The Center for Urban Responses to Environmental Stressors (CURES)

Announces a Request for Pilot Project Proposals

What is CURES?

The Center for Urban Responses to Environmental Stressors (CURES) is a cross-campus, community-engaged initiative that has been established to develop the leadership and research capacity to identify, evaluate, and mitigate Detroit's environmental health challenges in close collaboration with the community and environmental policy makers. The ultimate goal of CURES is to be an active partner in the collective goal of creating a healthier Detroit.

CURES is focused on understanding how chemical and non-chemical stressors in the urban environment affect the health and well-being of Detroit's vulnerable populations. Detroit is encumbered with an overabundance of industrial and post-industrial environmental toxicants, socioeconomic strains, violence, and housing decay. Identifying these health hazards and enhancing our understanding of how they impact our health is key to implementing effective remediation efforts. CURES is strategically designed to facilitate transdisciplinary research and training focused on: (1) the exposure to stressors that are especially prevalent in the urban industrialized environment, including chemical and non-chemical stressors, (2) the experiences of people who are particularly vulnerable to the adverse effects of such exposures (e.g., children, older adults, immigrants, and first responders), and (3) linking such environmental exposures to costly and serious public health disorders in Detroit's population.

The overall goals of CURES are (1) to provide leadership in environmental health science research by building capacity to enhance our understanding of the health effects from complex chemical and non-chemical urban environmental exposures, (2) to develop the next generation of environmental health researchers who are facile with transdisciplinary, translational team science, and (3) to interact with the community so as to leverage our research to contribute to a healthy Detroit.

What is the purpose of this RFA?

The guiding principal of CURES is to perform community-engaged research that addresses the most pressing environmental health concerns of Detroit's urban community. CURES uses input from its Community Advisory Board and the wider Detroit community to inform its research priorities. The primary goal of the CURES Pilot Project Program is to develop research capacity and expertise to address those priorities in close collaboration with the community.

This RFA seeks applications for community-engaged research projects that address environmental health problems of concern to the community. CURES is committed to performing community-engaged research in the truest sense. Community-engaged research entails full participation of community members in all phases of a research project, including identification of the environmental health concern to be studied, design of the research strategy to be followed, collection and interpretation of data, dissemination of results to the broader community, and discussions of possible remediation strategies based on the collected data.

Time Line

October 17, 2014, 10:00 – 11:30AM	Informational Meeting in the WSU Office of the Vice President for Research, 5057 Woodward Avenue, 6th floor, Conference Room A
November 4, 2014	Letters of intent (LOI) due by midnight
November 11, 2014	Notification of successful LOIs and invitation to submit proposal
December 16, 2014	Full applications due by midnight
January 16, 2015	Announcement of awards
February 1, 2015	Funding start date

Submission of Information

Submit Letters of Intent (LOI) in PDF format as an e-mail attachment to:

La'Quita Lowery
Manager, IEHS Business Operations
Phone (313) 577-6590
Lycarr@wayne.edu

Questions

If you have questions, please contact:

Dr. Thomas A. Kocarek
Leader, CURES Pilot Project Program
Phone (313) 577-6580
t.kocarek@wayne.edu

Dr. Melissa Runge-Morris
Director, Institute of Environmental Health Sciences
Director, CURES
Phone (313) 577-5598
m.runge-morris@wayne.edu

Dr. Bengt Arnetz
Deputy Director, CURES
Phone (313) 577-2644
barnetz@med.wayne.edu

What is the theme of this RFA?

This RFA seeks applications for community-engaged research pilot projects that address environmental health problems of concern to the community.

- The proposed research project must address an environmental health problem that is of concern to the community. This RFA does not restrict the choice of topic that will be considered responsive. However, the applicant must provide a compelling justification for the selected topic, both in terms of the importance of the environmental health problem and the likelihood that the proposed research project will have a substantial impact in addressing the problem.

- The project must adhere to the principles of community-engaged research, which is research that equitably involves community members and researchers in all aspects of the research process and in which all partners contribute expertise and share decision-making and ownership.

- The application must be accompanied by signed letters that indicate commitment to the project from all of the involved project leaders (both academic and community partners).

- The pilot project must be a research project that has the potential to generate peer-reviewed publications in high-impact journals and to be developed into a larger, longer-term project that is supported by extramural funding. While the project may involve some type of intervention, such interventions must include research that evaluates the impact of the intervention on some aspect of community health.

