

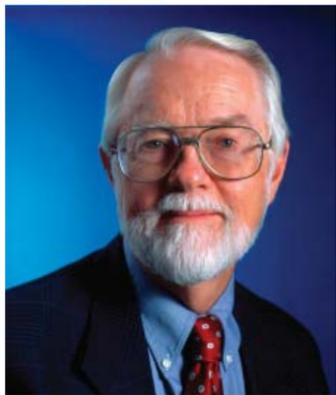
Inspired Leadership

Fouad R. Kandeel, M.D., Ph.D., leads the Department of Diabetes, Endocrinology & Metabolism. He also serves as the principal investigator on the *multicenter islet transplantation-alone* trial to determine the safety and efficacy of islet cell transplantation as a treatment for patients with type 1 diabetes. Among his many research endeavors is a study of genes related to the development of type 2 diabetes and cardiovascular disease in the Hispanic population. Foremost among Kandeel's accomplishments is the establishment of the Southern California Islet Cell Resource Center at City of Hope which supports clinical and basic science islet cell research throughout the western region of the United States. Kandeel also has established a Male Potency and Reproductive Clinic to address some of the unique complications that may result in male diabetes patients and has recently edited two textbooks on these topics for the benefit of scholars and practitioners.



Fouad R. Kandeel, M.D., Ph.D.,
director of the Department of
Diabetes, Endocrinology
& Metabolism

Arthur Riggs, Ph.D., professor of Biology, director emeritus of Beckman Research Institute and leader of all City of Hope diabetes and metabolic research programs, focuses his investigations on genetic structures and gene regulation. Recently inducted into the National Academy of Sciences, Riggs leads studies into a scientific realm he founded called epigenetics — a field which explores the reasons for inherited changes in genes while the DNA code remains unaffected. His novel discoveries concerning DNA methylation (where genes are silenced by adding groups of the chemical methyl to DNA) and X chromosome inactivation are generating new insights and possibilities for new therapy development. In his earlier work, Riggs' pioneering findings on genetic engineering led to the creation of synthetic human insulin, benefitting millions of patients worldwide. He holds 20 patents for biological processes and has published 156 peer-reviewed papers, with an additional 27 combined book chapters and invited articles.



Arthur Riggs, Ph.D., professor
of Biology; director emeritus of
Beckman Research Institute

Barry M. Forman, M.D., Ph.D., holder of the Ruth B. and Robert K. Lanman Chair of Gene Regulation and Drug Discovery, focuses his research into the molecular processes involved in diabetes. He has made significant contributions to the scientific understanding of human disease, including identifying new hormones and signaling mechanisms involved in diabetes and cholesterol metabolism. His technology is now being used by virtually all major drug companies to formulate new anti-diabetes treatments. His important discoveries in the field of nuclear receptors revealed the mechanisms that control cellular processes, providing scientists with new avenues to devise therapies for blocking and preventing disease. He holds 15 patents for molecular technologies and has published over 60 peer-reviewed articles and book chapters.

