



dedicated to finding a cure

JDRF Requests Expressions of Interest for Projects in the area of Target Validation and Advanced Target Validation to Develop Therapeutics against Diabetes Complications

Background and Purpose of Request

JDRF is committed to facilitating the translation of pre-clinical discovery of promising targets or therapeutics in type 1 diabetic complications to the clinic and patient. To this end, JDRF is soliciting expressions of interest in *translational* research which addresses type 1 diabetic complications of nephropathy, retinopathy, neuropathy, or novel systemic inflammatory signaling pathways. Complications under consideration in this announcement are restricted to vascular leak and neovascularization of retinopathy, fibrosis of nephropathy, nerve degeneration of peripheral neuropathy and systemic inflammatory pathways. The specific expressions of interest will address one of two of the following:

- **Target Validation or**
- **Advanced Target Validation**

Specific Goals of Request

Target Validation

Expressions of interest are sought from investigators interested in the validation of promising targets known to be important to Type 1 Diabetic Complications. To qualify for this EOI, the target must not be in the discovery stage, but rather be known to contribute positively or negatively to the complication process.

In this context, target validation is defined as the demonstration that the DNA, RNA or protein is directly involved in the type 1 diabetes complication plus shows promise as a suitable target for therapeutic drug development as shown by modulation of the target. Through this request, JDRF seeks to identify and support projects towards the validation of a novel or even known therapeutic target that perhaps may have not been accelerated in this field.

Examples of Target Validation

Target validation approaches should use both correlative and causative approaches. Examples of correlative approaches would be:

- Genomics, proteomics, bioinformatics
- Chemical Genomics
- Microarray analysis

Examples of causative approaches would be:

- Use of oligonucleotides to modulate in vitro and in vivo
- Use of siRNA in vitro and in vivo
- Use of transgenic or knockout mice
- Use of small molecule agonists or antagonists

Advanced Target Validation

Expressions of interest in this related discipline to the above must pass stringent qualifications as determined by JDRF to qualify for this area. An expression that wishes to be considered for this area must demonstrate that the target has passed the process of target validation and thus is ready to go the next phase of drug development.

An example of a target that is deemed validated will have demonstrated that it can pass the rigors of correlative and causative approaches through a multitude of the above approaches AND is a suitable substrate for drug development. Drug-relevant is defined as modulation of a DNA, RNA, or protein target through current scientific technology (medicinal chemistry etc) without effecting a toxic or lethal outcome. Validated targets in this EOI will be ready to go to the next critical phase of advanced target validation outlined below.

Examples of approaches in Advanced Target Validation

- Production of protein fragments for testing
- Screening of validated targets to define new small molecules (“hits”) that can be further optimized as “leads”
- Development of in vitro and in vivo assays to support the screening process
- Use of systems biological approaches to define the importance of a hit in the complex biological process specific to type 1 diabetes
- Testing of possible hits in a type 1 diabetic specific in vitro assay or in vivo efficacy study

Restrictions

This expression is open to academic investigators AND commercial drug development enterprises. An expression submitted from a joint academic/industry is welcome. It is recommended that prospective applications review the Research Emphasis Areas in Type 1 Diabetic Complication posted on the JDRF website to assess the program interests.

Expressions of interest should be no more than two pages in length and include the following information:

- Name, title and institution or industry of principal investigator, and any co-investigator or key collaborator
- Subject header: **Target Validation or Advanced Target Validation**
- Brief rationale and description of proposed research plan, including summary of published or preliminary data
- **Advanced Target Validation ONLY - must summarize target and state of validation in pathogenic pathway known to be relevant to human biology**
- Brief schematic of the milestones for the project
- Inclusion of known therapeutics that are similar, if known
- Clinical potential of the strategy proposed as well as pitfalls
- Total estimated budget and project duration (not to exceed \$250K per year for a maximum of 24 months including 10% maximum indirect costs)

PROGRAMMATIC CONTACT

Inquiries should be directed to John Gebhard, Ph.D. at jgebhard@jdrf.org; tel: +1-673-9929 or Barbara Araneo, Ph.D. at baraneo@jdrf.org; tel: +1-212-479-7662

EXPRESSION OF INTEREST

Expressions of interest should be submitted via Proposal Central (<http://proposalcentral.altum.com/default.asp?GMID=16>), using the template provided, no later than November 15, 2008 at 11.59 p.m. EST.

Principal investigators whose EOIs prove competitive and relevant to this RFA will be invited to submit a full proposal. **An Expression of Interest must be approved before gaining access to a full application.** *If your EOI is approved, log back on to your account on proposalCENTRAL to gain access to the full application.*

KEY DATES:

EOI deadline	November 15 th 2008
EOI decision by	December 1 st 2008
Full application due (Academic R+D)	January 26 th 2009
Pre-review critiques and questions due	March 16 th 2009
Applicant response due	April 6 th 2009
Final critiques due	April 27 th 2009
Final review	Weeks of May 4 th and 11 th 2009

ADMINISTRATIVE CONTACT

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PROPOSALCENTRAL

☐ <http://proposalcentral.altum.com/default.asp?GMID=16>
☐ pcsupport@altum.com
☐ (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.