
New JDRF Beta Cell Replacement Initiative in Australia
Request for Applications for Post-Doctoral Fellowship Awards

Release Date:	August 11th, 2008
Application Receipt Date:	December 30th, 2008

This RFA contains the following information:

- Background
- Purpose and Objectives of this RFA
- Eligibility
- Proposal Format Requirements
- Terms of Award & Stipends
- Application review
 - Peer Review Process
 - Review Criteria
 - Required Ethical Approvals
 - Contractual Agreement with JDRF Australia
- Receipt and Review Schedule
- Inquiries

Background

T1D is an autoimmune disease characterized by the destruction of the insulin secreting beta cells of the pancreas by cytotoxic T cells. T1D is difficult to control with the current therapies available, and as a result patients may suffer devastating consequences including accelerated cardiovascular and peripheral vascular diseases, nephropathy, retinopathy, neuropathy, oral diseases and premature death. Islet transplantation as a therapy for T1D has been an important focus of JDRFI support, and significant progress has occurred in recent years. However, serious obstacles remain for development of islet transplantation as a cure for T1D in the general population, most notably the toxicity associated with current regimens of immunosuppression and islet administration and the limited supply of human cadaveric islets. The recent successes in islet transplantation provide additional impetus for research to develop methods to attain an unlimited supply of islets for transplantation; to improve methods for harvesting pancreata and isolating islets; to improve techniques for the administration of transplanted islets; to enhance the engraftment and vascularization of transplanted islets; to develop approaches to prolong and enhance transplanted islets' function; and to monitor the functional mass of transplanted islets.

This Request for Application (RFA) was developed as a component of the JDRF Islet Transplantation Program (ITP) in Australia. The ITP was established by the JDRF with funding from the Department of Health and Ageing, and is designed to help take islet transplantation from being an experimental procedure to one broadly available for people with diabetes.

The ITP was established to develop multi-centre clinical studies, accompanied by mechanistic studies, which implement a single clinical islet transplantation protocol. ITP groups share information and resources to advance the field of islet transplantation. The exchange of information among this group will be an important part of all proposals to improve the current techniques of islet transplantation.

JDRF Beta Cell Replacement Initiative

Request for Application – PF Awards



dedicated to finding a cure

This RFA is not a program being run in isolation. It is created specifically as a supplement to the ITP clinical program underway to address and support the need for improved clinical outcomes. This RFA will fund projects that will ultimately assist in the development of improved clinical islet transplantation outcomes.

Purpose and Objectives of this RFA

To foster the growth of Type 1 Diabetes research community in Australia and to provide training opportunities to young scientists, JDRF is soliciting Post-Doctoral Fellowship proposals with research plans addressing the following:

Restoring euglycemia and insulin independence by transplanting a replenishable source of glucose-responsive, insulin-secreting cells in the absence of chronic immunosuppression

- Development of methods for *ex vivo* expansion of cadaveric islets and identification of relevant mechanisms and pathways
- Robust and reproducible *in vitro* methods for differentiation of human stem cells to functional islets or beta cells
- Identification, characterization, and differentiation of pancreatic stem cells and beta cell progenitors
- Reprogramming of non-beta cells to glucose-responsive, insulin-secreting beta cells
- Development of glucose-responsive, insulin-secreting cell lines suitable for therapeutic use in humans
- Prevention of rejection of insulin-secreting cells
- Approaches to maintain long-term beta cell viability and function after transplantation, including interventions to regenerate beta cells *in-vivo* post-transplantation
 - Discovery of biologic factors for potential use as therapeutics to promote beta cell regeneration and for target isolation
 - Discovery of New Molecular Entities (NME) for activating the regeneration of endogenous beta cells
 - Proof-of-principle investigations of potential regeneration therapeutics in animal models and clinical studies
- Development of assays that detect and quantify human alloimmune versus autoimmune beta cell rejection and protection
- Preclinical strategies to prevent islet graft rejection without long-term immunosuppression
- Develop clinically relevant, non-invasive beta cell-specific imaging methods that can quantify functional beta cell mass of the endogenous islets and/or in the transplanted grafts
- Develop biomarkers that can quantitatively reflect functional graft mass.
- Studies to develop, evaluate, and validate biomarkers for the induction, maintenance and/or loss of immune tolerance and/or for the onset of acute or chronic graft rejection
- Studies to improve the consistency, yield, and viability of human pancreatic islets during the islet isolation process

Advances are needed in the application of tissue engineering to improve islet transplantation outcomes and to generate renewable beta cell sources. The design must be directed at satisfying the cell and molecular requirements for long-term functional success while considering the clinical requirements of beta cell replacement therapy. Determining the fate and function of implanted devices/materials is also of critical importance. These materials and their degradation products (if any) must be non-toxic and non-immunogenic, as well as possess other properties specific for beta cells/pancreatic islets and the site of implantation. Topics of interest includes:

