are required</i> )
<b>Application Due Date(s)</b>	September 15, 2018, by 5:00 PM PST. 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.
<b>AIDS Application Due Date(s)</b>	Not Applicable
<b>Scientific Merit Review</b>	September – October 2018
<b>Advisory Council Review</b>	November 2018
<b>Earliest Start Date</b>	December 1, 2018
<b>Expiration Date</b>	November 30, 2019
<b>Due Dates for E.O. 12372</b>	Not Applicable

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## **Part 2. Full Text of Announcement**

### **Section I. Funding Opportunity Description**

#### **Nature of the Research Opportunity**

Pilot projects will be awarded in response to this FOA, PMIN-COBRE-001. These projects will be in the general area of personalized medicine ranging from basic science to translational applications. The general focus is discovery and utility of genetic and epigenetic markers for personalized medicine, although projects with other model systems will be considered.

For the purposes of this FOA, "personalized medicine" is defined as incorporation of an individual patient's genetic and genomic information (as reflected by their own genotypic, sequencing, family history, physiological data, etc.,) into decision-making about preventative strategies or clinical care for people.

#### **Background**

At least 1 in 20 people will have a genetic disorder during their lifetime; thus, a large opportunity exists to apply routine genetic analysis in health and medicine (PMID:19010252). Fortunately, for many patients, exome (the exon regions) and genome sequencing is now an economically feasible diagnostic test. Sequencing the protein-coding regions of the human genome (the exome) costs about \$300-\$400 today. More than 1 million human exomes have been sequenced and consequentially the pace of DNA sequencing is exceeding Moore's law for doubling of computational capabilities annually (PMID: 24567478). The challenge is to see how society can advance health through applications of genomics and genetic markers.

Although still largely a research endeavor, the use of genetic markers is becoming more commonplace in standard-of-care medical practice. Genetic markers have emerged with five general areas of overlapping clinical applications: (1) oncology; (2) Mendelian disorders; (3) prenatal screening and birth defects; (4) pharmacogenetics; and (5) undiagnosed diseases. Many genetic markers have already been identified—the

Genetic Testing Registry of the National Center for Biotechnology Information has genetic tests for 10,534 conditions in 5,034 genes developed by 481 laboratories (PMID: 29140470). Many of the loci on these genes (24,061 genetic loci) are in the genome-coding region (PMID: 23193275). Approximately 160,000 single-nucleotide polymorphisms are associated with disease (PMID: 26582918). Numerous genetic markers remain to be discovered, especially in the area of common disease where genetic risk scores (summarizing multiple variants of small effect sizes) are gaining wider acceptance.

Genetic markers can be used to assess an individual's health through four phases of disease progression: (1) the presymptomatic condition; (2) the symptomatic condition; (3) the choice of therapy; and (4) response to treatment of the condition. Uses and advantages of genetic markers are:

In presymptomatic or healthy states, genetic markers are used for disease subtyping, carrier screening, and assessing for disease risk and the need for preventative screening. Based on the anticipated continued growth in the discovery and utility of genetic markers in medicine, the specific personalized medicine niche of our COBRE is the "Discovery and utility of genetic and epigenetic markers for personalized medicine. Although genetic markers are also commonly used in forensics and agriculture, we will focus on their medical and health applications. This emphasis reflects the growing interest in the prediction of complex disease susceptibility using genetic risk scores and variant panels (PMID: 26839113).

Potential limitations of initial approaches, and/or drawbacks of genotype-driven strategies, should also be assessed objectively.

### **Scientific Knowledge to be Achieved**

This funding opportunity will focus on the discovery and utility of genetic and epigenetic markers for personalized medicine, although all other aspects of personalized medicine will be equally considered. The discovery of genetic markers is interdisciplinary. As such, it involves (1) bioinformatics for analysis and interpretation of sequencing results; (2) genomics to help interpret results; (3) clinical trial and biostatistics research to drive new discoveries; (4) genetics to support clinical trials and to apply in clinical research and practice; and (5) medical informatics to collect, organize, and analyze human phenotypes.

