

Juvenile Diabetes Cure Research Tax Check-Off Program Annual Report

January 1 - December 31, 2010



Tom Corbett, Governor

Table of Contents

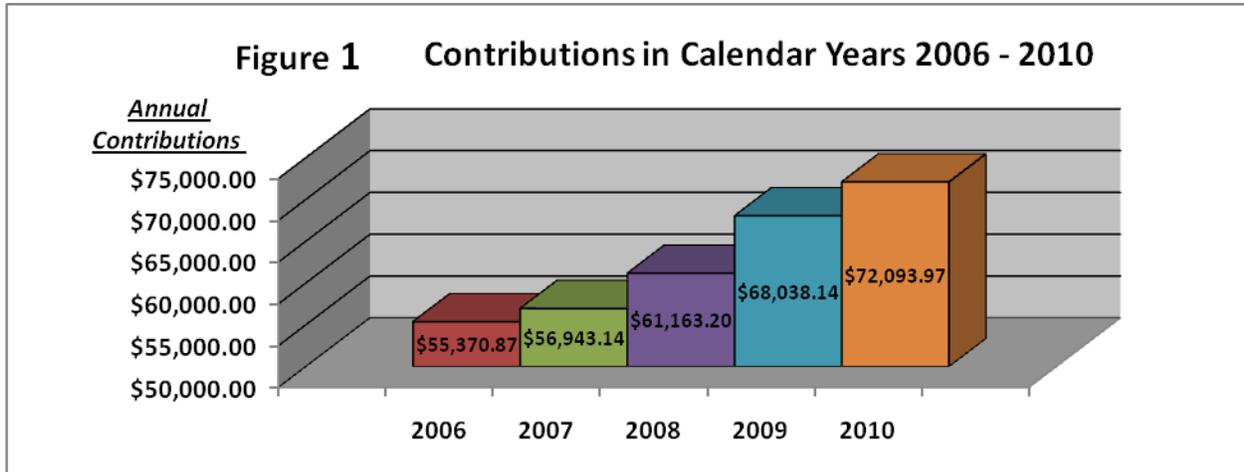
Juvenile Diabetes Cure Research Tax Check-Off Program	2
Tax Check-Off / Private Contributions	3
Administration of the Juvenile Diabetes Cure Research Tax Check-Off Program.....	3
Type 1 Diabetes Overview	4
Type 1 Diabetes Statistics	5
Diabetes Costs Overview	6
Research Results from the Juvenile Diabetes Cure Research Tax Check-Off Program Grant.....	7
Plans for Fiscal Year 2011-2012	8
For Additional Information	9
References	9

Juvenile Diabetes Cure Research Tax Check-Off Program

Created in September 2004 with the passage of Act 133, Juvenile Diabetes Cure Research, the Juvenile Diabetes Cure Research Tax Check-Off Program provides a state income tax check-off option for individuals to contribute a portion of their state tax refund to support research for juvenile diabetes, more commonly known as type 1 diabetes. The Program funds research grants focused on restoring normal blood levels, preventing and reversing complications of the disease and/or prevention of juvenile diabetes.

Tax Check-Off / Private Contributions

Tax Year 2009 (Calendar Year 2010) was the fifth year in which contributions were collected for this fund. Contributions to the fund in 2010 totaled \$72,093.97. The cumulative balance, as of December 31, 2010, was \$217,679.32.



Administration of the Juvenile Diabetes Cure Research Tax Check-Off Program

The Pennsylvania Department of Health (Department) Diabetes Prevention and Control Program is responsible for the administration of the Juvenile Diabetes Cure Research Tax Check-Off Program. A \$100,000 grant was awarded to The Pennsylvania State University College of Medicine to conduct vision impairment diabetic retinopathy research for patients with type 1 diabetes. Research began January 1, 2009, and ended on December 31, 2010.

