GLOSSARY

Acarbose – A drug that reduces hyperglycemia by altering intestinal absorption of carbohydrates.

Adipocyte – Fat cell.

Adipogenic – Inducing the formation of fat.

Adiponectin – A protein hormone produced in adipose tissue that affects metabolism in multiple ways.

Afferent neurons – Cells that carry nerve impulses from receptors or sense organs toward the central nervous system.

AGE proteins – Advanced glycation end products proteins. High concentrations of glucose in the blood and tissues may cause glucose to attach to protein molecules which link together forming large macromolecules called AGE proteins. These are thought to contribute to the complications of diabetes.

Agonist – A drug or other substance that mimics the action of a hormone.

Albuminuria – Abnormally high levels of the protein albumin in the urine; may be a sign of kidney disease.

Allele – Any of two or more alternative forms of a gene that occupy a specific site on a chromosome. Synonym of genetic variant. For example, certain alleles of *HLA* are the most significant genetic risk factors for type 1 diabetes.

Alpha cell – A type of cell found in the pancreatic islets that makes and releases glucagon, a hormone that raises the level of glucose in the blood and thus has an opposite effect to that of insulin.

Angiopathy – A disease of the blood vessels. Macroangiopathy involves large blood vessels and microangiopathy involves small blood vessels. Diabetes damages both types of vessels.

Angiogenesis – The growth of blood vessels. The control of angiogenesis in specific regions of the body could lead to new treatments for retinopathy and other diabetes-related vascular diseases by retarding or enhancing new blood vessel growth.

Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) – Classes of drugs used to treat high blood pressure. These drugs can slow the progression of kidney disease in patients with diabetes.

Antagonist – An agent that opposes the action of another. For example, insulin—which lowers the level of glucose in the blood—is an antagonist of glucagon, which raises it.

Antibodies – Proteins that the body's immune system produces to protect itself from foreign substances.

Antigens – Substances that are recognized by the immune system.

Antioxidants – Drugs or natural substances, such as vitamins C and E, that prevent or reduce the process of oxidation, thereby protecting the cells or tissues from the damage of toxic oxidative end products.

Apoptosis – A form of programmed cell death.

Artificial pancreas – A medical device for use in people with diabetes, intended to act in lieu of one or more of the major functions of the pancreas: in particular, automatically responding to elevated blood glucose by releasing an appropriate amount of insulin into the bloodstream. *See also*: "Closed-loop system."

Atherosclerosis – A disease in which fat and other material builds up in the large and medium sized arteries, leading to decreased or blocked blood flow.

Autoantibodies – Antibodies generated in a person that react against that person's own body. For example, antibodies created by a person's immune system against his or her own beta cells, which may lead to destruction of these insulin-producing cells, causing type 1 diabetes.

Autoimmune disease – Disorder in which the body's immune system attacks and destroys body tissue it mistakenly identifies as foreign. In type 1 diabetes, the immune system identifies certain proteins on the body's insulin-producing beta cells as foreign materials, attacking and ultimately destroying them.

Autonomic neuropathy – A disease of nerves that function automatically to control such internal organs as the bladder, digestive tract, genitals, and cardiovascular system, disrupting the functions of these organs. As an example, impairment of the nervous system's ability to regulate heart functions can cause sudden cardiac death.

Autophagy – Self-digestion of cellular components.

Bariatric surgery – Refers to any of several surgical procedures intended to result in significant weight loss by altering the size of the stomach and/or resecting and re-routing the small intestine.

Beta cell – A type of cell in the pancreatic islets that makes and releases insulin.

Bioinformatics – The application of statistics and computer science to large, complex biological data sets, such as the human genome sequence.

Biomarker – A substance or characteristic that can be measured and used to assess a biological state, such as a disease or a response to therapy.

Blood glucose – The sugar that is the major source of energy for living cells and is carried to each cell through the bloodstream. The hormone insulin helps cells to use glucose.

Biguanides – A class of drugs including metformin, which is used to help control blood glucose in people with type 2 diabetes.

Body mass index (BMI) – A measure of obesity, defined as body mass in kilograms divided by height in meters squared. BMI is used to help determine if a person is underweight, normal weight, overweight, or obese.

Brittle diabetes – A term used when a person's blood glucose level moves often from low to high and from high to low.