### **Objectives of this Research Program**

This FOA will support Pilot Projects to enhance or adapt ongoing successful basic science or translational personalized medicine projects, or initiate new ones, to expand the implementation of genetic and genomic medicine or preventative strategies.

The programmatic goals of these pilot grants are:

- To generate new preliminary discoveries in personalized medicine
- To produce preliminary data that will enhance the competitiveness of a new or resubmitted application for an NIH R03, R15, R21, K01, K08, BSF career awards, or other small awards.
- To grow personalized medicine research in Nevada and the IDeA network

- To enhance the use of our COBRE research cores (<https://www.unlv.edu/nipm/COBRE/GAACore>; <https://www.nevadacntn.org/clinical-and-translational-research-core>)
- To grow the Center of Excellence COBRE program by recruiting new participating members
- To identify candidate replacement projects and PIs as our new investigators graduate to independent funding.
- Recruit a pool PIs to be part of our phase II COBRE application.

Proposed pilot projects are not required, but may choose, to partner with experienced group(s) to expand sample size and generalizability and evaluate their proposed intervention(s) in different settings. The inclusion of diverse settings such as community hospitals, primary care practices, specialty groups, and military or Veterans' Administration hospitals, and under-served populations such as disadvantaged or non-European ancestry groups, is particularly encouraged, though the feasibility and advantages of such expansions should be clearly described. Similarly, expansion to multiple different medical or hospital systems, rather than within current members of an existing system, is also encouraged.

This initiative may support studies using animal models but must be combined with a human study component.

### **Program Formation and Governance**

The awards funded under this FOA will be highly collaborative. Close interaction among awardees and a cadre of COBRE grant members will be required to meet the obligations of this program.

Shortly after award, the awardees will meet with COBRE leadership and existing awardees as a consortium to share research plans; identify commonalities in approaches, barriers, and solutions; and present their research project or grant applications at NevBio, Science Café, Grant club, and/or COBRE seminar series if asked; and work with the COBRE group by regularly attending COBRE journal club, research core workshops, mentoring panel quarterly meetings.

Given the expected commonalities in infrastructural and institutional needs across Pilot Projects, awardees will have access to the COBRE research cores (Genome Acquisition to Analysis, and Clinical Trials cores; <https://www.unlv.edu/nipm/COBRE/GAACore>) and shared laboratory research space and equipment in the Nevada Institute of Personalized Medicine.

### **External Input into the Personalized Medicine Center of Excellence**

The Pilot Projects, as part of the Personalized Medicine in Nevada COBRE award, will be approved by, and report to an External Advisory Board (EAB). The EAB is appointed by and will advise NIGMS. The COBRE Advisory Board members will meet with awardees once a year in-person and once a year through teleconference and provide feedback on all pilot projects.

### **Data Sharing Under this Initiative**

To increase the value of the significant public investment in personalized medicine projects data produced under this FOA should become publicly available. Award recipients will adhere to NIH guidelines on sharing research data (see notice NOT-OD-03-032). Genomic data from Genome-Wide Association Studies (GWAS) will be deposited and available through dbGAP consistent with NIH policy for sharing of data obtained with NIH-supported Genome-wide Associate Studies (GWAS) (see notice NOT-OD-07-088).

## Section II. Award Information

<b>Funding Instrument</b>	Grant: A support mechanism providing money to an eligible entity to carry out an approved project or activity
<b>Application Types Allowed</b>	New, Continuation
<b>Funds Available and Anticipated Number of Awards</b>	The number of awards is contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications  NIH/UNLV intends to fund an estimate of 2 awards per year, corresponding to a total of \$150K per year. Future allocations amounts are expected to be similar but will depend on the annual continuation of the UNLV COBRE program
<b>Award Budget</b>	Up to \$75,000 total costs for one year
<b>Award Project Period</b>	The maximum period is 1 year, and competitively renewable

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

## Section III. Eligibility Information

### 1. Eligible Applicants (Principal Investigator)

All Nevada investigators who are eligible to apply for independent NIH funding, but have not been the PI of an R01 or similar senior level grant from another agency, and who have no conflict of interest, will be eligible to apply. Applicants cannot concurrently hold a COBRE, INBRE or CTR-IN at the time of the award. These individual(s) should have the skills, knowledge, and resources necessary to carry out the proposed research as the Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)) is invited to work with his/her organization to develop an application for support. Applicants must hold a full-time faculty position at the rank of Assistant or Associate Professor. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

