



JDRF Autoimmunity and Beta Cell Cure and Prevention Translational Centers

Request for Applications

Key Dates:

Release Date: August 6, 2012

Statement of Intent to Apply: October 1, 2012

Letter of Intent Due Date: November 1, 2012

Notice of LOI Decision: December 6, 2012

Application Receipt Date: January 21, 2013

Notice of Award Date: May, 2013

Earliest Anticipated Start Date: July, 2013

This RFA contains the following information:

- Goals and Research Objectives of the JDRF Translational Centers
- Centers Description
- Additional Activities: Consortium
- Eligibility
- Budget
- Instructions to Submit an Application
 - Statement of Intent to Apply
 - Letter of Intent
 - Application
- Review of Applications
 - Review and JDRF Board Approval
 - Review of the Translational Aspects and Potential of the Center
 - Review Criteria of Individual Projects
 - Review Criteria of Cores
 - Clinical Trials Review
- Terms of Award
- Program Contacts

Strategic Goals and Specific Objectives of the JDRF Autoimmunity and Beta Cell Cure and Prevention Translational Centers Program

The purpose of the JDRF Autoimmunity and Beta Cell Cure and Prevention Translational Centers Program is to support the development of therapies to cure and/or prevent human type 1 diabetes (T1D), an autoimmune disease resulting in loss of functional beta cell mass and insulin dependence. In established T1D, JDRF has set a strategic goal of modulating autoimmunity and restoring functional beta cell mass to achieve insulin independence. Specific objectives include inducing beta cell autoantigen immunoregulation, regenerating beta cells, alleviating stress on the beta cell and promoting beta cell survival. Such approaches may prove applicable not only in established T1D, but also in recent onset T1D, where restoring and maintaining beta cells will likely be required to induce durable insulin independence. Recent data suggest that there is extensive cross-talk between the beta cell and the immune system in the ongoing pathogenesis of T1D, and thus, reversal of the disease may require use of combination therapeutics targeting both the autoimmune process and beta cells (beta cell health/survival and regeneration). In the at-risk setting, JDRF has prioritized both primary and secondary prevention of T1D.

Centers are expected to address fundamental questions about human T1D and should focus on one or more of the following:

- Elucidate the pathogenic mechanisms underlying human T1D in order to identify and validate new approaches and targets for its prevention or reversal; targeting the interplay between the beta cell and immune system in human T1D is of particular interest
- Develop and/or evaluate in proof-of-concept (PoC) trials novel approaches and agents for inducing beta cell autoantigen-specific immune tolerance in human T1D
- Develop and/or evaluate in proof-of-concept (PoC) trials agents for the prevention of the destruction of pancreatic beta cells, regeneration of beta cells, or promotion of beta cell survival in human T1D
- Identify and/or validate novel biomarkers for the assessment and staging of risk and progression, reversal of the immune pathogenic responses, or beta cell health, function, or destruction in human T1D.

The JDRF Autoimmunity and Beta Cell Cure and Prevention Translation Centers must focus on human T1D and address a critical gap that will directly or have the potential to ultimately translate to the development and evaluation of therapeutic interventions to reverse or prevent human T1D. Centers are not required to conduct clinical intervention trials, but the research must have clear translational potential for therapeutic intervention in T1D. The JDRF Autoimmunity and Beta Cell Cure and Prevention Translation Centers Program is intended to complement, and not to replace, funding available for clinical trials from national and international research funding organizations, including consortia such as [NIH's Immune Tolerance Network and Type 1 Diabetes TrialNet](#).

This RFA will not support applications focused on overcoming alloimmunity or inducing transplantation tolerance. However, studies on beta cell autoimmune recurrence in the context of beta cell replacement will be considered.

In addition to delivering on the Center-specific research goals, the individual Centers are required to participate in an Autoimmunity and Beta Cell Centers Consortium (ABCC) – consisting of the Center Directors and JDRF scientific program staff, as detailed below. The ABCC will share and discuss emerging data, develop additional joint research projects to create synergies among the Centers, and further advance efforts to prevent and cure T1D.

