Georgia Cystic Fibrosis Research Development Center – Pilot Grant Program-Request for Applications – July 2023

The Georgia CF RDP Center is seeking up to two pilot proposals for potential funding for one or two years each, including $60,000/year for a basic research project and $80,000/year for a project that includes actual interface with human subjects. Projects should reflect overall research goals of the RDP:

"Enabling next generation therapeutic advancement in CF". The Georgia CF RDP will support research in a rapidly changing and aging CF landscape, including testing consequences of CFTR modulation, developing effective anti-inflammatory and immunomodulatory therapeutics, and enabling microbe-based therapeutics for resistant CF pathogens. In addition, the RDP will facilitate drug discovery for people with CF who lack disease-modulating therapies as well as assist in the development of cell- and gene-based therapies with a particular focus on immunologic response to these agents.

Eligibility: Junior faculty conducting CF research without significant NIH support (i.e., an R01), established scientists new to CF research, or experienced CF investigators pursuing a new project that represents a clear departure from their established research program. Independent faculty at all universities in the state of Georgia are eligible.

Available budget: Basic research projects will be allowed direct costs up to $60,000 per year for up to 2 years. Translational/clinical research projects which include a human component will be allowed up to $80,000 per year for up to two years. (Note: Use of already collected banked samples will be considered for the basic research award, not translational/clinical.) Indirect costs are not allowed.

Selection of Georgia RDP pilot projects:

- Highest quality science, with an emphasis on innovative basic, clinical, or translational CF research
- Projects should reflect overall research goals of the Georgia RDP Center stated above
- Project must propose to use at least one Georgia CF RDP Core Facilities (details of Core services are below):
    1. Immunophenotyping Core,
    2. Quantitative Metabolism Core, and/or
    3. Data Integration and Bioinformatics Core
- Strong potential to obtain external funding
- High risk/high impact studies
- Initiatives that establish interdisciplinary research and new partnerships between basic and clinical investigators are encouraged

Process: Eligible investigators are invited to submit a 2-page Letter of Intent, 1-page budget summary, and NIH biosketches for key personnel that will be reviewed by the RDP Program Steering Committee. Investigators who submit the highest quality LOIs will be invited to submit a full 6-page proposal.

Letter-of-Intent Details:

1) Two pages maximum, not including references cited.
2) Required sections include: Specific Aim(s), Significance, Overall Hypothesis, Innovation, Investigator(s), Summary of Approach, and Plan for Extramural Proposal Submission.

3) Address feasibility for successfully accomplishing the goals of the project within 1-2 years, and how the project will either make use of the RDP Cores or build upon them.
4) On a single page, provide a budget justification in broad strokes (e.g., as an outline). **PI/Co-PI salary support will be limited to a total of 5% of the proposed budget.** NIH salary cap should be applied. Equipment greater than $5,000 per item, personal computers not crucial to goals of the project, and travel not related to accomplishing the goals of the project are not allowed costs.
5) Provide an NIH-style biosketch for the PI and any other key personnel, using the NIH's definition thereof.
6) The LOI should be assembled as a single PDF document for submission to CFatlanta@emory.edu before 5:00 PM Eastern Time on Friday, **September 1st, 2023**

Questions: Contact RDP Pilot Program Co-Directors Nael McCarty, PhD (namccar@emory.edu) or Jessica Alvarez, PhD (jessica.alvarez@emory.edu)

DESCRIPTION OF PLANNED RDP CORES:

Overall, the proposed Georgia CF RDP aims to provide additional critical infrastructure for established and new CF researchers and complement ongoing NIH P30 Cores (listed **HERE**). The proposed Georgia RDP is centered on the theme, "Enabling next generation therapeutic advancement in CF". The overall structure will allow flexibility in a rapidly changing and aging CF landscape for testing consequences of CFTR modulation, for developing effective anti-inflammatory and immunomodulatory therapeutics, and enabling microbe-based therapeutics for resistant CF pathogens. In addition, the Georgia RDP will facilitate drug discovery for people with CF who lack disease-modulating therapies as well as assist in the development of cell- and gene-based therapies with a particular focus on immunologic response to these agents.

