Request for Proposals: AST Research Network / CareDx Directed Research Grant: Multi-Modality Research on Kidney Transplant Patient Care with KidneyCare

If you have any questions, please email research@myAST.org.

The application deadline is **extended through** 11:59 pm Pacific Standard Time on **July 30, 2021**.

A. Overview:
CareDx is collaborating with the AST Research Network to provide one individual investigator research grant to support transplantation and immunology research that tests the utility of KidneyCare, a multi-modality solution for kidney transplant recipients that combines donor-derived cell-free DNA (dd-cfDNA), gene expression profiling (GEP), and bioinformatics and artificial intelligence.

About *CareDx, Inc.*
CareDx, Inc. is dedicated to improving the lives of organ transplant patients by developing precision medicine tools. By combining the latest advances in genomics and bioinformatics technology, with a commitment to generating high quality clinical evidence through trials and registries, CareDx is at the forefront of organ transplant surveillance and pre-transplant HLA typing solutions.

B. General Information:
One grant will be awarded for one year at $50,000. Please submit your research proposal for the AST/CareDx grant planning on one year of funding. Research must commence on January 1, 2022 and conclude on December 31, 2022. The research start date cannot be deferred for any reason.

The recipient will sign a letter of agreement with the AST Research Network. Payments will be issued to the recipient's institution by the AST Research Network, and the recipient will report to the AST Research Network.

C. Research Focus:
The AST/CareDx grant will fund research that tests the utility of KidneyCare, a multi-modality solution for kidney transplant recipients that combines donor-derived cell-free DNA (dd-cfDNA), gene expression profiling (GEP), and bioinformatics and artificial intelligence.

Although rates of acute rejection have declined after solid organ transplantation, there is an unmet need to better define the molecular phenotype of rejection and provide non-invasive, precision medicine tools to better detect rejection. The standard-of-care for detecting allograft rejection is pathology-read biopsy, which suffers from sampling error, interobserver variability, and artefacts that result in often subjective and varying diagnoses of allograft rejection. Genomic medicine, including biomarkers such as donor-derived cell-free DNA, may permit non-invasive and earlier detection of allograft injury and rejection, and may allow for quantitative serial monitoring of graft health and response to rejection treatment. Another genomic medicine technique for monitoring allograft function is gene expression profiling (GEP) of peripheral blood (and possibly urine). GEP characterizes changes in gene expression (upregulation and downregulation of genes) that identify pathologic states.

GEP and dd-cfDNA, separately and in combination, show potential utility for monitoring allograft health and identifying graft injury sooner and more accurately than the standard-of-care. We seek

investigators who will test the value of GEP and dd-cfDNA for allograft surveillance through improved outcomes, reduction in mortality and mobility to patients, increased graft survival, improved quality of life and reduced costs to the health system. There is also scope for genomic medicine tools to guide immunosuppression and rejection treatment. Proposals that aim to determine if dd-cfDNA and/or GEP can improve outcomes through immunomodulation or guiding rejection treatment are also encouraged.

Artificial intelligence in transplantation is a nascent concept; however, shows strong potential for augmenting clinical decision-making and improving care. Recent work showed the validity of a machine-learned algorithm for predicting allograft survival after kidney transplantation. We seek proposals for research that demonstrate the clinical utility of artificial intelligence in transplantation, including the use of existing algorithms (e.g. iBox) to guide clinical care and improve outcomes or increase efficiencies for the health system. We also seek new artificial intelligence projects in any area of transplant care, including pre-transplant optimization of care, donor and recipient selection, peri-operative and post-operative care, and long-term management of patients.

D. Review Process and Notification:
1. Proposals are due by July 30, 2021.
2. Funding decisions will be made by an expert review committee from the AST Research Network with input from CareDx. Grants will be scored on the basis of novelty, research approach, feasibility of obtaining relevant data, and prior work, as well as other factors.
3. All applicants will be notified of their application status in September 2021.
4. For the selected individuals, the term of the grant will begin January 1, 2022.