Calorimetry – A method of measuring energy content or consumption, such as body heat (calories) used in activity. Tools used to do this are calorimeters.

Central obesity – An excess amount of fat stored in the abdominal area and assessed by measurement of waist to hip ratio.

Closed-loop system – A medical device that combines a glucose sensor and an insulin delivery system, automatically modulating blood glucose levels without patient involvement. *See also*: "Artificial pancreas."

Continuous glucose monitor – A medical device that automatically tests blood glucose levels every few minutes.

Coronary heart disease – A chronic state of inadequate blood supply to the muscles of the heart and the tissues around it. Also known as coronary artery disease.

C-peptide – A portion of the insulin protein which is clipped off the rest of the hormone and secreted along with it, sometimes used as a biomarker of insulin production by the pancreas.

Cytokines – Proteins secreted by different cell types of the immune system that serve as chemical messengers, promoting cell growth, immune interactions between antibodies and T cells, and immune reactivity.

Diabetic ketoacidosis (DKA) – A major acute complication of diabetes characterized by severe elevation of blood glucose and ketone levels usually occurring in persons with type 1 diabetes who have very low blood insulin levels. DKA occurs when the body begins using stored fat for energy, producing ketones and acids that build up to excessive levels in the blood. Without emergency treatment, the metabolic disturbances that result from ketoacidosis may lead to coma and death.

Diabetic nephropathy – Kidney disease that results when chronically elevated blood glucose causes damage to the small blood vessels and cells of the kidneys, impairing their ability to function, possibly leading to kidney failure (end-stage renal disease).

Diabetic neuropathy – Disease of the nerves that can affect any part of the nervous system: a single nerve (mononeuropathy); multiple nerves (polyneuropathy); the autonomic nervous system; or the central nervous system. *See also*: "Autonomic neuropathy; Peripheral neuropathy."

Diabetic retinopathy – Damage to the small blood vessels which supply oxygen and nutrients to the retina, at the back of the eye. This leads to changes in the flow of blood, weakening blood vessel walls, and stimulation of growth of harmful blood vessels. Retinopathy may be mild (background retinopathy) or it may become severe (proliferative retinopathy). In proliferative retinopathy, new blood vessels form which may rupture and bleed into the retina, threatening sight.

Diabetogenic – Causing diabetes.

DNA – An acronym for deoxyribonucleic acid, the genetic material.

DNA methylation – A type of chemical modification of DNA that is stable over rounds of cell division but does not involve changes in the underlying DNA sequence of the organism.

Dual-energy x-ray absorptiometry – A medical test for measurement of body composition, including adipose tissue (fat) and bone mineral density, which characteristically declines as part of osteoporosis.

Dyslipidemia – Unhealthy concentrations of serum lipoproteins—proteins in which fats (lipids) form a part of the molecule. For example, levels of high-density and low-density lipoprotein cholesterol affect a person's risk for heart disease.

Ectopic fat – The deposition of triglycerides within cells of non-adipose tissue that normally contain only small amounts of fat.

Efferent neurons – Cell that carry nerve impulses from the central nervous system toward muscles, glands, or other effector tissues.

End-stage renal disease (ESRD) – The point in any disease when the kidneys are so badly damaged or scarred that they fail, with the consequence that either renal dialysis or kidney transplantation is required for continued survival.

Energy balance – The balance between energy intake (food calories) and energy expenditure (body heat and activity).

Endoplasmic reticulum (ER) – A vast network of membranes within eukaryotic cells where all secretory and membrane proteins are assembled and proper folding, maturation, storage, and transport of these proteins take place.

Endothelium – The layer of cells that lines the heart and blood vessels.

Epigenetics – The study of modifications to DNA or proteins bound to DNA that do not change the DNA sequence, but which confer persistent effects on gene expression.

Euglycemia – Normal level of glucose in the blood. Also called normoglycemia.

Extracellular matrix (ECM) – Fibrous-like tissue that surrounds cells; an excess accumulation of this matrix may contribute to diabetic nephropathy.

Fatty acids – A component of fat. Fatty acids can be bound to glycerol to form a fat such as triglyceride. Fatty acids can circulate in blood as part of lipid particles or as "free" fatty acids attached to albumin (protein). The body (except the brain) may burn fatty acids for energy as a substitute for glucose.