The eventual significance of this research direction on public health outcomes could be enormous. Significant progress has been made using these funds. Thus far, the results of these studies have led to published manuscripts that describe roles for altered lipids and enzyme inhibition in diabetic retinopathy and complications:

1. Fox TE, Han X, Kelly S, Merrill AH 2nd, Martin RE, Anderson RE, Gardner TW, Kester M. *“Diabetes alters sphingolipid metabolism in the retina: a potential mechanism of cell death in diabetic retinopathy”* (DIABETES is the publication that contains the original article that provided initial data for this grant).
2. Fox TE, Bewley MC, Unrath KA, Pedersen MM, Anderson RE, Kim JK, Bronson SK, Flanagan JM, Kester M. *“Circulating sphingolipid biomarkers in models of Type 1 diabetes”* (The Journal of Lipid Research).
3. Fox TE, Young MM, Kester M, Gardner TW. *“Insulin Signaling in Retinal Neurons is Regulated Within Cholesterol-enriched Membrane Microdomains”* (American Journal of Physiology).
4. Fox TE, Kester M. *“Therapeutic strategies for diabetes and complications: a role for sphingolipids?”* (Advances in Experimental Medicine and Biology).

5. Fox TE, Young MM, Pedersen MM, Han X, Gardner TW, Kester M. “*Diabetes diminishes phosphatidic acid in the retina: implications for reduced mTOR signaling and increased neuronal cell death in diabetic retinopathy*” (under peer review at Investigative Ophthalmology and Visual Science).

The Pennsylvania State University College of Medicine has leveraged their findings for additional extramural funding as a bridge to national research funding from the National Institutes of Health (NIH) and American Diabetes Association (ADA):

1. National Institutes of Health National Eye Institute – The Role of Glycosphingolipids in Diabetic Retinopathy.
2. American Diabetes Association – Therapeutically modulating glycosphingolipid metabolism in a model of type 1 diabetes.
3. Presently seeking extramural funding to further explore the role of diminished caveolin-1 in ocular inflammation and vascular leakage.

Type 1 Diabetes Overview

Type 1 diabetes, previously known as insulin-dependent diabetes mellitus (IDDM), or juvenile-onset diabetes, is an auto-immune disease in which the immune system destroys the insulin-producing beta cells of the pancreas that regulate blood glucose. As a result, the pancreas no longer produces insulin, the hormone needed to convert sugar (glucose), starches and other foods into energy needed for living. This form of diabetes usually strikes children and young adults, although disease onset can occur at any age. In adults, type 1 diabetes accounts for approximately 5 percent of all diagnosed cases of diabetes. Risk factors may be autoimmune, genetic or environmental but the exact cause of type 1 diabetes is unknown with no known way to prevent it. In addition, there is no cure. Several clinical trials for preventing type 1 diabetes are currently in progress or are being planned.

The Scope of Diabetes: In the U.S., a new case of diabetes is diagnosed every 30 seconds; more than 1.9 million people are diagnosed each year.

The Cost of Diabetes: Nearly one-third of every Medicare dollar is spent on people with diabetes.

The Harm Caused by Diabetes: Damage to many organ systems (Diabetes is the leading cause of kidney failure, adult blindness, non-traumatic amputations and nerve damage.); increased heart disease risk (People with diabetes are two-to-four times more likely to have a heart attack or stroke.); and shortened life.¹

Type 1 diabetes is the third most prevalent childhood chronic disease in the United States. Type 1 diabetes has been diagnosed in children of all races, ages 10 to 19.² The disease comes on suddenly, causes dependence on injected or pumped insulin for life and carries the constant threat of devastating complications. While insulin injections or infusions allow a person with type 1 diabetes to stay alive, they do not cure diabetes, nor do they necessarily prevent the possibility of the disease’s devastating effects, which may include kidney failure, blindness, nerve damage, heart attack, stroke and amputations. Research focused on type 1 diabetes provides hope to detect its causes and to find a cure.

Type 1 Diabetes Statistics

On April 27, 2011, The World Health Organization reported that non-communicable diseases (NCDs) caused more than half of all deaths in 2008 and now pose a greater threat than infectious diseases, such as malaria, HIV and tuberculosis. NCDs, including diabetes, accounted for 36 million, or 63 percent, of the 57 million deaths worldwide in 2008.⁶

According to the Centers for Disease Control and Prevention (CDC), it is estimated that 25.8 million people of all ages in the United States have diabetes (with 18.8 million diagnosed and seven million undiagnosed).³ It is estimated that five to 10 percent of diabetic adults have type 1.³ The American Diabetes Association estimates that about one in every 400 children and adolescents has type 1 diabetes.⁴ Diabetes is one of the costliest chronic diseases.¹ Diabetes was the seventh leading cause of death listed on U.S. death certificates in 2007³ and the seventh leading cause of death in 2008 in Pennsylvania (2008 Vital Statistics).