E. Eligibility Criteria:
1. Academic Appointment and Institutional Resources:
   a. The applicant must have an academic appointment at an accredited institution of higher learning.
   b. An individual may apply for the research grant while still in training. However, he/she must have been offered and accepted a faculty position that will begin on or before initiation of the grant.
2. AST Membership
   a. The applicant must be an active member of the AST or have submitted a completed membership application by July 30, 2021.
3. Previous AST Funding/Funding from Other Sources
   a. There are no restrictions on past or current funding.
      i. The applicant may be a past or current recipient of an AST Research Network Fellowship or Faculty Development research grant.
      ii. The applicant may currently hold career development awards, mentoring awards, NIH or other independent research awards.
   b. If the applicant is currently receiving funding for a project similar to the topics described in this RFA, the applicant should explain how the funds of the CareDx grant would not overlap with the funds of the other research support.
4. Miscellaneous
   a. The proposed work is to be performed in a North American laboratory.
   b. Education: The applicant must have completed post-graduate training at the time of the application.
   c. Applicants who have a substantial relationship with CareDx that would present a real or perceived conflict of interest if awarded this grant must first contact the AST Research Network to declare the conflict before submitting an application.
   d. Citizenship: The applicant must be either: a) a U.S., Canadian, or Mexican citizen; b) a lawfully admitted permanent resident foreign national of the U.S., Canada, or Mexico with a valid visa during the awarded period; or c) a foreign national admitted lawfully for

residence in the U.S., Canada, or Mexico during the awarded period. J1 and H1B visa holders are eligible to apply.

F. Specific Application Requirements:
Applications must be completed in full by July 30, 2021 in order to be reviewed. Applications that do not conform to these guidelines will be returned without review.

1. Name, title, and institution of principle investigator, co-investigator, and/or key co-collaborator(s).
2. Abstract of the proposed research plan: This document should concisely summarize the project in 400 words or less. The abstract should introduce the project and note its relevance to transplantation. It should describe the long-term objectives and specific aims, research design, and methods for achieving these goals.
3. Applicant's NIH biosketch (five-page format) to include all usual and pertinent information, particularly describing other past and current research funding and prior published work.
4. The biosketch of additional personnel to be named on the grant (i.e. whoever would ultimately be listed at publication).
5. Complete proposed research plan: This document should be between four and six pages; the page limit does not include references. The following sections must be included:
    a. Aims: include the key questions posed or hypotheses to be tested.
    b. Introduction: provide the rationale for the research.
    c. Preliminary Results (if any): show preliminary results supporting the research plan
    d. Research Plan: explain how the questions or hypothesis will be studied, with emphasis on experimental design over the details of the specific methods to be used. Anticipated results and potential pitfalls and alternative approaches should be briefly discussed. Specific research (and, if applicable, training) goals to be reached at the end of the grant should also be provided.
        i. Research plan should include a description of relevant facilities/capabilities.
6. Budget
    a. The grant is intended to provide salary support for the researcher and supplies/materials. No other costs are permitted, including institutional overhead.

G. Funding Guidelines and Terms of Agreement:
Please review these guidelines and terms prior to completing your application. If you are ultimately awarded a grant, you will sign a letter of agreement (LOA) stating that you agree to these funding guidelines and terms, and the LOA will be co-signed by your institution's grant/research office.

1. Research must begin on January 1, 2022 and end by December 31, 2022. The research start date cannot be deferred.
2. Funding in the amount of $50,000 will be provided for one year of research.
3. Funding will not be released until visa status is confirmed (if applicable).
4. The grant is intended to provide only salary support for the researcher and supplies/materials. No other costs are permitted, including institutional overhead.
5. The grant is paid one installment to the recipient's institution.
6. Grant funding is not transferable from one recipient to another. If the grantee relocates, the AST will determine if the grant can be transferred to the recipient's new location, or if the grant must be surrendered and any remaining funds returned. If the grant is surrendered, a final report will still be required; see item 9 below.
7. The applicant must acknowledge the grant as a funding source in all manuscripts and presentations derived from the funded research using the following statement: "This work was supported by a grant from CareDx and the American Society of Transplantation Research Network." Copies of such publications must be submitted to the AST National Office.
8. Pursuant to regulations of the federal Physician Payment Sunshine Act (included in the Affordable Care Act), NPI numbers will be collected from grant recipients (if applicable), and

tax ID numbers collected from the recipients' institutions (if applicable). All payments will be reported to the Centers for Medicare and Medicaid Services Open Payments system, as payments from AST represent indirect transfers of value from the funding pharmaceutical company.

9. Reports are required at the following intervals depending on the term of the grant, and continuation of funding is contingent upon completion of these reports:
    a. Six-month progress report due June 30, 2022.
    b. Final report within 30 days of the conclusion of the grant term of December 31, 2022.
        i. A final report is required even if the grant is surrendered for any reason prior to the conclusion of the grant term.

The partnership between the AST and CareDx, Inc. in offering and administering this RFA should in no way be perceived as an endorsement by the AST for the use of KidneyCare or any other assays of cell free DNA as a diagnostic or monitoring tool in kidney transplant patients.