### Required Registrations

### Applicant Organizations

Applicant organizations must complete and maintain the following registrations as described in the SF 424 (R&R) Application Guide to be eligible to apply for or receive an award. All registrations must be completed prior to the application being submitted. Registration can take 6 weeks or more, so applicants should begin the registration process as soon as possible. The NIH Policy on Late Submission of Grant Applications states that 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) (formerly CCR) – 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 and SAM registration in order to complete the eRA Commons registration. Organizations can register with the eRA Commons as they are working through their SAM or Grants.gov registration. 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.

### **Program Directors/Principal Investigators (PD(s)/PI(s))**

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

## **2. Cost Sharing**

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

## **3. Additional Information on Eligibility**

### **Number of Applications**

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

Any PI application that is essentially the same as one already reviewed within the past thirty-seven months (as described in the NIH Grants Policy Statement) will not be reviewed, except for submission:



- To an RFA of an application that was submitted previously as an investigator-initiated application but not paid;
- Of an investigator-initiated application that was originally submitted to an RFA but not paid
- To an RFA of an application that was submitted previously as an investigator-initiated application but not paid; or
- Of an application with a changed grant activity code.

## **Section IV. Application and Submission Information**

### **1. Requesting an Application Package**

Applicants must download the PHS398 application forms associated with this funding opportunity at <https://grants.nih.gov/grants/funding/phs398/phs398.html>

### **2. Content and Form of Application Submission**

It is critical that applicants follow the instructions in the PHS 398 Application Guide, except where instructed in this funding opportunity announcement to do otherwise (in this FOA or in a Notice from the NIH Guide for Grants and Contracts). When the program-specific instructions deviate from those in the Application Guide, follow the program-specific instructions. Conformance to the requirements in the Application Guide is required and strictly enforced. Applications that are out of compliance with these instructions may be delayed or administratively withdrawn and not accepted for review.

### **Letter of Intent**

Although 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 contains allows COBRE staff to estimate the potential review workload and plan the review.

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

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

The letter of intent should be uploaded on our online Letter of Intent portal (<https://goo.gl/forms/wkWiHoEkT3bf3DOr2>).

### **Page Limitations**

All page limitations described in the PHS398 Application Guide and the Table of Page Limits must be followed unless otherwise stated in this FOA. **The research strategy section must be no longer than 5 pages and follow the format described in the Research Strategy section.**

### **Required Components**

The forms package associated with this FOA includes all applicable components, required and optional. Please note that some components marked optional in the application package are required for submission of applications for this FOA.

PHS398 Face Page (form page 1)

All instructions in the PHS398 Application Guide must be followed and the form must be signed by an Authorized Official.

PHS398 Project Summary (form page 2)

All instructions in the PHS398 Application Guide must be followed. The relevance section should describe how the proposed research is related to Personalized Medicine.

### **Biosketches of Project PI, Mentor, and Any Collaborators**

All instructions in the PHS398 Application Guide must be followed.

### **Detailed Budget**

All instructions in the PHS398 Application Guide must be followed. Allowable expenditures are research personnel and supplies, domestic travel to one meeting or workshop, and use of COBRE research cores. Funds may not be used for PI salary, subcontracts, renovation, or at external sites (other than for sample procurement services). Funds for food and meal are only allowed if related to nutrition research. Indirect costs are not allowed. None of the funds in this award shall be used to pay the salary of an individual at a rate in excess of the current salary cap. Current salary cap levels are published at [http://grants.nih.gov/grants/policy/salcap\\_summary.htm](http://grants.nih.gov/grants/policy/salcap_summary.htm)

### **Budget Justification**

All instructions in the PHS398 Application Guide must be followed. The justification should also state a commitment of at least 25% effort for the PI.

### **Review of Related Previously Submitted Grant (continuation format page)**

If the proposal is based upon a grant that was previously submitted to a federal agency and a review was received, the official review should be uploaded with the application. If this project is not based on a previously submitted application write "Not applicable".