In an effort to gain a better understanding and a better statistical picture of diabetes in children, the CDC and the National Institute of Diabetes and Digestive and Kidney Diseases funded the SEARCH for Diabetes in Youth study, a multi-center study focusing on children and youth with diabetes in the United States. This five-year study was a \$22 million national research project that ended in October 2005 and identified the number of children and youth under the age of 20 who have diabetes, both type 1 and type 2. The study provided the opportunity to learn more about the disease, its complications and its effects on the everyday lives of those who have it. It examined a diverse population of children and youth under age 20 from six geographic locations across the country. The published findings indicate:

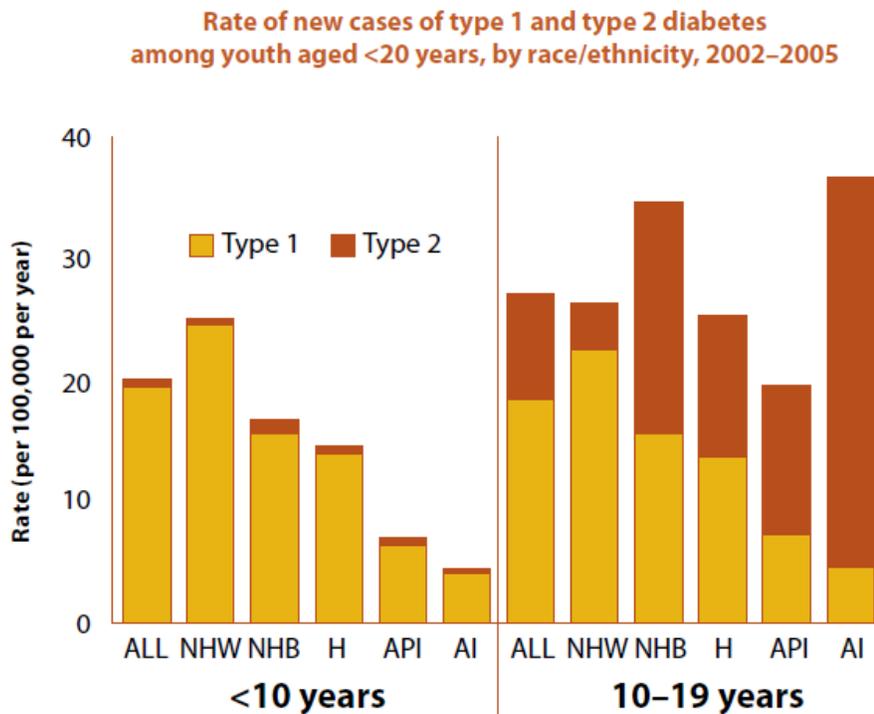
- The majority of new cases of diabetes in youth are type 1, with most occurrences in children under age ten.
- Of participants with type 1 diabetes, 56 percent had a first degree relative – a parent, sibling or grandparent – with the disease.
- Children diagnosed with type 1 diabetes had higher rates of obesity than children without diabetes.⁵

About 215,000 people younger than 20 years had diabetes (type 1 or type 2) in the United States in 2010. Estimates of undiagnosed diabetes are unavailable for this age group. During 2002–2005, 15,600 youth were newly diagnosed with type 1 diabetes annually, and 3,600 youth were newly diagnosed with type 2 diabetes annually. Among youth aged less than ten years, the rate of new cases was 19.7 per 100,000 each year for type 1 diabetes and 0.4 per 100,000 for type 2 diabetes. Among youth aged ten years or older, the rate of new cases was 18.6 per 100,000 each year for type 1 diabetes and 8.5 per 100,000 for type 2 diabetes.

Figure 2

Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2011

New cases of diagnosed diabetes *(continued)*



Source: SEARCH for Diabetes in Youth Study

NHW=non-Hispanic whites; NHB=non-Hispanic blacks; H=Hispanics; API=Asians/Pacific Islanders; AI=American Indians

http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf

Diabetes Costs Overview

Diabetes is one of the costliest chronic diseases, and timely investment in the diagnosis and treatment of diabetes is an excellent medical and economic decision. The number of new diagnosed cases of diabetes may be the tip of the iceberg, since a large study reported that there are an estimated 30 percent of undiagnosed cases of diabetes. The ramifications of undiagnosed and untreated diabetes can be serious, and the projected cost of not treating diabetes is extremely high.