Core 1: Immunophenotyping Core (IPC)

The IPC is designed as a forward-thinking Core that will provide testing platforms for novel cellular and genetic therapies (including immunogenicity of gene therapies), immunophenotyping of patient-derived samples, and the facilitation of immune and anti-inflammatory research in CF through optimized training and isolation/cryopreservation methods.

Services provided by the IPC Core are detailed below and include:

1) Human testing platforms for academic and Pharma industry labs
- Efficacy/immunogenicity of gene and cellular therapies
- Novel/repurposed agent testing in in human immune cell culture
- Biomimetic modeling with high-throughput 96 well assays
- Myeloid iPSCs CF variant lines

2) Immunophenotyping human samples
- CFTR function & expression
- Correlation of immune function with clinical outcomes

3) Cryopreservation & transmigration of immune cells
- Cryopreservation of whole blood, PBMCs, or specific cell types
- Transmigration of neutrophils/monocytes through airway epithelium for downstream testing

4) Investigator training in human immune cell models (faculty, staff, or trainee)

Core 2: Quantitative Metabolism Core (QMC)

The QMC is designed to facilitate the study of host cell and microbe metabolism in the presence or absence of therapeutic interventions. These include metabolite analysis, quantifying drug levels in a variety of biospecimens, spatial '-omics, and drug discovery support.

Services provided by the QMC Core are detailed below and include:

1) Quantitative small molecule determination in blood, airway, and cell samples

- Blood: Plasma, serum, erythrocytes
- Airway: Bronchoalveolar lavage (BAL), sputum, exhaled breath condensate (EBC), nasal lavage or filter paper
- Cell: Neutrophils, monocytes, epithelial cells, fibroblasts, bacterial cultures
- Other: Urine, Sweat, Saliva

2) Targeted and functional assays of therapeutics

- CFTR modulator drug levels in clinical and translational samples
- Cellular and enzymatic metabolic function, Redox
- Labeled nutrient tracing

3) Spatial metabolism & 'Omic discoveries

- Tissue and culture-based mass spec imaging
- Spatial metabolic gene/protein expression
- Untargeted metabolomics and lipidomics

4) Consulting/Training

- Method development, experimental design

Core 3: Data Integration and Bioinformatics Core (DIB)

The DIB is designed to: 1) provide biologic samples from people with CF (PwCF) of all ages to conduct biomedical research relevant to CF pathogenesis and therapeutics, 2) integrate extensive clinical data with the results of the biomedical research, 3) facilitate data sharing across cores, campuses, and institutions, and 4) educate on and provide support for computational approaches to big data and therapeutic discovery.

Services provided by the DIB Core are detailed below and include:

1) Provide **longitudinal biologic samples** from PwCF from infancy to old age as disease progresses, complications develop, and new therapies are started. Priority is given for studies on the immune response, inflammation, metabolomics (of host and/or pathogen), difficult to treat microbes, and new therapeutic strategies including gene therapy.

2) Host the **Georgia CF Data Warehouse (GACFDW)**. The GACFDW is a federated database system used to combine, utilize, and mine research data collected across our extensive CF research network. The Warehouse is hosted in a secured HIPAA-compliant Emory AWS account where we are able to leverage AWS services to transfer and store the collected data from this project.

3) Develop a cohort of **racially- and ethnically- diverse healthy control subjects** for longitudinal studies across the lifespan for comparison to PwCF.

4) Build **personalized data "toolsheds"** within the GACFDW that support data analysis, NIH compliant data sharing, and data preservation for the Georgia RDP investigators having NIH R01

and/or CFF awards.

5) Provide **standardized biostatistics, bioinformatics, and machine learning pipelines**that interface with the GACFDW, allowing users to automate tasks, including developing classification and regression algorithms.

6) Improve skills and workforce development through **canonical notebooks and hands on workshops** to inform on best practices in study design and biostatistics, data stewardship, bioinformatics, and systems approaches.