Gene – The unit of heredity in living things. Typically, a gene is a DNA sequence that encodes a protein or RNA that has some function within the organism.

Gene expression – The transcription of a gene into RNA and/or translation of that RNA into protein; may also refer to the rate of that transcription or translation.

Genetic variant – Any of two or more alternative forms of a gene that occupy a specific site on a chromosome. Synonym of allele. For example, variants of the gene *TCF7L2* are associated with an increased risk of type 2 diabetes.

Genome – Complete genetic complement of an organism.

Genome-wide association (GWA) studies – A scientific attempt to identify genetic contributors to health and disease by correlating known genetic variants throughout the genome with specific diseases, characteristics, or health outcomes.

Genotype/ genotypic – The genetic constitution of an individual, particularly in reference to that individual's allele or alleles for a particular gene. A genotype may or may not have a detectable impact on that individual's characteristics or health.

Gestational diabetes mellitus (GDM) – A form of glucose intolerance diagnosed during pregnancy, characterized by abnormally high levels of blood glucose. The level may return to normal after delivery or can be a precursor to the development of diabetes later in life.

Glucagon – A hormone produced by the alpha cells of the pancreas that counteracts insulin and raises blood glucose.

Glucokinase – An enzyme that catalyzes the formation of glucose-6-phosphate from glucose. It contributes to the glucose-sensing activity of beta cells.

Glucose – A simple sugar found in the blood that is the body's main source of energy. *See also*: "Blood glucose."

Glucose counterregulation – The net effect of hormones, such as glucagon, that counteract the effect of insulin and restore normal levels of glucose in the body if glucose levels drop too low (hypoglycemia).

Glucose intolerance – Abnormally high levels of blood glucose after an oral glucose tolerance test (OGTT). *See also*: "Impaired glucose tolerance."

Glutamic acid decarboxylase (GAD) – An enzyme produced by the beta cells in the pancreas that, along with insulin and the enzyme IA-2, is targeted by autoimmune T cells that destroy the beta cell's ability to produce insulin. Antibody response to this protein is found in most patients who develop type 1 diabetes, often appearing months to years before the progression to overt type 1 diabetes.

Glycemic – Relating to carbohydrates (sugars), particularly glucose.

Growth factors – Small molecules that stimulate the growth of specific types of cells. *See also*: "Vascular Endothelial Growth Factor (VEGF)."

HDL cholesterol – High density lipoprotein cholesterol, often thought of as the "good" cholesterol.

Hemoglobin A1c (HbA1c, or A1C) – A variant of the hemoglobin A protein, which is the major carrier of oxygen in the blood. HbA1c results from the addition of sugar molecules to hemoglobin A, which occurs more easily in people with chronically elevated blood glucose. Because HbA1c is very stable, it is a good biomarker for how well a person's blood glucose has been controlled over the previous 2 to 3 months.

Hepatic – Related to the liver.

Hexosamine – A class of amino sugars derived from six carbon sugars or hexose; involved in the metabolism of carbohydrates.

HLA antigens – *See*: "Human Leukocyte Antigens."

Homeostasis – A relatively constant state within the body that is naturally maintained by various sensing, feedback, and control systems, including the brain and hormone-producing glands.

Human leukocyte antigens – Genetically derived molecules on the surface of cells that determine the similarity of cells and susceptibility to disease and are involved in the activation of T lymphocytes.

Human Leukocyte Antigen (HLA) system – This system assures that the immune system recognizes the individual's own tissues as self rather than as foreign. In people susceptible to type 1 diabetes, this recognition system goes awry and produces an autoimmune response to insulin-producing beta cells.

Hyperglycemia – Abnormally high level of blood glucose, a hallmark of diabetes. Uncontrolled hyperglycemia may damage large and small blood vessels and lead to other complications of diabetes.

Hyperinsulinemia – A chronically high level of insulin in the blood that occurs because the body is producing large amounts of insulin in an effort to overcome insulin resistance.

Hyperlipidemia – An abnormally high level of lipids in the blood.

Hypertension – Abnormally high blood pressure.

Hypoglycemia – An abnormally low level of glucose in the blood.

Immune system – The body's system for protecting itself from viruses and bacteria or any "foreign" substances.