### **Letter of PI Time Commitment**

Applicants must submit a letter stating a time commitment for the PI of at least 25% effort for the period of the award from their dean, supervisor, or another institutional official.

### **Acceptance of Terms Letter Signed by PI**

Applicants must provide a signed letter stating that if the applicant is awarded the pilot grant that they will:

- Abide by NIH rules and policy
- Commit at least 25% effort (PI) to the projects
- Submit a grant application to a federal agency within six months of award completion and resubmit application within one year after the review is complete if the application is scored. To improve their chances of securing NIH funding, each new pilot PI may choose to receive coaching, including that relevant to writing their grant and paper submissions
- Complete a short online assessment one time and annual surveys reporting accurate data for 4 years after funding of the award
- Present their research project or grant plans at NevBio, Science Café, Grant club, and/or COBRE seminar series if asked



- Regularly attend COBRE journal club, research core workshops, mentoring panel quarterly meetings
- Submit one online mid-award and final progress report

### **PHS 398 Research Strategy (continuation format page)**

All instructions in the PHS398 Application Guide must be followed, with the following additional instructions:

Research Strategy: The research strategy must be no longer than 5 pages and have the following sections and format:

- Specific aims page or project summary of a future grant submission to a Federal Agency (1 page). The page should include the grant title, Federal agency, and funding mechanism. As in an NIH application this page should summarize the relevance to the five NIH review criteria.
- Preliminary studies inventory (up to 1/4 page) bullet list of preliminary data to be obtained during the pilot project to support the future grant submission to a Federal Agency
- A Research plan for preliminary studies (up to 3 pages)
- Usage of COBRE research cores (up to 1/2 page). Describe how the applicant will use the research cores indicating sample types, number of samples and analyses. The genomics acquisition and analysis (GAA) core will support pilot research projects through services and education for DNA and RNA sequencing, data processing, storage, management and protection, data integration and dissemination, and bioinformatic and statistical analyses. The experiments supported consist of exome and/or whole genome sequencing, or sequencing of an enriched portion of a genome (methylation or other targeted genomic segments, specific genes and pathways) and RNA sequencing. The core will conduct data quality control and data processing, establish and maintain analytic and annotation pipelines, and generate analysis-ready data for RPs and pilot projects. The core will assist with genetic analyses, bioinformatic and statistical supports based on project needs. Another COBRE core is the Clinical Trials Core (<https://www.nevadacntn.org/clinical-and-translational-research-core/>) through the Center for Neurodegeneration and Translational Neuroscience at the Luo Ruvo Center for Brain Health to support projects with a human subject research component.
- Usage of NIPM laboratory space (up to 1/2 page). If the investigator plans to use NIPM space and equipment in addition to the COBRE research cores, describe the equipment and type of space needed, and the amount of time it would be used.
- Mentoring plan (up to 1/2 page). Applicants may choose to select mentors from UNLV research match (<http://unlvresearchmatch.unlv.edu>) the Vivo system ([http://ctrin.unlv.edu/?page\\_id=558](http://ctrin.unlv.edu/?page_id=558)) or the National Research Mentoring Network (<https://nrmnet.net>). All PI applicants must have a mentor and include them mentor's Biosketch in the submission
- Milestones and timeline (up to 1/2 page)

Optimal Pilot Projects are expected to include: 1) a strong project related to personalized medicine, 2) an applicant with a strong training and publication history; 3) significant usage of the COBRE research cores; and 4) evidence of submission of competitive grants such as a previously scored grant.

### Optional Components

Follow all instructions in the PHS 398 Application Guide to ensure you complete all appropriate “optional” components.

**Protection of Human Subjects:** For research project involving human subjects the FORMS-E-application should be completed for the application and approved prior to the start of the project. Those projects that do not have IRB approval by **November 1, 2018**, will likely be administratively withdrawn or may be delayed. See FORMS-E-instructions <https://grants.nih.gov/policy/clinical-trials/new-human-subject-clinical-trial-info-form.htm> and application package <https://www.grants.gov/web/grants/forms/r-r-family.html>; Select HHS/PHS Human Subjects & Clinical Trial Information Applicants can work with the Clinical Trial Core (<https://www.nevadacntn.org/clinical-and-translational-research-core>) for preparation of their applications.