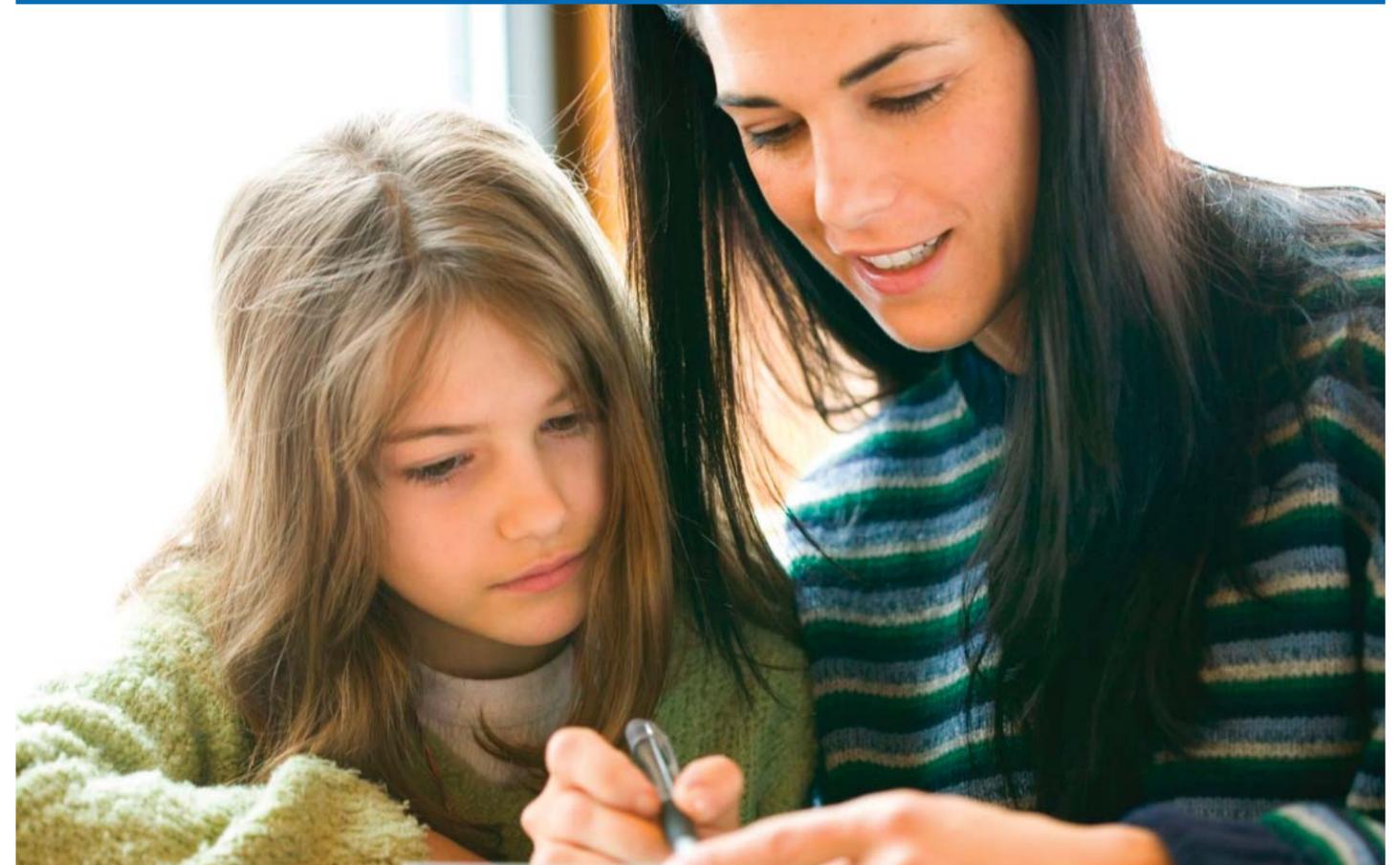


Barry M. Forman, M.D., Ph.D.,
Ruth B. and Robert K. Lanman
Chair of Gene Regulation and
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Advancing the Fight Against Diabetes



Diabetes_brochure_11_2007

The Growing Epidemic of Diabetes

- Nearly 20.8 million people — 7 percent of the U.S. population — have diabetes and it is occurring more frequently in children and adolescents.
- Almost 1.4 million new cases of diabetes were diagnosed last year.
- Scientists predict that one in three children born in 2000 may contract diabetes in their lifetime.

Our Pioneering Research

City of Hope is committed to developing better treatments and finding a cure for diabetes. Our scientists already have contributed to the fight against diabetes:

- Arthur Riggs, Ph.D., and Keiichi Itakura, Ph.D., genetically engineered bacteria that led to the production of unlimited quantities of synthetic human insulin (called Humulin), benefiting millions of patients.
- The late Rachmiel Levine, M.D., considered the “Father of Modern Diabetes Research”, discovered the basis of “insulin action,” describing how insulin helps the body’s cells use glucose, or blood sugar.
- Samuel Rahbar, M.D., Ph.D., first discovered the biomarker, hemoglobin-A1c, a strong predictor in evaluating long-term control of diabetes.
- Yoko Yamaguchi, Ph.D., identified the actual proteins that deliver insulin’s messages to cells.
- Barry Forman, M.D., Ph.D., identified how molecules work to treat resistance in type 2 diabetics — a process used by virtually all major drug companies to test new anti-diabetes agents.

Our team is not stopping there. Research is headquartered at the Leslie and Susan Gonda (Goldschmied) Diabetes and Genetic Research Center, a four-level, 41,000-sq. ft. facility, where our

scientists are working to develop better treatments and an eventual cure for diabetes.

Islet Cell Transplants: Producing Insulin

The islets of Langerhans, a part of the pancreas, are cells that produce insulin. Islet cells, obtained from healthy donors may provide new hope for patients suffering from diabetes. Doctors take the islet cells from the donor’s pancreas, purify them and then transplant them into the liver of a patient — patented processes developed at City of Hope.