- Encapsulation and immunoisolation technology that can protect pancreatic islets/beta cells from immune attacks with proof of concept tested in an *in vivo* animal model; meanwhile cell viability and function must be maintained
 - Novel materials and encapsulation methods for uniform micro- or macro-encapsulation of islets/beta cells to provide immunoisolation

JDRF Beta Cell Replacement Initiative

Request for Application – PF Awards



dedicated to finding a cure

- Coupling additional benefit of easy readout (e.g. imaging) of surviving and functional islet mass
- Novel biomaterial, encapsulation, or scaffold designs that may
 - Achieve innate and/or adaptive immunological isolation/ignorance for engineered devices;
 - Enhance islet engraftment, survival, and vascularization;
 - Meanwhile remain conducive to mass transfer of nutrients, oxygen, and other biological products necessary for islet survival and proper blood glucose regulation
- Development of strategies to promote vascularization and/or innervation within engineered islet tissue
- Promoting human stem/progenitor cell differentiation toward a physiologically-responsive insulin-producing cell
- Long-term maintenance of physiological beta cell phenotypes in an in vitro culture system for better characterization and understanding of the physical, chemical, and biomechanical aspects of beta cell biology

This RFA will complement and not replace other funding available through:

- ITP clinical program grants (initial commitments already made)
- ITP Pilot and Feasibility Studies and ITP Collaborative Research Projects grants
- Joint JDRF / NHMRC Program Grants
- JDRFI direct funding programs
- The Diabetes Vaccine Development Centre

Eligibility

Applicant

The fellowships are intended for those in a relatively early stage of their career. Ordinarily, their first degree (PhD, MD, DMD, DVM, or equivalent) will have been received no more than seven years before the fellowship. Since this program is targeted to those who would benefit from postdoctoral research training in preparation for later faculty appointments, applicants may not have faculty appointments. Any questions regarding eligibility should be directed to Dorota Pawlak (dpawlak@jdrf.org.au) and Albert Hwa (ahwa@jdrf.org).

Sponsor

The applicant must be sponsored by an investigator who is affiliated full-time with an accredited institution and who agrees to supervise the applicant's training. The sponsor does not necessarily need to have a background in diabetes, but the research project must be type 1 diabetes-related.

Location

Fellowship research may be conducted at Australian for-profit and non-profit, and public and private organizations—such as universities, colleges, hospitals, laboratories, units of state and local governments, and eligible agencies of the federal government.

Proposal Format Requirements

All applications must be completed using the templates provided on the [proposalCENTRAL website](#), under [ITP Post-doctoral Fellowships](#).

Research Plan

The research plan must address critical issues in beta cell replacement therapy, as explained in the section "*Purpose and Objectives of this RFA.*"

JDRF Beta Cell Replacement Initiative

Request for Application – PF Awards



dedicated to finding a cure

The postdoctoral fellowship research plan must be organized as follows: a) Specific Aims, b) Background and Significance of this work to beta cell replacement therapy and islet transplantation (provide a brief historical background of your proposed research, including major findings by you and/or others in relevant fields. Explain why you have chosen this problem), c) Preliminary Results (if available), d) Research Designs and Methods. Describe, in detail, plans for solving problems, hypothesis, methodology, expected results, experimental subjects, controls, potential pitfalls and the rationale for the chosen approach), e) Other aspects (formal and informal) of the program that will contribute to the total training environment (examples include, but are not limited to, clinical experience with diabetic patients, interaction with senior professional with expertise in diabetes, participation in staff conferences, teaching, consultation, etc.), f) List any planned coursework, g) List pertinent literature references (no page limit). All information in items a through d may not exceed 7 pages, not counting tables and figures.

In addition, a Future Career Plans statement and a Training Plan statement must be included at the end of the Research Plan section (see below).

Future Career Plans Statement

The applicant must include a statement of career goals and indicate the relevance of these goals to islet transplantation and beta cell replacement therapy.

Sponsor Application Requirements

The sponsor must provide a biographical sketch, a list of previous trainees, and a statement of the plan for training the applicant. This statement must outline a detailed training program (e.g. seminar, symposium, mentor-trainee meetings, etc.) for the applicant as well as confirm the availability of facilities to conduct the research project. The sponsor must also include accurate and complete information regarding all other sources of grant support (current and pending), including title, abstract, annual and total amount of grant, inclusive funding period, and percentage effort of the applicant.

Recommendation References

Three (3) recommendation references assessing the scientific abilities and potential of the applicant must be submitted. Please note that the recommendation references are confidential and will not be released to the applicant. *The recommendation references must be submitted directly to proposalCENTRAL by the referee. Please note applications will not be validated until all references are submitted.* Sponsors cannot be references, but should complete the Training Plans section of the application.

Terms of Award & Stipends

Awards will be made for duration of up to 2 years, assuming satisfactory progress. The fellowship term is 12 months for each fellowship year, and fellows must devote 100 percent of their effort to the project outlined in the application.

