# ISPAD-JDRF Research Fellowship Research Progress Report

| Principal Investigator | Date Sent | Due By |
|---|---|---|
| Petter Bjornstad, MD | 7/30/2018 | 8/10/2018 |
| **Project Name**<br>**D**iabetic **K**idney **A**larm (**DKA**) Study – Tubulopathy in diabetic ketoacidosis | **Amount of Grant**<br>$25,000.00 | |

This progress report should include the following. Use additional pages as needed.

1. A summary of project accomplishments during the reporting period.
2. A detailed explanation of any changes in focus or major changes in protocol. Provide justification for all changes.
3. A detailed explanation of specific problems encountered. Include a description of current efforts to resolve the problems.
4. A list and copies of all publications, including reprints, abstracts, manuscripts and presentations resulting from work accomplished during the reporting period.
5. Outline of work to be accomplished in next reporting period.
6. Other relevant information
7. Included below is an abstract of the study.

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1. Summary of project accomplishments:
   - Obtained SARC, IRB and Research Institute Approval
   - Secured ThermoFisher Kryptor Compact Plus instrument in lab to measure copeptin concentration as a reduced cost
   - Enrolled 15 patients so far (out of 40) [~38%]
   - Completed 15 visits for 0-8 and 12-24-hour time intervals
   - Completed 13 visits for 3-month follow-up (the remaining two are not due for their 3-month follow-up yet)

2. No major changes in protocol besides expanding eligibility to include participants with known type 1 diabetes to improve recruitment. This change will also allow us to evaluate differences in tubular injury markers between participants with known vs. new-onset type 1 diabetes presenting in DKA (diabetic ketoacidosis).

3. Recruitment has picked up since we expanded eligibility to include participants with known type 1 diabetes presenting in DKA. If recruitment slows down again we may consider expanding eligibility to mild DKA as well.

4. No publications to date but planning on presenting preliminary data at the *International Society of Pediatric and Adolescent Diabetes* meeting as an oral presentation in October. For this presentation, we will perform an interim analysis on available data.

5. Continue enrollment of participants, study visits and data collection

6. No other relevant information.

7. BACKGROUND: Type 1 diabetes (T1D) presents most commonly in childhood and translates to a lifetime of exposure and risk for early death from cardiovascular disease (CVD) and diabetic kidney disease (DKD). Over 1.25 million American children and adults have T1D, and most youth diagnosed with T1D in the US present with DKA; the incidence of DKA in youth at diagnosis of T1D in Colorado between 1998-2012 increased by 55%, which is much higher than reported in Canada or United Kingdom.

   GAP: DKA is characterized by dehydration, metabolic acidosis and hyperglycemia, all risk factors for tubular injury, but it is unknown whether DKA is sufficient to cause tubulopathy.

   HYPOTHESIS: The overarching hypothesis of this study is that irreversible tubulopathy exists in DKA and that it is related to urine uric acid (UUA)-mediated injury.

   METHODS: This observational study will prospectively examine markers of renal health from diagnosis of DKA through 3-months of follow-up. Boys and girls (age 3-21) with T1D presenting with DKA to the Children's Hospital Colorado (CHCO) ED.

   RESULTS: Pending

   IMPACT: If the results of the pilot study demonstrate evidence of irreversible tubulopathy in DKA, the next step would be a clinical trial to evaluate strategies to protect the tubules in youth with new onset T1D with DKA. The study findings will also be relevant to the rising number of overweight and obese youth who are at risk of type 2 diabetes, a condition associated with even higher rates of DKD than in T1D.