Immune tolerance – The process by which the immune system considers a protein or other molecule as self, and does not mount a destructive response against cells or tissues containing that protein.

Immunosuppressive drugs – Drugs that prevent an immune response to foreign or self proteins. Often administered to prevent rejection of transplanted tissue and to prevent autoimmune disease.

Impaired glucose tolerance (IGT) – A disorder in which blood glucose levels are intermediate between normal and diabetic. Because studies have shown that IGT increases the risk of developing type 2 diabetes and its macrovascular complications, IGT is sometimes referred to as "pre-diabetes."

Inflammation – Part of a complex biological response to certain stimuli, particularly infection. While inflammation is a normal and valuable immune system process, chronic inflammation may contribute to diseases including diabetes and coronary heart disease.

Insulin – A hormone secreted by the beta cells of the pancreas that regulates the metabolism of glucose.

Insulin analog – A form of insulin modified to have desirable properties for therapy. It may have more rapid onset of action or be more long-lasting.

Insulin pump – A mechanical device that pumps insulin into the body through a plastic tube that is connected to a needle inserted into the body. The pump may also be activated by the person to deliver extra boosts of insulin when needed, e.g., at mealtimes.

Insulin receptors – Specialized protein molecules on the outer surface of a cell that bind circulating insulin, allowing insulin to produce its effects on the cell, including taking up glucose from the blood and using it for energy.

Insulin resistance – Impaired ability of muscle and fat cells to respond to the hormone insulin. Insulin resistance is a major contributor to and precursor of type 2 diabetes and may appear many years prior to the onset of clinical disease.

Ischemia – Poor blood supply to an organ, such as the heart, that is often marked by organ dysfunction and pain.

Islet transplantation – Transplanting pancreatic islets (as opposed to a whole pancreas or a section of a pancreas) from a donor into a person whose pancreas has ceased to produce insulin.

Islets of Langerhans – The pancreatic structure containing alpha, beta, and delta cells, which produce and secrete hormones such as insulin that aid in the metabolism. (Referred to as "islets" in the Strategic Plan.)

Ketoacidosis – *See*: "Diabetic ketoacidosis."

LDL cholesterol – Low density lipoprotein cholesterol, sometimes called the "bad" cholesterol.

Leptin – A hormone that is secreted by fat cells and controls a key pathway in regulation of food intake and energy balance.

Lipids – Fat or fat-like substances often used to store energy in animal (or plant) tissues. Lipids include cholesterol and triglycerides. Elevated levels of lipids in the blood are associated with diseases such as atherosclerosis.

Loci – Plural of locus.

Locus – The position of a sequence within the genome.

Lymphocytes – Small white blood cells that are critical components of the immune system and of the autoimmune response in type 1 diabetes. There are several types of lymphocytes. B cells are primarily involved in the production of antibodies. Helper T cells release chemicals that activate and direct the movements of other cells to help fight infection or attack foreign matter, including the production of antibodies by B cells. Suppressor T cells suppress the activity of B cells.

Macrovascular – Related to large blood vessels. Macrovascular complications of diabetes can lead to coronary disease, cerebral artery disease, and peripheral vascular disease.

Macular edema – Eye disease in which leaking fluid from the blood vessels pools in the center of the retina and impairs central vision functions, such as reading.

Magnetic Resonance Imaging (MRI) – A technique for obtaining images of the internal structure or processes within the body. The nuclei of certain atoms absorb the energy in a strong magnetic field, causing them to spin. The spinning nuclei can be detected and pinpointed in the body to produce an image.

Major Histocompatibility Complex (MHC) – Genes that control the body's immune response. They produce molecules that are expressed on the white blood cells of the immune system, including the human leukocyte antigen (HLA) molecules that contribute to the autoimmune response in type 1 diabetes.

Matrix – A mixture of proteins found between tissue cells (also called extracellular matrix).

Maturity Onset Diabetes of the Young (MODY) – A type of diabetes distinct from type 1 or type 2 diabetes characterized by early onset and a primary defect in insulin secretion, caused by a single genetic flaw that can be inherited from either parent.

Mesenchymal stem cells – A group of cells that can differentiate into a number of important cell types, including bone- and fat-producing cells (osteoblasts and adipocytes).