Translational Centers Description

The Centers Initiative aims to provide leading scientists and clinicians with the opportunity to bring together in a collaborative and performance-based, milestone-driven environment the diverse expertise needed to develop and rapidly translate new and emerging ideas into clinical benefits for people with

T1D. Centers will be organized around a priority goal and should support collaborations both among scientific disciplines and between basic scientists and clinical researchers. The component projects of the Center should be closely aligned and interdependent and should be clearly aligned with the Center's priority goal. Synergy within a center is expected and the synergies among Projects and Cores (see below for description) should be robust and well outlined in the LOI and final application. Centers should be coordinated, collaborative, multidisciplinary, integrated, and dynamic entities where new projects (including pilots) may be initiated and other projects terminated as dictated by scientific progress. An administrative Core, for coordination of Center activities, is required. Centers should be organized around therapeutic or translational goals and need-not be organized around a common region or institution; a JDRF Center may have principal investigator (PI) members from multiple regions or institutes.

Pivotal to the Center is the Center Director, an established investigator who is expected to provide strong intellectual and scientific leadership and create an environment that fosters communication, innovation, and high-quality research. Junior PIs are encouraged to lead Projects or Cores.

Special consideration will be given for a clinical trial or activities leading to a trial. However, a clinical trial is not a required component of a Center. Overall, the Centers should have a strong clinical translation mission, with defined goals and outcomes, and will show progress from basic or pre-clinical research towards clinical research or human clinical trials. JDRF will work with the Center investigators to promote the accelerated translation of their findings to the clinic, including addressing issues of manufacture of clinical-grade compounds, medicinal chemistry, and addressing regulatory activities. Technology sharing, whenever possible, across centers will be strongly encouraged.

The JDRF Autoimmunity and Beta Cell Cure and Prevention Translational Centers will have the potential to provide exceptional and comprehensive training environments for junior investigators and trainees. It is expected that the Centers will utilize their unique infrastructure and resources to enhance training opportunities for junior scientists in the Center. JDRF will further enable these activities through the provision of short-term training awards described further under the section "Additional Activities: Consortium" below.

As a resource for T1D research, Centers will be expected to attract additional funding from other appropriate sources, such as the investigators' institution, NIH, EU, industry, and others to enhance their mission.

Proposals that include industry collaboration as part of the Center or from groups with a track record of human translation are strongly encouraged. JDRF maintains relationships with a number of experienced partners that have an interest in such collaborations and can assist applicants with making appropriate connections if we are contacted early in the process.

Additional Activities: Consortium

Centers awarded funding will be part of the **JDRF Autoimmunity and Beta Cell Centers Consortium (ABCC)**. The JDRF Center Directors and JDRF scientists will serve on the ABCC Steering Committee, which will define the goals of the Consortium and will identify opportunities for creating synergies across the Centers. The members of the Steering Committee will meet monthly by teleconference and once a year at a face-to-face meeting. The ABCC will convene at a retreat every 18 months; in addition, bimonthly data calls will be implemented to facilitate information exchange and training. JDRF retains the prerogative to appoint external reviewers for any aspect of the individual Centers as well as the Consortium efforts as deemed necessary.

Additional resources will be made available, in years 2-4, for collaborative consortium activities, including a Pilot & Feasibility (P&F) Program (open to Center investigators and to the research community at large) and short-term Training Grants in Translational Research, to foster cross-training opportunities for junior

investigators involved in the Centers. The ABCC Steering Committee will be involved in establishing the procedures for the solicitation and review of projects supported through the P&F and Training programs. Participation of the Center in the ABCC and the participation of the Center Director on the Steering Committee are required.