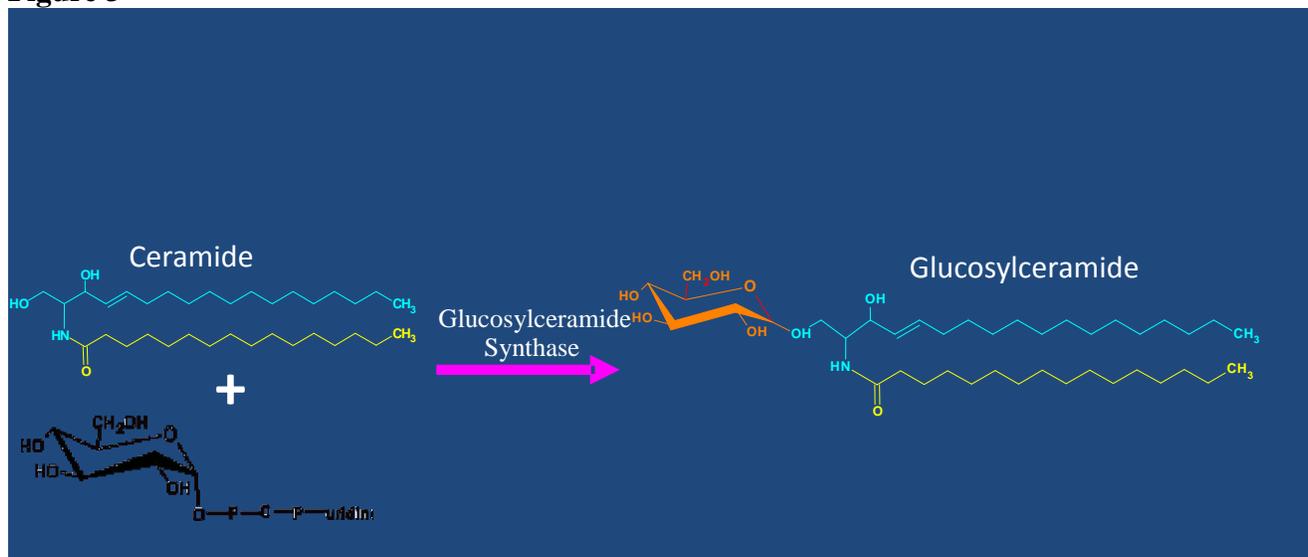
- National Estimated Diabetes Costs for 2007
 - ✓ Total (direct and indirect): \$174 billion
 - ✓ Direct medical costs: \$116 billion
 - ✓ Indirect costs: \$58 billion (disability, work loss, premature mortality)
- Pennsylvania Estimated Diabetes Costs for 2006 (American Diabetes Association's Diabetes Cost Calculator)
 - ✓ The total cost of diabetes for people in Pennsylvania in 2006 was estimated at \$6,789,000,000.
 - ✓ This estimate includes excess medical costs of \$4,496,000,000 attributed to diabetes and lost productivity valued at \$2,293,000,000.

- ✓ Totals for diabetes related hospital charges in Pennsylvania from 2000-2007 have reached more than \$5 billion and over 1,000,000 days in the hospital (Department analysis of 2000-2007 Pennsylvania Health Care Cost Containment Council [PHC4] Diabetes Data).
- ✓ In 2007 alone, the hospitalizations, for which diabetes was the principal diagnosis, accounted for over 132,200 hospital days and incurred over \$833 million in hospital charges (Department analysis of 2007 PHC4 Diabetes Data).

Research Results from the Juvenile Diabetes Cure Research Tax Check-Off Program Grant

Research Summary: Thanks to this grant, medical science now knows that too much of a type of glycolipid in the type 1 diabetic retinas of both rat and mouse models causes insulin to fail to be processed properly, as well as causing detrimental effects of inflammation, vascular dysfunction and neuronal cell death. An enzyme called glucosylceramide synthase (GCS) catalyzes the reaction that creates glucosylceramide in the retina. Juvenile Diabetes Cure Research Tax Check-Off Program grant funds were successfully used to identify and validate GCS as a target in reducing or eliminating diabetic complications.