Meta-analysis – A study that combines data and results from multiple previously published studies, and applies statistical methods to answer questions that could not be addressed by the previous works, or more precisely than was possible in the previous works.

Metabolic syndrome – A combination of medical disorders that increase the risk of developing both cardiovascular disease and type 2 diabetes. Precise definitions vary, but the syndrome is generally marked by several of the following: central obesity (large waist circumference), high blood pressure, unhealthy levels of fats in the blood, and impaired glucose tolerance or elevated fasting blood glucose. (Also called Syndrome X.)

Methylation – Addition of a small chemical group (methyl group) to another molecule. Methylation of DNA and proteins bound to DNA in chromosomes affects how genes are expressed and is a form of epigenetic modification.

Microangiopathy – *See*: "Angiopathy."

Microarray – A two-dimensional array of a large number of small samples (e.g., DNA, RNA, protein, or other chemical compounds), that can be assessed for one or more scientifically interesting properties through high-throughput screening.

Microbiome – The complete collection of microbes that live in a particular environment (such as a human being) and/or their collective genomic information.

Microvascular – Related to small blood vessels. Microvascular complications of diabetes affect the eye, kidney, and nerve and can lead to blindness, kidney failure, and limb amputation.

Mitochondria – Compartments within cells that convert calories derived from food into fuel the cells can use for most biological processes.

Monoclonal antibodies – Antibodies of a single type that recognize a particular antigen, usually mass-produced from a cell hybrid that is formed by the fusion of a normal antibody-producing cell to a tumor cell.

Murine – Pertaining to rats and mice.

Myocardial infarction – Damage to the heart due to coronary artery disease. Also known as heart attack.

Neovascularization – The growth of minute new blood vessels in a new location, such as out from the retina in diabetic eye diseases.

Nephropathy – *See*: "Diabetic nephropathy."

Neuropathy – *See*: "Diabetic neuropathy."

Non-Insulin-Dependent Diabetes Mellitus (NIDDM) – Former term for type 2 diabetes.

"Omics" – systematic approaches to studying the complete collection of a particular set of biological compounds from an organism. For example, genomics is the systematic study of the whole genome, proteomics is the study of all of an organism's proteins, and metabolomics is the study of the chemical intermediates and products of an organism's metabolic processes.

Oral hypoglycemic agents – Class of drugs that are taken by mouth and are used to lower blood glucose levels by stimulating the pancreas to release more insulin, increasing tissue glucose uptake, decreasing glucose production by the liver, or inhibiting glucose absorption.

Oxidation – The process by which the oxygen content of molecules is increased, changing their chemical structure.

Oxidative stress – Damage due to the accumulation of toxic end products resulting from oxidation in cells and tissues (*See also*: "Reactive oxygen species"). This process has been implicated in diabetic complications, as well as in atherosclerosis and cancer.

Pathogenesis – The processes which occur in the development of a disease.

Penetrance – The proportion of individuals with a particular genetic trait who also exhibit the characteristics associated with that trait. For example, the fraction of people with a gene that can cause a disease who actually develop the disease.

Periodontitis – Inflammation of the tissue that surrounds the teeth, gums, and/or the jaw bone.

Peripheral neuropathy – Nerve disease that causes pain and sensory loss, usually affecting the feet and lower extremities; can lead to foot ulcers and even to amputation, especially when accompanied by impaired circulation.

Phagocyte – A white blood cell that ingests and destroys other cells or foreign matter. In type 1 diabetes, phagocytes and T cells attack and inflame the pancreatic islets, as part of an autoimmune process that ultimately destroys the insulin-producing beta cells.

Phenotype/phenotypic – Having to do with the characteristics of an individual (or group) that can be detected and that result from the interaction of genetic and environmental factors.

Phosphorylation – The metabolic process of adding a phosphate group to an organic molecule; important in diabetes because it is involved in the breakdown of glucose, action of insulin, cell signaling, and other processes.

Plasticity – Capacity to change.

Platelets – The smallest cells in the blood, necessary for blood clotting.

Polymorphism – A genetic variant.

Positron Emission Tomography (PET) – A radiographic technique that, through the use of special tracers, can show the metabolism of glucose in the body, especially the brain.