Eligibility

Applicants must hold a D.M.D., D.V.M., M.D., Ph.D., or equivalent and have a faculty position or equivalent at a college, university, medical school, or other research facility. Applications may be submitted by domestic and foreign non-profit organizations, public and private, such as colleges, universities, hospitals, laboratories, units of state and local governments, and eligible agencies of the federal government. Ordinarily, for-profit organizations will not be considered to lead the center, but these organizations are encouraged to be members/collaborators of a Center (see "[Industry Discovery & Development Partnerships](#)" section for description of special program for for-profit entities). There are no citizenship or country requirements and racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as principal investigators and directors.

Budget

A maximum of US \$1.5 million per year total costs may be requested. Funding requests for up to 5 (3+2) years may be requested by individual Centers. Annual continuation of funding will be based on the outcome of annual evaluations. Funding beyond year 3 will be based on evidence of progress and promise as assessed by JDRF with input from an external expert panel. Since the nature and scope of research supported by this RFA may vary, it is expected that the size and length of awards may vary. If a Center requests five years of funding, this request must be clearly justified.

A budget should be presented for each individual project and Core. Funds requested must be used only for expenditures directly related to the research of the grantee. Costs for renovation, alteration or other infrastructure costs are not allowed. Core support may be requested for the normal operating expenses of shared facilities used by multiple investigators in the Center. Such expenses include salaries for technicians, equipment, materials and supplies, and maintenance contracts. In addition, salaries for a limited number of research trainees and other personnel whose participation will enhance the productivity of the Center may be requested.

Budgets should be quoted in United States dollars and provided for the entire project period. Clinical trials should be budgeted and will be funded based on meeting established trial milestones including enrollment, patient follow-up, etc.

Interested parties should note the following:

- JDRF is committed to the publication and dissemination of all information and materials developed using JDRF resources. All recipients of JDRF awards must agree to this principle, and must take steps in order to facilitate availability of data and samples.
- Applicants will be required to provide information about how any proposed Center activities will relate to the activities of NIH-supported studies (ITN, TrialNet, etc.)
- JDRF IP policy

A Statement of Intent to Apply is requested prior to submitting a Letter of Intent. However, a Statement of Intent is not mandatory.

A Letter of Intent is mandatory and must be approved before submitting a full application.

Instructions to Submit an Application

Statement of Intent to Apply

Those who have made a decision to submit an application are requested to announce their intent by sending an email to Deborah Kenyon at dkenyon@jdrf.org by October 1, 2012. The Statement of Intent to Apply message should contain the following information:

- Title and goal of the Center
- List of titles and lead PIs for each of the proposed Projects and Cores
- Any additional key collaborators

This will facilitate the recruitment of an appropriately composed peer-review committee. Please note that a Statement of Intent to Apply is not required and a Letter of Intent can be submitted even in the absence of a filed Statement of Intent to Apply.

Letter of Intent

Prospective applicants should submit a letter of intent (LOI). **The JDRF Center LOI template on proposal Central must be used to complete the application.** The LOI should include the following:

- A descriptive title of the proposed Center and a clear mission statement, the Center's priority goal;
- The name, address, telephone number, and email address of the Center Director;
- An estimated budget;
- The identities of other key personnel and participating institutions;
- The titles and a short description of component projects and cores;
- Research project descriptions indicating the translational significance, gap-filling nature and potential impact of the proposed studies for type 1 diabetes. Indicate how this Center proposal differentiates from other work being done in the field and whether and how this builds on current JDRF or other funding;
- Description of the synergism among any projects/cores within the Center
- Plan for research to lead to clinical trials, including collaborative efforts
- If a clinical trial is proposed as part of the Center, the following information should also be provided: clinical trial plan, including the target patient group and the intervention tested.
- Projected timelines and milestones for each year of the proposal
- Clear description of the deliverables and next steps if successful

All LOIs must be submitted through the JDRF on-line application system – proposalCENTRAL (<https://proposalcentral.altum.com/>), by **November 1, 2012**. Successful LOI applicants will be notified and will then have access to the full application at <https://proposalcentral.altum.com/> no later than December 6, 2012.

Application

The JDRF Center Application Template must be used to complete both the LOI and the application and both must be submitted via proposalCENTRAL.