Figure 3



Research Next Steps: A potential next step of this research would involve “knocking down” the production of the enzyme that catalyzes the reaction of the glycolipid by delivering small segments of ribonucleic acid (RNA) to locations where the enzyme is produced. These small segments can be encapsulated using recently developed nanotechnology techniques, and can make the reduction or elimination of the type 1 diabetic complications (improperly functioning insulin receptor, inflammation, vascular dysfunction and neuronal cell death) in the retina extremely likely.

This type of molecular-based therapy will become an important part of the health care industry. There are many diseases that are prime candidates to be cured by molecular-based therapies, especially autoimmune illnesses, such as asthma, rheumatoid arthritis and type 1 diabetes.

Future Research Needs/Prospects: These would include 1) to determine if polymorphisms in the GCS gene are associated with diabetes and/or metabolic syndrome; 2) to determine the upstream regulators of GCS; 3) to develop a non-labile, non-toxic small interfering ribonucleic acid (siRNA) formulation that targets GCS as a therapeutic to ameliorate diabetic complications.

Research Implications: Should research to create an encapsulated siRNA – one that remains stable in the body and turns off the malfunctioning gene(s) producing the GCS enzyme – be successful, the same techniques could be applied to other autoimmune illnesses by identifying the enzymes causing the problems in other autoimmune diseases and developing siRNA and delivery mechanisms to turn off those malfunctioning genes.

The American Autoimmune Related Diseases Association lists more than 100 autoimmune illnesses, including type 1 diabetes. The eventual impact of this research on public health could be profound.

Plans for Fiscal Year 2011-2012

The Diabetes Prevention and Control Program will release a Request for Application (RFA) in 2011. The purpose of the resulting grant will be to conduct research that focuses on juvenile diabetes as it relates to restoring normal blood levels, preventing and reversing complications from the disease and/or preventing juvenile diabetes. Research funds from the program will allow researchers to initiate their research with the intention of seeking sustainable funding from national funding sources.



This report was prepared by the Diabetes Prevention and Control Program, Division of Nutrition and Physical Activity, Bureau of Health Promotion and Risk Reduction, Pennsylvania Department of Health. For more information, contact:

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To contribute to the Program Fund:

Individuals may indicate the amount of their state tax refund they wish to contribute to the Juvenile (Type 1) Diabetes Cure Research Fund. Contributions may be payable to the Juvenile Diabetes Cure Research Fund and sent to:

Pennsylvania Department of Health
Bureau of Administrative & Financial Services
Division of Budget
625 Forster Street
Health and Welfare Building
Harrisburg, PA 17120

For Additional Information

For additional information regarding Type 1 diabetes, including managing the disease and current research being conducted, please visit the following:

- Centers for Disease Control and Prevention, <http://www.cdc.gov/diabetes>
- American Diabetes Association, <http://www.diabetes.org>
- Juvenile Diabetes Research Foundation, <http://www.jdrf.org>
- SEARCH for Diabetes in Youth, <http://www.searchfordiabetes.org>

References

1. Juvenile Diabetes Research Foundation. Fact Sheets: General Diabetes Facts, Type 1 Diabetes (Juvenile Diabetes) Facts. (Updated January 2011). http://www.jdrf.org/index.cfm?page_id=102586
2. National Institute of Diabetes and Digestive and Kidney Diseases. National Diabetes Statistics, 2007 fact sheet. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, 2008.
3. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2011. http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf
4. American Diabetes Association. Diabetes Statistics, Data from the 2011 National Diabetes Fact Sheet (released Jan. 26, 2011), <http://www.diabetes.org/diabetes-basics/diabetes-statistics/>
5. SEARCH for Diabetes in Youth. SEARCH Countdown Article: Who Has Diabetes? Retrieved April 27, 2011, <http://www.searchfordiabetes.org/documents/countdown.pdf>
6. New WHO report: deaths from noncommunicable diseases on the rise, with developing world hit hardest. News release, 27 April 2011, Moscow, Paul Garwood, Communications Officer http://www.who.int/mediacentre/news/releases/2011/ncds_20110427/en/index.html