Budgets up to AUS\$90,000 per year for up to 2 years may be requested. The stipend request must be consistent with the amounts shown below (see Table below) based on years of relevant postdoctoral experience, inclusive of 9% compulsory and contributory superannuation. Salary support for additional staff is not allowable.

There are no indirect costs allowed for fellowships and JDRF will make no deductions for payroll tax, holiday loading etc. Funds in excess of the stipend, up to a total budget of \$90,000 per year, can be used for travel to scientific meetings (up to \$2000/year), journal subscriptions, books, training courses, laboratory supplies, or equipment (in Year 1 only). The purchase of a personal computer is allowed (up to \$2000) only during Year 1 of the award.

JDRF Beta Cell Replacement Initiative
Request for Application – PF Awards



dedicated to finding a cure

<i>Postdoctoral Fellowship Allowances</i>		
Years of Experience	Stipend	Maximum Total
0	AUS \$ 49,095	AUS \$ 90,000
1	AUS \$ 51,669	AUS \$ 90,000
2	AUS \$ 55,335	AUS \$ 90,000
3	AUS \$ 57,456	AUS \$ 90,000
4	AUS \$ 59,562	AUS \$ 90,000
5	AUS \$ 62,090	AUS \$ 90,000
6+	AUS \$ 64,508	AUS \$ 90,000

All awards must adhere to standard JDRF grant administration procedures.

Application Review

Peer Review Process

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by JDRF in accordance with the review criteria stated below.

The applicant’s professional ability and promise for a research career in islet transplantation and beta cell replacement therapy will hold the highest priority in selection and will be assessed on the basis of the letters of recommendation, career plans, prior clinical and research training, academic transcripts, and the mentor’s endorsement. Location in a department that will provide a stimulating research environment is an additional factor that will be considered in evaluating applicants.

Review Criteria

The scientific review group will address and consider each of the following criteria in assigning the application’s overall score, weighting them as appropriate for each application.

APPROACH: Are the conceptual framework, design, 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 tactics?

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?

APPLICANT: Is the applicant appropriately trained and well-suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator 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: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

Required Ethical Approvals

JDRF reaffirms its commitment to research within the framework of the highest scientific and ethical standards. The relevant regional legislation on ethical review requirements for human pluripotent stem cells applies to all projects to be funded by this Program. For research utilizing

JDRF Beta Cell Replacement Initiative

Request for Application – PF Awards



dedicated to finding a cure

human pluripotent stem cells, all applicants are required to provide evidence of appropriate ethical review by the Regional Ethical Committee. In addition, JDRF has convened its own Oversight Committee, which will provide a separate ethical review for all applications utilizing human embryonic stem cells, human embryonic germ cells/tissues, and human fetal tissues. Approval from both committees is required for funding.

All required ethical approval document(s) must be received by the JDRF before funding can begin. The Funded Applicant will provide certification, in English, as to the content of all ethical approval documents provided in other languages.

Contractual Agreement with JDRF Australia

All applicants who are ultimately selected for funding through this RFA will also be required to enter a contractual agreement with JDRF Australia, from whom funding will be provided through support from the Department of Health and Ageing.

Upon receipt of the application, the proposed contract with JDRFA will also be provided via electronic correspondence. Applicants are advised to discuss concerns regarding the contract terms with their sponsors and institutions early in order to prevent delays in activating the award.

Receipt and Review Schedule

Release Date: August 11th, 2008

Full Application Receipt Date: December 30th, 2008

Anticipated Award Date: March, 2009

Inquiries

Inquiries concerning this program are encouraged and should be directed to JDRF staff:

Scientific Inquiries:

Albert Hwa, Ph.D.

Scientific Program Manager, Beta Cell Replacement

Juvenile Diabetes Research Foundation International

120 Wall Street, 19th Floor

New York, NY 10005, USA

Tel: +1 (212) 479-7663

Email: ahwa@jdrf.org

Robert Goldstein, M.D., Ph.D.

Chief Scientific Officer

Juvenile Diabetes Research Foundation International

120 Wall Street, 19th Floor

New York, NY 10005, USA

Tel: +1 (212) 479-7523

Email: rgoldstein@jdrf.org

ProposalCentral Inquiries

Nicholas A. Roose

Grant Coordinator

JDRF Beta Cell Replacement Initiative

Request for Application – PF Awards



dedicated to finding a cure

Juvenile Diabetes Research Foundation International
120 Wall Street, 19th Floor
New York, NY 10005
Tel: +1 (212) 479-7694
E-Mail: nroose@jdrf.org

Other Inquiries:

Mike Wilson
Chief Executive Officer
Juvenile Diabetes Research Foundation Australia
Level 4 / 80 Chandos Street
St Leonards NSW 2065
Tel: 02-9966-0400
Email: mwilson@jdrf.org.au

Dorota Pawlak
Research Development Manager
Juvenile Diabetes Research Foundation Australia
Level 4 / 80 Chandos Street
St Leonards NSW 2065
Tel: 02-9966-0400
Email: dpawlak.@jdrf.org.au