**Vertebrate Animal Research:** If the proposed research involves vertebrate animals, applicants must complete the Vertebrate Animals section, and verify IACUC approval for the project prior to by **November 1, 2018**. IACUC approval must have been granted within three years to be valid.

**Resource Sharing Plan:** Individuals are required to comply with the instructions for the Resource Sharing Plans (Data Sharing Plan, Sharing Model Organisms, and Genome Wide Association Studies (GWAS)) as per NIH requirements.

**PHS398 Research Grant Table of Contents (form page 3):** Follow instructions in the PHS398 Application Guide.

**Appendix:** An Appendix is not allowed. Do not use the Appendix to circumvent page limits.

### 3. Submission Dates and Times

Part I. Overview Information contains information about Key Dates. Applicants are encouraged to submit applications before the due date to ensure they have time to make any application corrections that might be necessary for successful submission.

Organizations must submit applications at the online portal (<https://goo.gl/forms/KINeW5yWOWHw7kEA2>). If a Changed/Corrected application is submitted after the deadline, the application will be considered late.

### 4. Intergovernmental Review (E.O. 12372)

This initiative is not subject to intergovernmental review.

### 5. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. Pre-award costs are not allowable.

### 6. Other Submission Requirements and Information

Applications must be submitted electronically as described in this FOA. Paper applications will not be accepted.

Upon receipt, applications will be evaluated for completeness. Applications that are incomplete and/or nonresponsive will not be reviewed.

### **Post Submission Materials**

The only post-submission materials allowed are papers published since submission, official grant reviews obtained since submission, or documentation for approval of IRB, IUCUC or Biosafety applications since submission.

## **Section V. Application Review Information**

Applications will be reviewed by applying standard NIH review criteria.

### **1. Criteria**

Only the review criteria described below will be considered in the review process. All submitted applications are evaluated for scientific and technical merit following the NIH peer review system.

### **Overall Impact**

Reviewers will provide an overall impact score to reflect their assessment of the potential for this pilot project to lead to impactful funded research and the potential for this pilot to produce the key preliminary data for a successful grant application.

### **Scored Review Criteria**

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

### **Significance**

Does the project address an important problem or a critical barrier to progress in the field? 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? How likely is the project to improve the assessment and expand the implementation of personalized medicine?

### **Investigator(s)**

Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, or 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? How suitable is the research team to perform personalized medicine research and assess its impact? How likely is the PI to leverage this support into a new funded grant award?

## **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? How likely is the proposed project to contribute valuable new information to the evidence base on personalized medicine?

## **Approach**

Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? 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? Are criteria for success, a plan to leverage the pilot project into future grant applications and next steps for the project clearly defined? Are definitive early results likely to be available for a grant application within six months of the end of the award?

If the project involves clinical research, are the plans for 1) protection of human subjects from research risks, and 2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?

## **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? Does the applicant take advantage of the COBRE cores and research team?

## **Additional Review Criteria**

As applicable for the project proposed, reviewers will evaluate the following additional items while determining scientific and technical merit, and in providing 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 six 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 six 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 Human Subjects Protection and Inclusion Guidelines.

### **Inclusion of Women, Minorities, and Children**

When the proposed project involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children. For additional information on review of the Inclusion section, please refer to the Human Subjects Protection and Inclusion Guidelines.

### **Vertebrate Animals**

The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia. 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**

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

### **Renewals**

The awardee may apply for a competitive renewal for an additional year of funding.

### **Revisions**

Not Applicable

### **Additional Review Considerations**

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

### **Applications from Foreign Organizations**

Not Applicable

### **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**

Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: 1) Data Sharing Plan; 2) Sharing Model Organisms; and 3) Genome Wide Association Studies (GWAS).

### **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.

## **2. Review and Selection Process**

Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) convened by the Personalized Medicine in Nevada COBRE.

As part of the scientific peer review, all applications:

- May undergo a selection process in which only those applications deemed to have the highest scientific and technical merit (generally the top half of applications under review) will be discussed and assigned an overall impact score.
- Will receive a written critique.
- Appeals of initial peer review will not be accepted for applications submitted in response to this FOA.

