NGS-Based Pilot Projects – Sequencing, Bioinformatics, and Analysis
Request for Applications

Purpose and Overview

To advance the cellular and molecular understanding of individualized and population health, undiagnosed diseases, adverse events, and more, the partnership between CTSI and the Mellowes Center for Genomic Sciences and Precision Medicine (MC), is seeking proposals for small-scale research projects that utilize any combination of the genomic, transcriptomic, or epigenomic technologies and bioinformatics platforms available in the MC. Responsive proposals will describe projects that 1) improve our understanding of disease initiation, progression, or therapeutic resistance, 2) show promise to clinically improve disease prevention, early detection, diagnosis or treatment, or 3) develop novel data that empower future studies translating 'Omics data into the practice.

Thus, responsive projects will be setup to rapidly identify discoveries for better understanding health for our communities through robust, multidisciplinary, and Team Science approaches, that leverage 'Omics technologies.

Number of Awards and Budget

- This mechanism will fund at least 2 projects up to $25,000 each for MC services that include sample preparation, sample sequencing or high-throughput assay, and/or bioinformatic analytics.
- Projects requiring greater than $25,000 to accomplish the outlined aims can be supplemented with other funding sources (see below).

Timeline

- Project Interest Forms are due by **May 24, 2024**
- Completion of a 30-minute consultation with the MC 'Omics technology and bioinformatics team by **May 31, 2024**
- Full applications are due by 5:00 p.m. on **June 21, 2024***
- Recommendation for funding will be made after peer review, by **mid-July 2024**
- Planned start date: **August 1, 2024**
  Human and/or animal study regulatory approvals must be in place before the award start date. If samples are not available within 6 months of the project start date, the award will be void.

** Funding Proposals: applications for this award are not required to be submitted in eBridge. Instead of starting a funding proposal in eBridge, please submit the online REDCap grant application to CTSI by 5:00 p.m. on June 21, 2024.*

Eligibility

- Faculty meeting MCW PI eligibility, or PI eligibility at another CTSI partner, that have an imminently implementable project involving NGS-based methodologies (see MC Technology & Bioinformatics Platforms below).
  - Projects should have a ready hypothesis
  - Sequencing data should meet minimum QC metrics appropriate for the NGS technology.
- Agree to abide by NIH data management sharing policy. (NIH 2023 Data Management Sharing Policy)
- Completion of a 30-minute consultation with the MC 'Omics technology and bioinformatics team to ensure appropriate allocation of resources and clear communication of project size and

design. Approximately one week after consultation the Mellowes Center will provide a statement of work (SOW) with an expected timeline and budget specific to your project.

Grant Application Instructions

Link to the grant application will be sent to PI upon completion of the 30-minute MC consultation.

Application Format:
Use standard 11-point font, single space, and half-inch margins throughout the document. Consecutively number all pages.

- **Scientific Abstract:** Provide a summary of the project (250-word limit).
- **Research plan:** Provide the aim(s) of the study, background, significance and rationale for the use of NGS-based methodologies and analysis. Describe sample availability (e.g. MCW tissue bank, lab storage), data set(s) to be analyzed (e.g. doi, SRA identifier, or clear file format description), and expected impact of proposed study (3-page limit).
- **Future Plans:** Provide clear information on how the award will lead to external grant funding (1/2 page limit).
- **References.** List references cited (not counted in page limit).

Supporting Documentation

- **NIH Biographical sketches.** Provide an NIH Biosketch in the most current NIH format for each PI and co-investigator.
- **Statement of Additional Funding Support.** If initial consultation indicates costs beyond the award amount, include source of additional funds along with a copy of the statement of work.

Evaluation Criteria and Reporting

Grants will be reviewed by a panel assembled by CTSI and Mellowes Center Leadership. Proposals showing promise to support submission of a high-impact paper or a larger proposal for extramural funding will be prioritized.

Awardees will be required to respond to routine post-award surveys and to present their data at a research seminar (to be scheduled by MC)**.**

EXAMPLES OF POTENTIAL PROJECTS

MC Technology & Bioinformatics Platforms

- **DNA-Based testing**
  - Sample types include frozen cell pellets, flash-frozen tissue, isolated total DNA
  - Tumor and/or somatic variant calling and analysis
  - Germline variant calling and analysis for cancer patients to investigate etiology or predisposition
  - Differences in variant (SNV, MNV, INDEL, CNV) frequencies between cases and controls
  - Analysis of specific inheritance patterns among duos, trios, or quads
- **RNA-Seq differential expression analysis (bulk, low input analysis available)**
  - Sample types include frozen cell pellets, flash-frozen tissue, isolated total RNA (from 10pg to 1ug), single cell preparation
  - Differential expression by pairwise conditions or among groups of conditions/phenotypes
  - Results summary *via* PCA (dimensionality reduction), volcano plot, heatmaps, and pathway analysis
- **RNA-Seq Single cell or Spatial**

    - Sample types include viable single cell suspensions from disassociated tissues, FFPE blocks, tissues sections on slides
    - Report on quality metrics of the sample sequencing, processing through Cell Ranger, Seurat and Loupe pipelines as appropriate for conditions
    - Consideration of differential expression among clusters or conditions of the samples (unsupervised)
- **DNA accessibility profiles *via* ATAC-Seq**
    - Sample type includes lifted and pelleted cells (at approximately 100,000 cells per condition)
    - Report on genome-wide patterns of peak position and intensity differences
    - Summary on genes and their proximal regulatory regions
- **DNA CpG Methylation *via* RRBS** or **EPIC methylation arrays**
    - Sample types include frozen cell pellets, flash-frozen tissue, isolated DNA (150ng - 1ug)
    - Global profile summaries, CpG calling and quantification, region-based quantification (tiling or DMRs), annotation with TFs and/or marks
    - Differential CpG and DMR calling among conditions
    - Summary of genes and their proximal regulatory regions with altered methylation
- **Histone-based ChIP-Seq and/or cut-and-run**
    - Actively growing tissue culture cells, fixed cell pellet (consultation available regarding method of fixation and total numbers needed) or prepared library
    - Report on genome-wide patterns of peak position and intensity differences
    - Summary on genes and their proximal regulatory regions

REPORTING

As an NIH supported program, the CTSI is required to collect benchmark, annual progress, and long-term outcomes reports of all Pilot awarded projects. Timely progress and reporting of the funded research project is a requirement of the award.

These CTSI Pilot – Mellowes Center Awards are funded by the Medical College of Wisconsin (MCW). All applications and awarded projects must follow respective processes including but not limited to reporting requirements.

FUNDING ACKNOWLEDGMENT

Please acknowledge the National Institutes of Health (NIH) CTSA award when publishing or presenting any outcomes resulting from your study by including the CTSI Funding Acknowledgement.

Questions?

Please contact Renee McCoy, CTSI Pilot Award Program Director, at rmccoy@mcw.edu.