PPAR gamma – A nuclear hormone receptor involved in the differentiation and function of fat cells. Certain classes of oral diabetes drugs act through this receptor. *See also*: "Thiazolidinedione drugs."

Protein kinase C (PKC) – An enzyme that transfers phosphate groups to specific proteins, changing their biological activity. Several hormones and growth factors activate PKC, including VEGF, which may contribute to diabetic proliferative retinopathy. Inhibitors for the different types of PKC are being studied for treatment for diabetic retinopathy, nephropathy, and cardiac disease.

Proteinuria – Proteins in the urine; measurements of small amounts of protein (microalbuminuria) can detect kidney disease at an early stage. Large amounts of protein (macroalbuminuria) reflect late stages of kidney disease.

Reactive oxygen species (ROS) – Chemically-reactive molecules containing oxygen that are generated normally during cellular metabolism. An excess of ROS can damage cellular structures.

Receptors – Any one of a group of protein substances found on the surface of or within a cell that bind with specific molecules, antibodies, viruses, or hormones.

Renin Angiotensin System (RAS) – Renin — an enzyme made and stored by the kidneys—helps produce angiotensin—a substance in the blood that causes vessels to constrict and thus raises blood pressure. Drugs actings on the pathway lower blood pressure and protect against diabetic nephropathy.

Retinopathy – *See*: "Diabetic retinopathy."

RNA – Ribonucleic acid. Chemically similar to DNA, RNAs of different sequences and structures have numerous roles in the body.

SNP – Single nucleotide polymorphism; a particular position within the genome that varies from individual to individual.

Stem cell – A cell with the capacity to divide and form multiple cell types.

Sulfonylureas – A class of orally active hypoglycemic drugs commonly used to treat type 2 diabetes by promoting increased insulin secretion by the pancreas.

Sumoylation – Attachment of one of a family of small proteins (small ubiquitin-like modifiers, or SUMO proteins) to another protein in cells to modify its function.

Telemedicine – The provision of consultant services by off-site health care providers to health care professionals on the scene or directly to patients – for example, by closed-circuit television or over the Internet.

Thiazolidinedione drugs – A class of insulin sensitizers that improve the body's use of insulin by acting on a protein called PPAR gamma. Examples include rosiglitazone and pioglitazone.

Tomography – A technique of x-ray photography by which a single plane is pictured without the outlines of the structure of other planes. *See also*: "Positron Emission Tomography (PET)."

Transcription factors – Proteins that can bind to or form complexes on DNA to regulate the expression of genes and control cell growth and function.

Transgenic – Pertaining to the experimental insertion of a segment of DNA from one genome into the DNA of a different genome. For example, this technique is used to make genetically-modified mice.

Triglyceride – A type of lipid that circulates in the blood. High levels of triglycerides may be associated with atherosclerosis. Because insulin is needed to remove triglycerides from the blood, people with diabetes have elevated levels of triglycerides in their blood.

Type 1 diabetes – A condition in which the pancreas makes little or no insulin because the beta cells have been destroyed by an autoimmune response. Because the body is thus unable to use glucose for energy, insulin must be replaced through injection or another mechanism such as an insulin pump. Previously referred to as Insulin-Dependent Diabetes Mellitus (IDDM) and juvenile-onset diabetes.

Type 2 diabetes – The most common form of diabetes, which results from insulin resistance and/or reduced capacity to produce insulin. About 90 to 95 percent of the people with diabetes have type 2 diabetes, which is associated with obesity and controlled with diet, exercise, and/or medication including oral hypoglycemic agents and insulin. Previously referred to as Non-Insulin-Dependent Diabetes Mellitus (NIDDM) and adult-onset diabetes.

Ubiquitination – Addition of a small protein known as ubiquitin to another protein, usually targeting it for degradation.

Unfolded protein response – A self-protective response of cells against endoplasmic reticulum (ER) stress resulting from accumulation of unfolded/misfolded proteins in the ER.

Variant – *See*: "Genetic variant."

Vascular endothelial growth factor (VEGF) – A molecule that stimulates new blood vessel growth.

Vitrectomy – A surgical procedure in which the gel found behind the lens of the eye is removed because it contains blood and scar tissue that blocks sight. The cloudy gel is replaced with a clear fluid.

Xenobiotic – A chemical found in an organism in which it does not naturally occur.