Applications will compete for available funds with all other recommended applications. Following initial peer review, recommended applications will receive a second level of review by External Advisory Board and NIGMS. The following 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 COBRE program priorities.

## **3. Anticipated Announcement and Award Dates**

After the peer review of the application is completed, the PD/PI will be emailed his or her Summary Statement (written critique). Information regarding the disposition of applications is available in the NIH Grants Policy Statement. Award dates are expected to be on, or about December 1, 2018. The RFA is expected to be adapted and reissued in January 2019

## **Section VI. Award Administration Information**

### **1. Award Notices**

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

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

Awardees must comply with any funding restrictions described in Section IV.5. Funding Restrictions. Selection of an application for award is not an authorization to begin performance.

Any application awarded in response to this FOA will be subject to the DUNS, SAM Registration, and Transparency Act requirements as noted on the Award Conditions and Information for NIH Grants website.

## **2. Administrative and National Policy Requirements**

All NIH grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the NoA. For the terms of an award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General and Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities. More information is provided at Award Conditions and Information for NIH Grants.

### **Cooperative Agreement Terms and Conditions of Award**

The following special terms of award are in addition to, and not in lieu of, otherwise applicable U.S. Office of Management and Budget (OMB) administrative guidelines, U.S. Department of Health and Human Services (DHHS) grant administration regulations at 45 CFR Parts 74 and 92 (Part 92 is applicable when State and local Governments are eligible to apply), and other HHS, PHS, and NIH grant administration policies.

The administrative and funding instrument used for this program will be the cooperative agreement, an "assistance" mechanism (rather than an "acquisition" mechanism), in which substantial NIH programmatic involvement with the awardees is anticipated during the performance of the activities. Under the cooperative agreement, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients in a partnership role; it is not to assume direction, prime responsibility, or a dominant role in the activities. Consistent with this concept, the dominant role and prime responsibility reside with the awardees for the project as a whole, although specific tasks and activities may be shared among the awardees and the NIH as defined below.

### **The PD(s)/PI(s) will have the primary responsibility for:**

- Determining research approaches, designing protocols, setting project milestones, and conducting research.
- Participating in group activities, including meeting with the COBRE leadership and EAB, to share design and analysis techniques and promote comparability across studies wherever possible.



- Ensuring active collaboration in group activities, if applicable.
- Implementing EAB recommendations for designing, implementing, evaluating, and disseminating pilot projects, as appropriate and feasible.
- Sharing detailed process, outcome, and evaluation data derived from the pilot projects.
- Determining needs for additional consent, IRB approval, and/or CLIA-certified genotyping prior to implementing the pilot projects.
- Developing and implementing appropriate educational resources for patients and their clinicians.
- Sharing results according to the NIH data sharing policy.
- Adhering to policies regarding data access, publication, and intellectual property established by NIH and the EAB for this program.
- Cooperating with other awardees in the development and design of research methods, protocols, tools, and strategies.
- Accepting and complying with study policies established by NIH, and with additional non-conflicting policies approved by the EAB.
- Cooperating with other awardees in the publication and dissemination of program results and the eventual release to the scientific community of methods, tools, and results, and other resources.
- Not disclosing confidential information obtained from other members of the program.
- Notifying the COBRE PI of all major interactions with another member of the EAB.
- Submitting periodic progress reports, as agreed upon by the COBRE PI and EAB.
- Attending and participating in EAB meetings and accepting and implementing the guidelines and procedures of the EAB and NIH, as appropriate.

Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, and NIH policies.

NIGMS staff have a substantial programmatic involvement that is above and beyond the normal stewardship role in awards, as described below:

The Program Officer is a scientist of the NIGMS staff who will have a substantial scientific and programmatic involvement during the conduct of this activity through technical assistance, advice, and coordination. The Program Officer will have the following substantial involvement:

- Participating with the EAB members in the group process of setting research priorities, deciding optimal research approaches and protocol designs, and contributing to the adjustment of research protocols or approaches as warranted. The Project Scientist will assist and facilitate the group process and not direct it.
- Serving as a liaison, helping to coordinate activities among and for the awardees, including acting as a liaison to the NIH, and as an information resource for the awardees about genome research activities. The Project Scientist will also coordinate the efforts of the program with other groups conducting similar studies.
- Attending all Steering Committee meetings as a voting member and assisting in developing operating guidelines, quality control procedures, and consistent policies for dealing with situations that require coordinated action. The Project Scientist

will be responsible for working with the Coordinating Center as needed to manage the logistic aspects of the program.