Applicants must provide information about how any proposed Center activities will relate to the activities of NIH-supported studies (ITN, TrialNet, etc.) where relevant.

The Center proposal should contain the following: a Table of Contents, a Center overview and individual projects and cores.

- 1) Table of Contents — prepare a detailed table of contents that will enable reviewers to find specific information readily. Organize the table of contents so that the Center Overview and each individual project and core are listed as headings in the table of contents. Identify each project by title, and assign each project a number, each core unit a capital letter, and provide the name of the investigator responsible for each component. Number the pages consecutively.

- 2) Center Overview — a concise goal statement that expresses the Center’s priority goal. A more detailed description of the additional goals of the Center and each individual project/core, the relationship of the projects and cores to each other and how they are aligned with the Center’s priority goal, how the project team will be coordinated, and the Center and a composite budget and milestones for the entire Center. Please provide current or past JDRF Center funding and provide progress and success of JDRF and non-JDRF Center or multi-investigator programs. The Center Overview should not exceed 15 pages.
- 3) Individual Projects and Cores — each project or core includes a detailed budget, biographical sketches and information about other support for the applicants, and a detailed research plan/ core description with milestones. The research plan/ core description for each project/core should not exceed 10 pages. Tables, charts, figures and references are not counted as part of the page limits. Individual projects and cores may vary in timelines and duration; some projects could be shorter in length than the overall Center.

Review of Applications

Review and JDRF Board Approval

The Center application will be evaluated competitively by an external expert peer review committee based on the criteria described below. The final funding approval is made by the JDRF President and CEO and the JDRF International Board of Directors.

Review of the Translational Aspects and Potential of the Center

The relationship and contributions of each individual research project and core to the overall theme of the Center application and its translational potential will be evaluated by the review committee. The following criteria are among those considered by the review committee:

- **Relevance:** Does the proposed research meet the goals and objectives of the RFA?
- **Significance:** Is the Center addressing a fundamental question or challenge in human T1D that if addressed successfully will have a major impact on understanding and preventing/curing human T1D?
- **Approach:** Is the approach taken by the Center scientifically valid and technically feasible?
- **Innovation:** Is the proposed research novel and addressing key gaps or major challenges using innovative approaches?
- **Translational Impact Potential:** Will the Center program move the field significantly and meaningfully closer to a cure or prevention of human T1D? What is the potential impact of the Center’s program on the lives of those living with T1D? What is the likelihood of the program being commercially viable?
- **Collaboration:** How does the cohesiveness of the Center and the coordination of individual projects and core(s) contribute to the common theme? Do the Center investigators have a proven track record of effectively collaborating with other research groups on research projects? Are they likely to become collaborative members of the JDRF ABCC?
- **Organization, Communication and Synergy:** Will the organizational aspects of the Center structure allow the proposed research to occur? Assessment of the plans for meetings, other interactions, and exchange of data, material and techniques. Comment on the geographical distribution of the Center members, keeping in mind that the inclusion of researchers from different institutions is encouraged. Is there clear synergy among the Center’s Projects and Cores?
- Assessment of the **leadership and scientific ability of the Director of the Center:**
 - His or her ability to develop a program of integrated research projects with a well-defined central research focus; and
 - Her or his commitment and ability to devote adequate time and effort to the program.
 - Past success in JDRF on non-JDRF funded multi-investigator programs

- **Training:** How will the research setting permit and enhance translational research training?
- **Appropriateness of the proposed budget** and duration in relation to the proposed research. Is the overall budget appropriate and efficient?
- **Institutional and other sources of support:** What resources have been leveraged? What is the institutional commitment to the Center (financial support, time protection, and laboratory space and equipment, etc.)? Are there any other sources of financial support for the request, which could include: cost-sharing arrangements with the sponsoring institution(s), industry (keeping in mind that university-industry collaborations are strongly encouraged), or other agencies; estimates of institutional expenditures involved in upgrading or constructing laboratory facilities; estimates of indirect institutional support such as provision of services and computing resources.