- Based on strengths of CURES investigators in studying the effects of environmental stressors on the immune system, metabolic disease, cancer, and mental health, applications that address environmental problems that are relevant to these areas are especially encouraged.

- Successful applications will also include plans to utilize one or more of the services that are provided by the CURES Integrative Health Sciences Facility Core (IHSFC). The purpose of the IHSFC is to facilitate translational research in the Center, and its services include biostatistical support and access to specialized cell models and the Michigan Neonatal Biobank. Also, while not specifically required, proposed use of the Exposure Signatures Facility Core will also be viewed favorably during the review of the applications. Brief descriptions of the services offered by these two facility cores are provided at the end of this document.

What are the terms of this RFA?

1. **Number of awards:** CURES plans to fund 3 pilot projects.

2. **Funding time and amount:** Each pilot project will be funded for ~1.2 years at a total amount of up to $80,000 in direct costs. There will be no funds allocated for administrative and facility costs (indirect costs). Successful applicants will receive up to $40,000 as soon as they have completed all pre-award requirements (described below), expected to occur approximately February 1, 2015. On approximately April 1, 2015, the projects will receive the remainder of the award.

3. **Eligible applicants:** Eligible applicants will be teams that include at least one academic investigator and one community member. An academic investigator must have the role of PI on the project. A community member may have the role of either co-PI or co-investigator. Eligible academic investigators will include all current CURES members as well as non-CURES members at Wayne State University (WSU) and Henry Ford Health System (HFHS) who declare their willingness to join CURES and abide by its policies. Each academic PI must have a faculty or other appointment that would enable him/her to submit an extramural research grant application as a PI.

   A list of current CURES members and members of the CURES Community Advisory Board can be found on the CURES website: http://iehs.wayne.edu/index.php

4. **Requirements:**
   1) The proposed research project must be responsive to this RFA – i.e., it must be a community-engaged research project that addresses an environmental health problem of concern to the community
   2) The proposed research project must be of outstanding merit – i.e., there must be a high likelihood that the proposed research project will have a substantial impact in addressing the problem
   3) As indicated above, an academic investigator must have the role of PI on the project and a community member may have the role of either co-PI or co-investigator. Additional collaborating participants (e.g., co-investigators, collaborators, consultants) are encouraged.
   4) While not absolutely required, another desirable characteristic of the proposed project will be the inclusion of a new investigator (as defined by NIH), since this will facilitate the mentoring mission of CURES. **We anticipate that at least one of the pilot projects that are funded will have a new investigator as PI.**

What may funds be used for?

Funds **may** be used as follows:

1. To purchase supplies, reagents, or equipment (clear justification required). Computers costing less than $5,000 and software fees are allowed.
2. For technical support salaries
3. For incentives for community partners and community research participants.

Funds **may not** be used as follows:

1. For salary support of faculty
2. For travel, except local travel (e.g., mileage for staff collecting environmental samples)

How do I apply?

The first step is to submit a letter of Intent (LOI) that is no more than 3 pages in length. The LOI should:

- Clearly explain why the proposed research is responsive to this RFA
- Include a “Statement of Impact” that explains why the project is significant and innovative, and why it will have a substantial impact on the field
- Identify the co-PIs and other participants and describe their positions, roles, and qualifications
- Provide a brief description of the project, including hypotheses, specific aims, and methods to be used
- Provide an estimate of the total budget and expected use of the funding (one paragraph)

LOIs will be reviewed by a subcommittee that is selected from the CURES Internal Advisory Board and Community Advisory Board. This committee will select those proposals that will be invited for submission of a full application. In the case of overlap among proposals, CURES may suggest collaboration. Details for preparing full applications will be provided to successful applicants when they are notified of their selection but the format will essentially be that of an NIH R03 with some additional requirements, as indicated:

a) Cover Page
b) Abstract and Personnel
c) Research sites
d) Biographical Sketches of key personnel
e) Other Support for key personnel
f) Available resources
g) Budget and Justification
h) Specific Aims (1 page)
i) Research Strategy (6 pages)
    a. Significance
    b. Innovation
    c. Approach (Preliminary Data should be incorporated into this section)
j) References Cited
k) Human, Vertebrate Animal, and Hazardous Materials Assurances of Compliance - Investigators using animals or human subjects in their research must obtain protocol approval from the Institutional Animal Care and Use Committee (IACUC) or the Human Investigation Committee (HIC), as applicable, before funds can be spent on activities that require such approval.
l) Plans for Submission to external funding agencies
m) Letters of commitment from all project leaders (both academic and community members).
n) Letters of support from the departmental chairs/directors of the PIs academic units. If you are the departmental chair, provide a letter from your Dean or Vice President.