- Reporting periodically on the progress of the program to the Director of the Personalized Medicine COBRE.
- Retaining the option to recommend the withholding or reduction of support from any project that fails to achieve its goals or comply with the Terms and Conditions of award.
- Serving as a liaison between the Steering Committee and the Expert Scientific Panel, attending Expert Scientific Panel meetings in a non-voting liaison member role, and arranging for timely preparation and distribution of meeting minutes.
- Serving on subcommittees of the Steering Committee and the Expert Scientific Panel, as appropriate.
- Assisting awardees in the development, if needed, of policies for dealing with situations that require coordinated action.
- Providing advice in the management and technical performance of the award.
- Assisting in promoting the availability of the data and related resources developed in the course of this program to the scientific community at large.
- Participating in data analyses, interpretations, and, where warranted, co-authorship of the publication of results of studies conducted through the program.
- If re-consent is necessary, plans for re-consent, including consent forms, must be reviewed by the NHGRI Program Official prior to implementation.
- The Program Official may withhold or reduce support from any awardee that fails to achieve its goals or comply with the Terms and Conditions of Award.
- Other NHGRI staff may assist the awardees as designated by the Program Official.
- Additionally, an NHGRI Program Official will be responsible for the normal scientific and programmatic stewardship of the award and will be named in the award notice.

### **Scientific Panel**

An External Advisory Board (EAB) will evaluate the progress of the program. The EAB will provide recommendations to the NIGMS about the progress and scientific direction of all components of the program.

The EAB will be composed of 4-5 scientists matching expertise as closely as possible, although the membership may be enlarged permanently or on an ad hoc basis as needed. The EAB will meet once a year, one in-person meeting, and one telephone conference. At least once a year, there will be a joint meeting with the EAB to allow direct interaction with the EAB. Twice a year the SP will make recommendations regarding progress of the program to the NIGMS about changes, if any, which may be necessary for the program.

### **Dispute Resolution**

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to Dispute Resolution. A Dispute Resolution Panel composed of three members will be convened. It will have three members: a designee of the Steering Committee chosen without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two; in the case of individual disagreement, the first member may be chosen by the individual awardee. This special dispute resolution procedure does

not alter the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D and DHHS regulation 45 CFR Part 16.

### **3. Reporting**

Awardees will be required to submit the annual Progress Report through an online survey as part of the COBRE assessment. Financial statements will be required as in the NIH Grants Policy Statement.

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

### **Section VII. Center Contacts**

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

#### **Application Submission Contacts**

Online Pilot Grant Application Portal: <https://goo.gl/forms/KINeW5yWOwHw7kEA2>

Email: [bob.thorson@unlv.edu](mailto:bob.thorson@unlv.edu)

**Grants Information** (Questions regarding application instructions and process, finding NIH grant resources)

Telephone 301-710-0267

TTY 301-451-5936

Email: [GrantsInfo@nih.gov](mailto:GrantsInfo@nih.gov)

#### **Scientific Research Contact**

Martin Schiller, Ph.D.

Nevada Institute of Personalized Medicine, UNLV

Telephone: (702)895-5546

Email: [martin.schiller@unlv.edu](mailto:martin.schiller@unlv.edu)

#### **Peer Review Contact(s)**

Laurel Raftery, Ph.D.

School of Life Sciences, UNLV

Telephone: (702)774-1404

Email: [laurel.raftery@unlv.edu](mailto:laurel.raftery@unlv.edu)

#### **Financial/Grants Management Contact(s)**

Ms. Sarah Love

Nevada Institute of Personalized Medicine, UNLV

Telephone: (702)895-1297

Email: [sarah.love@unlv.edu](mailto:sarah.love@unlv.edu)

**Section VIII. Other Information**

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