Review Criteria of Individual Projects

Each individual project will be evaluated by a peer review committee. Reviewers will be asked to: 1) assess each project on its own merits; 2) assess each project as part of the Center and whether it should be included in the Center; and 3) assess the Centers track record in collaborative projects and their likelihood of being productive members of the ABCC. Reviewers will be provided with the full Center application to assist them in their evaluation. The following questions are among those that will be considered during the review of the individual projects:

- **Alignment with Center Priority Goal:** does the study clearly support the Center's priority goal?
- **Significance:** Does this study address an important problem, a scientific or technical challenge, and address a gap that the Center has identified? If the aims of the application are achieved, how will scientific knowledge be used to advance the Center's goals? What will be the effect of these studies on the concepts or methods that drive the broader T1D field? How does the program compare to the competitive landscape in both academia and industry?
- **Innovation:** Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?
- **Approach:** Are the conceptual framework, design, milestones, methods and analyses adequately developed, well integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative approaches? Is the approach technically feasible?
- **Investigator(s):** Is/are the investigator(s) appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator(s) and other researchers (if any)?
- **Environment:** Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?
- **Budget:** Is the budget appropriate? Are clinical trials budgeted based on enrollment?

Each individual project will be assessed based on the criteria described above and it is possible that individual projects may not be approved as part of a funded Center application.

Review Criteria of Cores

Reviewers will be provided with the full Center application to assist them in their evaluation. The following questions are among those that will be considered during the review of the cores:

Relationship to Projects: Does the core provide a necessary service driving progress toward the Center's priorities? How will the core provide service to each project?

Infrastructure: Is the Core adequately equipped to accomplish the work? What is the quality of relevant facilities or services provided by the core (including procedures, techniques and quality control)

and criteria for prioritization and usage? Are there core resources that could expand to support non-JDRF funded projects?

Core Personnel: Is the Core Director appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of Core personnel?

Budget: Is the budget reasonable? Are the core expenses distinct from project expenses?

Each individual core will be assessed based on the criteria described above and it is possible that individual cores may not be approved as part of a funded Center application.

Clinical Trials Review

If a clinical trial is proposed as part of a Center, JDRF will conduct a clinical trial review for this component of the Center. For details on the application and review process please refer to JDRF's web site.

Terms of Award

JDRF Cure and Prevention Translational Centers will be supported for a maximum of \$1.5 million total costs per year for a period of up to 5 (3+2) years. Funding beyond year 3 will be based on evidence of progress and promise based on successful external evaluation at the end of the 3rd year. Indirect costs cannot exceed 10% of direct costs minus equipment costs and/or subcontract costs if indirect costs are included in the budget submitted by the subcontracting organization. Evidence of institutional commitment in the form of dollars or non-financial resources is also required. Support beyond the funded period will be determined based on a competitive review of the accomplishments, future plans of the center, and JDRF portfolio requirements.

JDRF is committed to the publication and dissemination of all information and materials developed using JDRF resources. All recipients of JDRF awards must agree to this principle, and must take steps in order to facilitate availability of data and samples. IP Policy.

JDRF Autoimmunity and Beta Cell Centers Consortium (ABCC)

Full participation of the Center in the Centers Consortium and the participation of the Center Director on the Steering Committee are required.

Evaluation and Continuation of Funding

JDRF will perform regular Center Evaluations in the form of on-site or reverse-site visits with an outside panel of experts. Year-to-year funding is subject to modification based on the assessment of progress. At a minimum, evaluation and continuation of funding will require an annual written progress report, due two months prior to the anniversary date of the award. A detailed process for evaluation of progress will be determined at time of award.

Program Contacts

Please direct any scientific inquiries regarding this funding opportunity to:

Jessica Dunne, Ph.D.

Senior Scientific Program Manager, Immune Therapies Program

Tel: (212) 479-7595

e-mail: jdunne@jdrf.org

Please direct any administrative inquiries regarding this funding opportunity to:

Amanda Rieder

Grant Coordinator

Tel: (212) 479-7575

e-mail: arieder@jdrf.org