



dedicated to finding a cure

JDRF requests expressions of interest for collaborative tissue engineering and biomaterials projects to improve beta cell replacement

Background and Purpose of Request:

One of JDRF's therapeutic goals is to restore beta cell function in type 1 diabetes by replacement/transplantation of beta cells. Pancreatic islet transplantation has been efficacious in select patients in improving metabolic control and quality of life, and in preventing severe hypoglycemia in patients with "brittle" or difficult to control type 1 diabetes (T1D). Despite improvements in cadaveric pancreas procurement, islet isolation, and islet purification, major scientific and technical challenges remain that must be addressed before beta cell replacement will be widely incorporated into the clinical management in established type 1 diabetes; examples include the insufficient human islet supply, an alternative transplantation site, and islet sensitivity to certain immunosuppressives. JDRF's role is to enable the scientific community to address these challenges with the ultimate goal of developing safe and effective transplantation approaches available to large numbers of individuals with type 1 diabetes.

Currently the field of islet transplantation is challenged by islet graft failures over time and the lack of a replenishable human cell source. Recent meeting reports on encapsulated porcine and human islets transplanted into non-human primates or patients continue to indicate that encapsulation may be a promising approach to provide long-term islet protection from the immune system. Early reports on attempts at producing beta cells from stem cells suggest the viability of the concept "bottled beta cells off the shelf." It is thought that the field will benefit from the involvement of bioengineers by applying quantitative and rational engineering principles to improving aspects of beta cell replacement therapy, such as immunoisolation and higher efficiency at deriving beta cells from stem cells.

Specific Goals of Request: JDRF is soliciting expressions of interest (EOIs) to encourage collaborations among bioengineers, chemists, immunologists, stem cell biologists, transplant researchers, and pancreatic islet biologists to incorporate engineering concepts and designs into current efforts toward improving beta cell replacement as a therapy for type 1 diabetes. Expressions of interest are sought from applicants interested in using the engineering principles to improve:

- Goal 1: Strategies to enhance long-term transplanted islet survival and function;
- Goal 2: Approaches to augment the differentiation of stem/progenitor cells towards physiologically-responsive insulin-producing cells and long-term maintenance and/or expansion of those cells in vitro

To achieve this, JDRF is soliciting EOIs for proposals addressing aspects of the following:

- Goal 1: Advances are needed in the development of novel engineered materials, devices, and/or culture systems that promote cell and graft survival, both in vivo and in vitro. Examples of pertinent topics include (not intended to be exclusive or all-encompassing):
 - Novel encapsulation and immunoisolation technology that can protect pancreatic islets/beta cells from immune attack with proof of concept tested in an in vivo animal model
 - Novel biocompatible materials and encapsulation methods for uniform micro- or macro-encapsulation of islets/beta cells to provide immunoisolation

- Designs must address mass transfer issues for appropriate beta cell survival and function
 - Novel biomaterials or scaffold designs that may
 - Achieve innate and/or adaptive immunological isolation/ignorance for engineered devices;
 - Enhance islet engraftment, survival, function, and vascularization;
 - Meanwhile remain conducive to mass transfer of nutrients, oxygen, and other biological products necessary for islet survival and proper blood glucose regulation
- Goal 2: To evaluate the development of alternative beta cell source for transplantation, bioengineered devices or culture systems, novel biomaterials and culture designs (examples include co-culturing, three-dimensional cultures, and perfusion systems) are needed to provide mechanical support as well as physical, chemical, and biomechanical cues in forming functional human beta cells or pancreatic islets. Examples of pertinent topics include (not intended to be exclusive or all-encompassing):
 - Promoting human stem/progenitor cell differentiation toward a physiologically-responsive insulin-producing cell
 - Development of strategies to promote vascularization and/or innervation within engineered tissue
 - Long-term maintenance of physiological beta cell phenotypes in an in vitro culture system
- ❖ Any novel material or device should address potential clinical utility, such as safety and manufacturing issues
- ❖ Proposals using novel biomaterials for the purpose of encapsulating islets/beta cells must indicate significant advance of the new materials/technology over reported encapsulation results to date

Expression of Interest should adhere to instructions printed in the template. It should include, where applicable, the following information:

- Name, title, institution, and contact information of principal investigator, co-investigator and / or key collaborator
- Designation of team members with necessary bioengineering/material science/stem cell biology/beta cell biology/immunology/transplant expertise
 - Collaboration between **Group 1: bioengineering/material science/chemistry** and **Group 2: stem cell biology/beta cell biology/immunology/transplant** expertise is required
- Specify whether the proposal addresses Goal 1 or Goal 2
- Brief details of approach proposed, including rationale and references to published or preliminary data (preliminary data need not be presented in detail)
- Short and long-term development goals set forth as milestones, as well deliverables
- Biosketch for each PI and co-PI
- Total estimated budget and project duration (up to 3 years)

Recommendation on funding level

Collaborative projects involving one PI in Group 1 and one PI in Group 2 may request up to total \$350,000 per year, up to three years. Innovative approaches and novel material development projects without significant preliminary data may request up to total \$150,000 per year for one year. Applicants should discuss with JDRF Program Staff when proposing multi-group projects with higher budget figures. Indirect costs may not exceed 10% of the direct costs.

Applicants are strongly advised to consult with JDRF Program Staff to discuss the responsiveness of their proposal to this program. Enquiries in this area should be referred to Albert Hwa, Ph.D., ahwa@jdrf.org, +1-212-479-7663, Adrienne Wong, Ph.D., awong@jdrf.org, +1-212-479-7642, or to Julia Greenstein, Ph.D., jgreenstein@jdrf.org, +1-212-479-7682.

Key Dates

- Expression of Interest should be submitted no later than January 12th, 2009 at 11.59 p.m. EST on proposalCENTRAL (<https://proposalCentral.altum.com/login.asp>). For questions regarding submission, please contact grantsupport@jdrf.org.
- Submitted expressions of interest will be acknowledged with brief responses as to their suitability for further development by the relevant JDRF Program Staff no later than two weeks from submission.

Announcement Date	EOI Deadline	Invitation of Full Applications	Full Online Application Deadline	Notification
09/03/2008	01/12/2009	01/23/2009	03/09/2009	06/2009

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PROPOSALCENTRAL

✉ <https://proposalcentral.altum.com/Login.asp>

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☎ (301)-916-4557 ext. 227, or toll free in the US, (800)-875-2562 ext. 227

Assistance can be obtained Monday through Friday between 8:30am and 5pm U.S. Eastern Time.