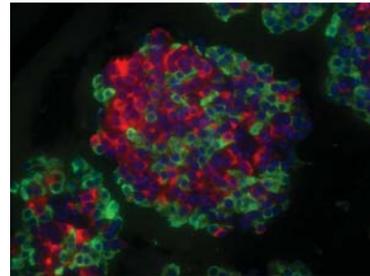
Patients then begin producing insulin on their own. In 2001, City of Hope established the Islet Cell Transplantation

Program, **one of seven National Institutes of Health-sponsored Islet Cell Resource Centers in the U.S. and the only one in the western United States.** Scientists are now developing ways to reduce the need to give patients drugs that suppress the immune system (which have many adverse side effects) to prevent rejection of the transplanted cells. Our team also is studying how to improve immune tolerance for safer islet cell transplantation, and developing stem cells into islet cells to increase the number of islet cells available for transplant.

We are also an official Juvenile Diabetes Research Foundation (JDRF) Islet Cell Transplant Center and have been granted \$3.3 million in funding over the next five years from the JDRF for improving islet cell replacement therapies for patients with type 1 diabetes.

Reversing Diabetes

Type 1 diabetes occurs when the body destroys its own pancreatic cells. Our team has shown that they



Regenerated islet producing cells responsible for producing insulin.

can reverse type 1 diabetes in mice through bone marrow transplantation. In this new approach, our researchers replaced unhealthy T-cells (immune cells) in mice with healthy bone marrow cells from a donor. They paired this therapy with antibodies, an immune system protein, which stopped the body from attacking islet cells. Early results are encouraging further study to determine if this therapy could help cure type 1 diabetes altogether. Another new treatment approach “boosts” the power of the body’s certain special T-cells to suppress the autoimmune attack on islet cells.

Nuclear Receptors to Control Diabetes

City of Hope’s Department of Gene Regulation and Drug Discovery is exploring the promise of designer drugs — targeted therapeutics that directly undermine type 2 diabetes, atherosclerosis (the dangerous thickening of the artery walls) and other metabolic diseases linked to obesity. Researchers are targeting specific proteins in the cell nucleus, called nuclear receptors, that control gene activity. By harnessing basic cellular functions through these receptors, our team seeks to conquer diabetes.

Scientists have discovered 35 nuclear receptors whose function remains unknown. By studying these “orphan receptors,” our researchers made discoveries that led to many discoveries, including a new hormone involved in diabetes and atherosclerosis. It was the first new steroid hormone to be identified in years, creating a starting point for new ways to treat these diseases. Our team also identified an orphan receptor involved with blood sugar regulation —now being targeted as they develop drugs for diabetes.

Eliminating the Effects of Diabetes

City of Hope researchers are dedicated to ending common secondary health problems associated with diabetes such as heart and kidney disease and

neurological problems. Researchers are developing new ways to combat the biological processes that lead to these dangerous diabetes-related complications. Aging processes in the body are often accelerated in persons suffering from diabetes, so researchers are trying to learn why. City of Hope scientists are studying the formation of *advanced glycation end products* (AGEs) — molecules that lead to stiffening of connective tissues and tissue damage in the kidney, retina, vascular walls and nerves. Our team has developed many AGE-inhibitor drugs that prevent diabetic complications. One inhibitor compound, *LR-90*, has shown promise in mice as a possible prevention for kidney disease. City of Hope scientists also have uncovered other mechanisms in the body that influence the risk of vascular illnesses, like atherosclerosis and hypertension (high blood pressure). They also are studying how to regulate genes and related signals in blood, kidney and fat cells to figure out ways to prevent complications that arise from diabetes.

Our Distinctive Strengths

We are a fully independent, biomedical research institution with the vision, drive and infrastructure to accelerate new treatments from the laboratory to patients. With unparalleled accomplishments, over a half-century of experience in diabetes research and our own genetic engineering and manufacturing capabilities onsite, we are offering new hope now.

Help Us Conquer Diabetes

Individual donors play a major role in enabling our scientists to pursue studies that have and will save lives worldwide. Our development staff is eager to show you how you can play an integral role in helping us achieve our lifesaving mission. Please contact our Development Center at 800-232-3314 or via e-mail at giftplanning@coh.org. Learn more at www.cityofhope.org.