Pre-award responsibilities. Successful applicants will be required to attend a pre-award meeting with the CURES Business Manager, at which they will be advised about account establishment and monitoring as well as the requirement to acknowledge support received from CURES and the WSU Office of the Vice President for Research in any publications that contain data that are generated under the Pilot Project award. Necessary IRB and/or IACUC approvals must be obtained as soon as practicable.

Award-time responsibilities. PIs must provide updates on their research progress for annual progress reports and meetings with the CURES External Advisory Board. Also, PIs must present their research findings each year at one of the CURES Center-wide research meetings. **Pilot project recipients will also be required to present their results at one of the CURES Community Outreach and Engagement Core's Environmental Health Forums.**

Post-award responsibilities. Upon completion of a project, the PIs will be required to submit a report that contains the following information:

1) A list of any publications (i.e., research articles, review articles, abstracts; submitted, in press, or published) or patents that resulted from the pilot project award.
2) A list of any grant applications submitted (funded, pending, or non-funded) that resulted from the pilot project award in which the applicant was listed either as PI or co-investigator.
3) A list of collaborations that developed as a result of the pilot project award.

Pilot project recipients will be expected to submit applications for extramural funding to continue their projects as soon as practicable.

Please adhere to the following formatting requirements when preparing LOIs:

- Font: Use an Arial, Helvetica, Palatino Linotype, or Georgia typeface, a black font color, and a font size of 11 points or larger. (A Symbol font may be used to insert Greek letters or special characters; the font size requirement still applies.)
- Type density, including characters and spaces, must be no more than 15 characters per inch. Type may be no more than six lines per inch.
- Use standard paper size (8 ½" x 11).
- Use at least one-half inch margins (top, bottom, left, and right) for all pages.

CURES Facility Cores

1. Integrative Health Sciences Facility Core (IHSFC)

Directors: Samiran Ghosh, Ph.D. (sghos@med.wayne.ed) and Graham Parker, Ph.D. (gparker@med.wayne.edu)

The purpose of the CURES IHSFC is to facilitate translational research by providing:

1. Biostatistical support for study design and advice on Institutional Review Board (IRB) applications for human investigation studies (Dr. Samiran Ghosh)
2. Access to cellular models that recapitulate human tissues, organ systems and developmental stages in the laboratory (Dr. Graham Parker)
3. Access to the Michigan Neonatal Biobank (www.mnbb.org), a repository for de-identified dried blood-spot specimens collected from Michigan's Neonatal Screening Program (Nancy Christ, nchrist@med.wayne.edu)

2. Exposure Signatures Facility Core (ESFC)

Directors: Douglas Ruden, Ph.D. (douglasr@wayne.edu), Susan Land, Ph.D. (sland@med.wayne.edu), and Paul Stemmer, Ph.D. (pmstemmer@wayne.edu)

The ESFC provides CURES researchers with an interactive environment that allows them to integrate genomic, epigenomic, and proteomic technologies at all phases of investigation, from the design phase through generating preliminary data and cost analyses, to conducting the research and writing the methodologies, and finally data analysis and interpretation.

Summary of Available Services

Core services are divided into three categories: (1) fully-established services (e.g., DNA sequencing); (2) fee-for-service with established prices, which may vary depending on sample type, quantity, and reagent availability, (e.g., genotyping); and (3) studies requiring new technology development. Core staff, in collaboration with investigators and data analysis groups, design experimental approaches to optimize results and provide investigators with a detailed cost analysis and documented methods. Investigators are encouraged to submit preliminary samples prior to an experiment in order to standardize methods and make modifications to optimize results. Services include:

Genomic Services (provided through the Applied Genomics Technology Center, Dr. Susan Land Director)

