

## JDRF REQUESTS PROPOSALS FOR: IDENTIFICATION OF AREAS OF ARTIFICIAL PANCREAS ALGORITHM ENHANCEMENTS THROUGH BIG-DATA ANALYSIS (PART 1)

### PURPOSE

JDRF is committed to advancing the effectiveness and usability of artificial pancreas (AP) systems to treat type 1 diabetes (T1D). One focus area addressing both of these objectives is to improve the AP algorithm, which doses insulin autonomously based—mostly—on readings from a continuous glucose monitor and records of previously delivered insulin. JDRF challenges applicants to help understand how much better next-generation algorithms might be if researchers/developers leverage a large real-world data set from which to glean insights and identify areas for AP algorithm enhancements.

### BACKGROUND

T1D is characterized by the loss of the body’s ability to produce insulin, a hormone which regulates blood glucose levels tightly in individuals without diabetes. With no endogenous insulin production, people with T1D rely on exogenous insulin. The delivery of this insulin, though, must be carefully regulated; too much insulin results in potentially acutely dangerous low glucose levels (hypoglycemia), while too little insulin can result in problematic high glucose levels (hyperglycemia) and/or a potentially dangerous condition known as diabetic ketoacidosis (DKA). In short, it is essential that a person with T1D is dosed the right amount of insulin at the right time. Moreover, even if a person with T1D were able to provide this degree of control, it would necessitate an unacceptably high burden of self-management.

AP devices [interchangeably, automated insulin delivery (AID) devices] are currently the most advanced device-based treatment for T1D. These devices integrate three components to provide (at least partially) automated insulin delivery:

- 1) The sensor: a continuous glucose monitor (CGM) which continuously measures glucose levels in the body,
- 2) The actuator: an insulin pump, which has continuous access to the body to deliver insulin, and
- 3) The controller: an algorithm, which predominantly uses the information stream from the CGM and information about previously delivered insulin to calculate the optimal insulin infusion dose for the current conditions, and commands the insulin pump to deliver this calculated dose.

There is an ever-growing body of evidence demonstrating the ability of AP devices to both improve biochemical outcomes related to T1D (e.g., increasing time spent in a healthy glucose range while reducing exposure to hypo- and hyperglycemia) and simultaneously decrease the onerous responsibility of self-management. The algorithms used in these devices have advanced greatly, but have until now been developed largely based on first principles, simulation data, and/or limited real-world data.

JDRF is hopeful that the emergence of advanced “big data” analysis techniques such as machine learning enabled by access to large real-world data sets can result in better, more sophisticated, and possibly even personalized AP algorithms, or at least components thereof.

### OBJECTIVES

With the ultimate goal of developing therapies/products for commercialization in the future, proposals are sought from academic or non-academic organizations with serious intentions to use a provided set of “big data” to:

- 1) Help elucidate relationships/learnings with actionable recommendations that could be incorporated into next-generation AP algorithms, and/or

- 2) Develop or improve mathematical constructs that may be incorporated into next-generation AP algorithms.

Open publication/dissemination of results, methodologies, and even code is highly encouraged. Research groups with intentions to develop proprietary approaches are also welcome to apply, provided they have further intentions to incorporate their technologies into therapies/products for commercialization.

## DATA SET

JDRF will make available a large real-world data set provided by Tidepool via their [Big Data Donation Project](#), appropriately de-identified, for researchers/developers to use to achieve the above objectives. Data from at least 100 unique individuals with T1D (and possibly hundreds more, as described below) will be available and will include the following therapy-related time-stamped variables:

- Glucose values from a CGM
- Insulin delivery amounts from an insulin pump
- Glucose values from a blood glucose meter (BGM) or flash glucose meter (FGM)
- Blood glucose inputs from an insulin pump and/or BGM
- Carbohydrate inputs from an insulin pump
- Physical activity inputs [(type and relevant details such as duration and distance); note: these data may be limited depending on data requirements]
- Basal events from an insulin pump, e.g., temp basal, suspend
- Settings from an insulin pump, e.g., basal programs, insulin-to-carbohydrate ratios, correction factors

In addition, for each individual, the following **contextual** information is available:

- Actual time (of day, week, month, season, etc.).
- Date of birth (month/year)
- Date of T1D diagnosis (month/year)

Applicants should specify their data requirements in their proposals. Please refer to [Tidepool's data model](#) for a full list of available data types. The exact number of datasets that can/will be delivered will be dependent upon the project's specific data requirements and data availability. As part of the data requirements specification, applicants will need to specify A) the minimum required time-length of each data type (e.g., 6 months, 2 years, etc.) for each individual, and B) the minimum number of required individuals. Following funding decisions, grantees will work with Tidepool to finalize dataset details.

## RESEARCH OUTCOMES

Researchers/developers are charged with achieving the above objectives specifically related to (although not necessarily limited to) quantifying:

- The effect of incorporating any/all of the **contextual** information relative to not including this information, and/or
- The effect of incorporating a learning/adaptive mathematical construct leveraging any/all of the **contextual** information relative to not including such a construct.

