

Editorial:

Can high-dose omega-3 fatty acids and high-dose vitamin D3 (cholecalciferol) prevent type 1 diabetes and sustain preservation of beta-cell function after disease onset?

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Modulation of inflammation and immunity could prevent, delay or halt the progression of autoimmunity in Type 1 Diabetes (T1D). Vitamin D and omega-3 long chain polyunsaturated fatty acids (LCPUFA) could attain such modulation^{1,2}. Contemporary administration of high dose vitamin D and omega-3 PUFA was recently tested in pilot clinical trials to determine if progression of autoimmunity could be halted following T1D onset³⁻⁵. The rationale for this combination strategy is that Omega 3 LCPUFA (eicosapentaenoic acid, EPA, and docosahexaenoic acid, DHA) and Vitamin D can have beneficial effects not only on inflammatory markers, but also on immunomodulation-increasing regulatory T cells (Tregs), while decreasing Th17 cells and Th1/Th2 ratios^{1,2}. In contrast, arachidonic acid (AA) showed an opposite effect on Tregs, Th17 cells and Th1/Th2 ratios. A very high AA/EPA ratio has been observed in subjects diagnosed with T1D and other autoimmune conditions (F.Cadario and C. Ricordi, personal communication and manuscript in preparation). This may reflect a diet-related pro-inflammatory baseline condition. This condition could predispose to or trigger the subsequent development of autoimmunity. In this direction, anti-inflammatory nutrition could have an important synergistic role, in addition to Vitamin D and Omega 3 LCPUFA supplementation, as already explored by Cadario and collaborators in pilot and ongoing clinical trials. If the initial results will be confirmed, similar strategies to reduce exogenous insulin requirements and

promote persistence of residual endogenous insulin production could be of assistance to reduce the risk of complications in T1D⁶⁻⁹.

The recently reported maintenance of C-peptide production above baseline for over 2 years post diagnosis⁵ is very encouraging and warrants randomized controlled trials. Additional mechanistic studies, including assessment of cytokine profiles and inflammatory markers, will be required to determine the effect of the proposed combination therapy for prevention of T1D, as well as for preservation of beta-cell mass and function in patients with recent onset of T1D.

Because of the significant interest raised by these preliminary results, the 1st PreDiRe T1D (Preventing Disease and its Recurrence in Type 1 Diabetes) Symposium was organized to discuss initial results, possible alternatives and complementary combination strategies, to eventually generate consensus on the possibility to extend these interventions to disease prevention strategies (Figure 1).

In summary, the use of combination high-dose omega-3 LCPUFA and high-dose vitamin D₃ (Cholecalciferol) therapy has been well tolerated in pilot trials and may have beneficial effects on the maintenance of beta-cell function before and after T1D onset. Randomized controlled trials are required to validate this hypothesis and initial clinical results. Similar combination therapies aimed at modulating inflammation and promoting immunomodulation may be tested to prevent, reverse, or halt the progression of other autoimmune diseases.

In this issue of CellR4, we share the protocol for the Poseidon Clinical Trial (Pilot Study of OMEGA-3 and Vitamin D in High-Dose in Type I Diabetic Patients, ClinicalTrials.gov Identifier: NCT03406897), recently allowed by the FDA. Its

availability in open access could facilitate implementation by interested physicians and centers, and could stimulate the use of a similar design in the context of other autoimmune diseases.



2018 PreDiRe T1D SYMPOSIUM

Preventing Disease and its Recurrence in Type 1 Diabetes

April 20, 2018

Location

Diabetes Research Institute, University of Miami
1450 NW 10th Avenue, Miami, Florida 33136

Symposium Objectives

- To review findings from the ongoing screening programs
- To review emerging strategies to halt progression of autoimmunity
- To build consensus on a prevention protocol that could be applicable for both prevention of T1D and to prevent disease recurrence after a successful intervention strategy, such as immunotherapy or biologic replacement

Co-Chairs

Sonia Chritton
 President, Children With Diabetes Research Foundation

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 Founding President, The Cure Alliance

Type 1 diabetes (T1D) affects 1.3 million people in the U.S. Their expected medical expenses and income loss due to diabetes totals \$643 billion annually, with an increase of 3-5% each year. The JDRF, the American Diabetes Association, and the Endocrine Society have recognized that T1D should be diagnosed when a child develops multiple islet autoantibodies (stage 1) irreversibly leading to dysglycemia (stage 2) and symptomatic hyperglycemia (stage 3 T1D). Major ongoing studies are testing interventions at stages 1 and 2, to prevent or delay life-long insulin dependence. Mass-screening for stage 1 T1D provides access to the prevention trials and prevents life-threatening diabetic ketoacidosis at diagnosis.

Follow this link to indicate if you are interested in attending in person or by webinar:
<https://www.eventbrite.com/e/pre-di-re-t1d-symposium-tickets-43128745238>

For additional information please contact: PreDiReT1D@gmail.com

Figure 1. Overview and objectives of the 2018 PreDiRe T1D (Preventing Disease and its Recurrence in Type 1 Diabetes) symposium.

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