1. DNA isolation magnetic bead technology (small scale, Qiagen EZ1 Advanced or larger scale QIAsymphony) or manual processing is available for the following sample types: blood, buccal, saliva, frozen tissue, and formalin-fixed paraffin sections. Options include RNase treatment, glycogen addition for small samples, and additional protease treatment.
2. Next-generation sequencing utilizing an Illumina HiSeq 2000 (the 2500 upgrade has already been purchased). Options include: library preparation for DNA-Seq, RNA-Seq, microRNA-Seq, ChIP-Seq, Exome-Seq, and Amplicon-Seq. Output from the HiSeq includes files containing the basecalls for each sample (*.bcl) which is demultiplexed (if necessary) and converted to *.fastq files using CASAVA 1.8. The quality of the sequencing run is determined using the FastQC software as well as the parameters from the First Base Report produced by the HiSeq. The reads are aligned to the reference genome using Novoalign or TopHat, which takes the *.fastq files as input and produces *.sam and *.bam files as output, respectively. The remaining analysis options depend on the requirements set forth by the investigator. From the aligned reads, we can determine differential expression (Cufflinks or Partek) or alternative

splicing (Cufflinks or Partek), and do variant calling (samtools and GATK [Genome Analysis Toolkit]).

3. DNA sequencing (Sanger) utilizing an Applied Biosystems 3730. Options include: primer design, sample amplification, and amplicon purification before sequencing. Optimization of sequence reactions is available for hard-to-sequence templates such as GC-rich regions.
4. Genotyping services, including primer and probe design (when the assays are not commercially available), assay optimization, troubleshooting, and limited analysis. Options for single-nucleotide polymorphisms include 5'-nuclease assays (TaqMan, QuantStudio 12K Flex Real-Time PCR system-OpenArrays with fixed or custom content, digitalPCR, or single assays), GoldenGate (custom multiplexed panels up to 1536-plex and fixed-content panels such as the Cancer Panel, Illumina iScan) and Infinium (fixed content panels of up to 1.2 M, Illumina iScan) assays, length polymorphisms (Applied Biosystems 3730), and SNP chips (fixed content, Affymetrix)
5. DNA methylation studies, including bisulfite treatment of DNA, DNA sequencing (AB 3730), Illumina Infinium Methylation Bead Arrays (fixed and custom panels, Illumina iScan), Sequenom MassArray system, and PyroMarkQ24 (Qiagen)
6. Arrayed comparative genomic hybridization studies using SureScan technology (Agilent)
7. Somatic mutation analysis using the MassArray system (Sequenom) or PyroMarkQ24 (Qiagen)
8. RNA isolation obtained from cell lines, blood, paraffin slices, and tissue is available. The quality of the RNA is determined using a 260nm/280nm (NanoDrop or DropSense Spectrophotomer) and the 28S/18S and RNA Integrity Number (RIN) (Agilent Bioanalyzer 2100 or TapeStation).
9. Expression analysis options, including quantitative RT-PCR (TaqMan, QuantStudio 12K Flex Real-Time PCR System-OpenArrays with fixed or custom content, digitalPCR, or single assays), SureScan arrays (Agilent), GeneChips (Affymetrix), Sentrix arrays (Illumina iScan), and DASL assays for RNA isolated from formalin-fixed paraffin tissues (Illumina iScan).
10. GIPZ lentiviral shRNA library viral supernatant or individual clone preparation is available for the whole genome human shRNA library developed by The RNAi Consortium licensed from Open Biosystems.

Proteomic Services (Provided through the Proteomics Core, Dr. Paul Stemmer Director)

11. Protein identification using nano-LC/MS/MS instruments
12. Protein quantitation using spectral counting, isobaric tags and Stable Isotope Labeling with Amino acids in Cell culture (SILAC) with data acquired on the Orbi Elite, Q Exactive, or the LTQ and the Multiple Reaction Monitoring strategy using the TSQ Vantage system
13. Proteomic profiling using two-dimensional chromatographic separations or MuDPIT technologies
14. Analysis of post-translational modifications using nano-LC-MS/MS with fragmentation by ETD, higher energy collisional dissociation (HCD), or collision induced dissociation (CID).
15. Robotic protein digestion using the Genomic Solutions Investigator ProGest
16. Protein interaction and protease activity analysis by fluorescence polarization measurement using the Beacon 2000 fluorescence polarization system or the Tecan Polarion microplate reader
17. Peptide labeling and purification using an HPLC with UV and Fluorescence Detectors. Fluorescence measurement using a QM-6 spectrofluorometer equipped for simultaneous dual-emission recording and with removable dual-emission polarizers all controlled by software on an accompanying work station
18. Data Analysis using Mascot, Sequest, X!tandem, and Peaks algorithms with data compilation and secondary analysis using Scaffold.