

## **AMERICAN DIABETES ASSOCIATION-ENTELOS TYPE 1 DIABETES COLLABORATION**

### **Summary**

The American Diabetes Association and Entelos, Inc. entered into a two-year collaboration to address key scientific questions related to the onset and progression of type 1 diabetes. In the first year, the Entelos Development Team will create a non-obese diabetic (NOD) Type 1 Diabetes PhysioLab<sup>®</sup> platform. This research will optimally position the collaboration for translational efforts, including the development and application of a Human Type 1 Diabetes PhysioLab platform in the second year of the collaboration. Application of these platforms will help clarify how interactions between immune components affects glucose control and the onset of diabetes, enabling the investigation of pathways contributing to and regulating autoimmunity and  $\beta$  cell destruction. Such insights will help clarify and characterize the major research questions surrounding disease onset and progression, and contribute to approaches to evaluate and halt or reverse disease progression.

Assisting the Entelos Development Team is a scientific advisory board, hand-selected by the ADA.

- Mark Atkinson, Ph.D. – Professor, University of Florida, Department of Immunology and Transplantation
- Jeff Bluestone, Ph.D. – Professor, UCSF
- Diane Mathis, Ph.D. – Professor of Medicine, Harvard Medical School; Head Section on Immunology, Joslin Diabetes Center
- George Eisenbarth M.D., Ph.D. – Professor, University of Colorado Health Science Center; Executive Director, Barbara Davis Center for Childhood Diabetes
- Aldo Rossini, M.D. – Professor, University of Massachusetts Medical School

Upon completion of the the first-generation NOD Type 1 Diabetes PhysioLab platform, Entelos will make the technology available to the greater scientific community through grants awarded by the ADA.

### **Challenges in Type 1 Diabetes**

Type 1 diabetes is a multifactorial autoimmune disease that affects approximately one million people in the United States alone. As disease onset often occurs early in life, primary disease and associated complications pose significant social and financial costs. The disease arises from the autoimmune destruction of islet  $\beta$  cells in the pancreas and the subsequent loss of glucose control. However, the understanding of type 1 diabetes pathogenesis and efforts to prevent, halt, or inhibit the disease are significantly impaired by the inherent difficulties associated with studying these processes in prediabetic and diabetic humans. These difficulties include the challenge of identifying individuals that will develop type 1 diabetes, as well as practical considerations in studying the involved tissues.

Since the study of type 1 diabetes pathogenesis in humans is difficult, much of the current understanding regarding disease progression and pathogenesis is derived from rodent models. The NOD mouse is a particularly well studied model in which the majority of females spontaneously develop diabetes. In these mice, the importance of numerous immune components to disease development has been experimentally established, and numerous therapies have been shown to inhibit the development of type 1 diabetes. Despite multiple successes in protecting the NOD mouse from disease, however, success in advancing therapies

from the NOD mouse to human patients has been limited. Currently, no preventative treatments are available for human type 1 diabetes.

### **Collaboration Goals**

The goals of the ADA/Entelos collaboration in type 1 diabetes are:

- Improve the scientific understanding of type 1 diabetes pathogenesis through the use of predictive mathematical models, starting with the NOD mouse
- Improve the rationale for advancing potential therapies from the NOD model into human clinical trials