Specific focuses of research/development efforts may include (but are not necessarily limited to) elucidating relationships/learnings and/or developing mathematical constructs related to:

- Identification or anticipation of events that meaningfully affect glucose control, e.g., insulin sensitivity changes/fluctuations, meals, exercise, stress, sleep, infusion set issues, lifestyle changes – and moreover actionable recommendations for how to handle them to improve glucose control
- Enhancing glucose prediction accuracy, including predicting hypoglycemic and hyperglycemic conditions

Examples of questions this research might help answer include (but are *certainly* not limited to):

- How informative is time? Are some individuals more “predictable” than others in terms of insulin sensitivity changes/fluctuations and/or personal habits/patterns? Can time-related learnings be incorporated into next-generation AP algorithms to improve controller performance and/or enhance usability of AP devices?
- How informative is age and/or time-since-T1D-diagnosis (“T1D age”)? Can individuals be stratified based on age range and/or T1D age range? Can age-related learnings be incorporated into next-generation AP algorithms?
- How effective can a learning/adaptive mathematical construct leveraging contextual information be in explaining an individual’s glucose control or the factors that affect it over a duration of time? Can such a construct be incorporated into next-generation AP algorithms?

## VALIDATION

A key “validation” step will be required for all award grantees. At a date in the future, additional data for each individual in the original data set will be made available for researchers to use to test their findings. Grantees will be responsible for using this validation data to demonstrate the integrity and repeatability of the results; in some cases, JDRF may request that grantees work with Tidepool through this validation step to further ensure the integrity and repeatability of the results.

Depending on the specific project, this validation data set may be roughly contiguous with, and more recent than, the original data set, i.e., for each individual, the validation data will pick up where the original data left off. In all cases, researchers must use the validation data set for testing purposes only; they may not use the validation data to inform the learnings obtained from the original data set. (Learning/adaptive constructs may, of course, still adapt over the course of the validation data set, but their mechanism may not be altered.)

The purpose of this crucial validation step is to ensure that the conclusions drawn from the original data still apply to the validation data.

JDRF may choose to merge complementary or synergistic approaches prior to the validation step.

## MECHANISM

In response to this announcement, proposals can be submitted to JDRF’s **Strategic Research Agreement (SRA)** or **Industry Discovery and Development Program (IDDP)** grant mechanisms.

For more information on the Strategic Research Agreement mechanism, please refer to our website: <http://grantcenter.jdrf.org/information-for-applicants/grant-mechanism-descriptions/strategic-research-agreements/>

Each application may request up to \$200,000 (including up to 10% indirect costs), for a maximum of one year.

## ELIGIBILITY

Applications may be submitted by non-academic domestic and foreign for-profit and non-profit organizations, public and private. Academic applicants must hold an M.D., D.M.D., D.V.M., Ph.D., or equivalent and have a faculty position or equivalent at a college, university, medical school, or other research facility. Applications from for-profit entities or industry collaborations with academia may be submitted to this RFP; however, additional information will be requested from for-profit entities if awarded a grant.

There are no citizenship requirements for this program. To assure continued excellence and diversity among applicants and awardees, JDRF welcomes applications from all qualified individuals and encourages applications from persons with disabilities, women, and members of minority groups underrepresented in the sciences.

## FULL PROPOSAL

Prospective applicants should submit a full proposal online via RMS360 (<http://jdrf.smartsimple.us>) to be considered for funding. The proposal template provided on the RMS360 website must be used to complete the application. Proposal section templates in MS Word [**10 page maximum**] should be type-written, single-spaced and in typeface no smaller than 10-point font and have no more than six vertical lines per vertical inch. Margins, in all directions, must be at least ½ inch. Complete information should be included to permit review of each application without reference to previous applications.

Proposals should use the template provided and include the following information:

- Background/rationale, published or preliminary work/data, hypotheses, specific aims, deliverables of project, collaborative framework if applicable
- Description of motivation and plan to publish results and methodologies (and if open-source, what license will be used), or otherwise to develop/translate project deliverables into therapies/products
- Estimated budget
- Biosketches for all principal investigators

By submitting a proposal to the RFP you agree that proposals may be shared with Tidepool at any time following submission.

Applicants are encouraged to consult with JDRF Scientific Staff to discuss the alignment of their proposal to this RFP and to develop the projected study concept.

## ANNOUNCEMENT INTRODUCTION AND PUBLIC Q&A

JDRF will hold an announcement introduction meeting via web and teleconference on **Tuesday, November 6 at 12:00pm (noon) US Eastern Time**, to which all interested prospective applicants are invited. JDRF scientists will give an overview of the goals of this initiative, explain the application process and answer initial questions on applications.

Click here to [Join Webex meeting](#)

Meeting number: 735 903 307

Meeting password: Jdrf2018

### Join by phone

Dial in (US): 1-650-429-3300

Dial in (International): [Global Call in Numbers](#)

Conference Code: 735 903 307

## DEADLINES

- **RFP release date** Friday, October 19, 2018
- **Proposal deadline** Wednesday, November 28, 2018
- **Response to applicants** April 2019
- **Earliest anticipated start date** June 2019

## SUBMISSION INSTRUCTIONS

Applicants should register and submit their completed proposal in RMS360 (<http://jdrf.smartsimple.us>).

## REVIEW CRITERIA

Proposals will be evaluated based on JDRF's standard confidential award policy and according to the following criteria:

- Significance
- Relevance to T1D
- Approach
- Innovation
- Plans for publishing and/or development/translation
- Investigator experience
- Environment

## CONTACTS

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If you have any grant-specific questions as you work within RMS360, please contact the administrative contact listed above.

For any **non-grant-specific** inquiries or issues, please contact SmartSimple Support Services via email support@smartsimple.com or phone (866) 239-0991. Support hours are Monday through Friday between 5:00am and 9:00pm US Eastern Standard Time.