

## **Tethys Bioscience – Scientific Background**

Diabetes is a complex disease driven by multiple underlying biological factors. Aside from phenotypic risk factors (e.g., obesity and high blood pressure) and imprecise diagnostics such as the blood glucose test, physicians have few tools available to assist in identifying those patients at highest-risk for the disease before progression, a critical time period when lifestyle and/or medication intervention can prevent irreparable damage from occurring.

### **The Power to Predict and Prevent**

Tethys products are based on the knowledge gained from a wide range of studies showing that prevention is possible. The company's first product, the PreDx™ Diabetes Risk Test, is a simple-to-use blood test that evaluates a patient's risk of progression to type 2 diabetes within five years and presents that risk in the form of a Diabetes Risk Score, a number between 1 (lowest risk) and 10 (highest risk). This individualized risk score correlates with a percentage risk of developing diabetes within five years, as determined by analysis of a large, retrospective study.

### **PreDx™ Development**

To create the PreDx™ Diabetes Risk Test, Tethys leveraged a deep understanding of the biological underpinnings of diabetes, as well as proprietary methods of analyzing molecular information and statistical modeling to identify an individual's corresponding risk.

Development began with a comprehensive search of scientific and clinical literature in an effort to identify an extensive list of the biomarkers associated with development of the disease. Biomarkers screened covered known pathways associated with diabetes progression, and each was assessed for utility and relevance.

To discover those biomarkers most predictive of diabetes, Tethys utilized samples from the Inter99 cohort, a Danish population-based primary prevention study of cardiovascular disease and type 2 diabetes. Blood samples from healthy subjects were tested using sensitive Molecular Counting Technology, resulting in quantification of 89 potential diabetes markers. This list was later narrowed down to the roughly 20 biomarkers determined to have higher or lower levels common to those in the study who had gone on to develop diabetes.

Following rigorous modeling and testing, Tethys developed the proprietary algorithm that became the PreDx™ Diabetes Risk Test. The final product utilizes biomarkers related to inflammation, lipid and carbohydrate metabolism and coagulation to assess changes related to multiple aspects of the disease process, not just glucose metabolism.

### **The PreDx™ Difference**

The PreDx™ focus on protein biomarkers is a key differentiator from other prognostic approaches. Unlike genetic tests, which describe an unalterable, gene-based risk, the PreDx™ Diabetes Risk Test describes a modifiable risk alterable through lifestyle and/or medication intervention. In this way, the patient and physician receive knowledge needed to make lifestyle changes to stave off progression to serious health problems before it occurs.

### **PreDx™ Future Applications**

In addition to PreDx™ Diabetes Risk Test, Tethys is developing similar tests for osteoporotic bone fracture and serious cardiovascular events, indications where there is growing evidence as to the potential of early intervention for those at highest risk.

*The PreDx Diabetes Risk Test is performed exclusively by the Tethys Clinical Laboratory.*