

THE LASER

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Stopping the Spiral: Chronic Hyperglycemia, Oxidative Stress, and the Complications of Type 2 Diabetes

One of the most difficult aspects of living with diabetes—and one that PNRI scientists are investigating with hopeful results—is its inexorable progress toward destructive complications. The tissue damage that type 2 diabetes causes leads to well-known and wretched health problems. Retinopathy, amputation, kidney disease, nerve damage, heart attack and stroke—all of these are the by-products of the central condition of type 2 diabetes: chronic hyperglycemia.

Researchers in the laboratory of Dr. Paul Robertson at PNRI are developing a new understanding of this condition. They have discovered a new explanation of why it is so destructive, and proposed a suggestion of how its effects may be blocked or forestalled.



Robertson lab group—(front) Sabrina Mak, Theresa Mangahas, and Naoko Tonooka; (rear) Tao Zhang, Felipe Guillen, Elizabeth Oseid, Jamie Harmon, and Huarong Zhou

Glucose Toxicity of the Beta Cell

The central condition of diabetes is an increased level of sugar, or glucose, in the blood. This condition is reflected in the very name of the disease. Its technical name *diabetes mellitus* includes the Latin word *mellitus*, or “sweet.” In some cultures the

informal name for diabetes even today is “the sugars.” Both names reflect the fundamental connection between diabetes and sugar. Sugar is not the cause of the disease, but because the body fails to metabolize sugar properly it accumulates in the blood. This build-up of blood sugar is called *hyperglycemia*.

In persons without diabetes, hyperglycemia is generally rare. Normally, insulin works by enabling muscles and other tissues of the body to take up glucose from the blood and convert it into energy. Insulin does this job in just the right amounts and at just the right time. The tissues of the body also play their part properly: stimulated by insulin, they absorb glucose from the blood and store and process it. In type 2 diabetes, however, either one or both of these processes is defective, so sugar remains in the blood and over time becomes a toxin.

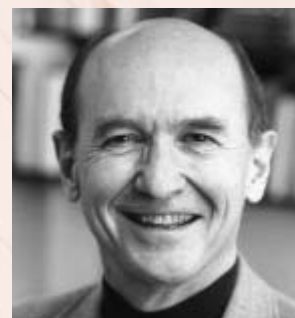
Doctors and scientists have long recognized the toxic effects of elevated levels of glucose. They have named it *glucose toxicity*. They have also understood its key role in the secondary consequences of type 2 diabetes—the destruction of tissues like eyes, nerves, kidneys, and heart. But this conventional understanding has not been able to account for the relentless progress of the disease. Why does it keep getting worse?

Robertson and his colleagues have proposed a new hypothesis. In addition to peripheral tissues, they have demonstrated that prolonged hyperglycemia damages the pancreas’s beta cell as well. Robertson explains that the beta cell is the body’s only source of insulin. So the damage it experi-

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PERSPECTIVES

by R. Paul Robertson, M.D.



The Future of PNRI Is Diabetes Research

This issue of *The Laser* gives me the opportunity to make an announcement I am very excited about. We are refining our mission at PNRI. It is now more targeted than in the past. PNRI’s scientific focus for the future will be the prevention and cure of diabetes.

Approaching our fiftieth anniversary in 2006, we are at an important moment in our institutional history. PNRI has had a distinguished past—having been founded by Dr. William Hutchinson, parenting the Fred Hutchinson Cancer Research Center, fostering creative research by practicing physicians in clinical care and medical devices, and since 1997 making breakthrough advances in diabetes and cancer research. Even as we evolve in this more focused direction, our two National Academy of Science members will continue to pursue their highly important cancer research investigations.

18 million Americans have

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Diabetes at PNRI—Science That Matters to You

Pacific Northwest Research Institute conducts the most comprehensive program of diabetes science in the Northwest. Our work extends from the early development of beta cells to the mechanisms of defective insulin secretion and insulin resistance in type 2 diabetes.

Pacific Northwest Research Institute (Việän Nghieän Cöu taï Vuöng Taây Baéc Thaùi Binh Döng) thöic hieän chöông trình khoa hoïc toaøn dieän nhaát trong vuöng Taây Baéc veä beänh tieäu nöðöng. Coäng vieäc chuèng toái bao goàm nhieäu chuú ñeä roäng raõi töø vieäc nghieän cöu tieän trình phaüt trieän cuä cauc teá baøø beäta öü giai ñoaïn phoái thai cho ñeän cô cheä hoaït nöäng cuä cô theä khi maéc cauc tình traïng öü beänh tieäu nöðöng loaïi 2 nhö saün sinh thieäu insulin vaø khauèng laïi insulin.

太平洋西北研究所的糖尿病研究是综合性的，我们从胰岛细胞的胚胎生长开始，扩展至胰岛素分泌途径的缺陷和2型糖尿病胰岛素抵抗等的机制研究

Este instituto conduce el Programa mas amplio de la ciencia de la Diabetes en el Noroeste. Nuestro trabajo se extiende desde el desarrollo embrionario de la celula Beta hasta los mecanismos de la secrecion de Insulina defectuosa y la Insulina Resistente en el tipo de Diabetes # 2.

PNRI is doing science that matters. Together, we can create a future without diabetes.

CIENCIA QUE TE INTERESA A TI

PNRI PACIFIC NORTHWEST
RESEARCH INSTITUTE



FROM THE EDITOR:

REACH 2010: Supporting Community Health

by Rich Murphy

The meeting in PNRI's Renshaw Room brought together representatives from a broad coalition of organizations committed to preventing diabetes and improving its management and treatment. The coalition is called Project REACH 2010—Racial and Ethnic Approaches to Community Health—and it is currently being funded by the Centers for Disease Control and Prevention. PNRI has joined the coalition in an effort to serve com-

Health and Roxana Chen from Seattle/King County Public Health.

One of the most important dimensions of the public health diabetes challenge is that proportionally more people of color are afflicted by type 2 disease than are whites. Health services too—from effective treatment to accessible information—are less likely to reach these affected communities. The mission of the REACH 2010 Coalition

*...community support for people with diabetes.
It is a fundamental part of our mission.*

munities particularly hard hit by diabetes and to reduce health disparities. Our meeting at PNRI was part of an ongoing effort to make this important work sustainable.

Dr. Cheza Garvin was there, director of the Public Health Department's Office of Chronic Disease Prevention and Healthy Aging. So was Dr. Noel Chrisman, Professor of Community Health in the School of Nursing at the University of Washington. Among others attending were Melissa Ponder from International Community Health Services, Valerie Baldisseratto from SeaMar Community Health Centers, Melissa Foster from Harborview Medical Center, Mariah Koh from the Diabetes Prevention Program, Sandra Bazan-Diallo from Public Health, and Lois Watkins, the Public Health Coordinator of the REACH Coalition. The group was chaired by Devon Love from the Center for Multi-cultural

is to reduce these diabetes health disparities. The coalition appreciates language and cultural differences, values diverse traditions, and provides services tailored to the needs of different racial and ethnic communities.

PNRI is working with REACH to increase opportunities for diabetes education and self-care, personal awareness of potential risk, public awareness, and community support for people with diabetes. It is a fundamental part of our mission.

PNRI's research targets the key mechanisms of diabetes. But prevention and effective treatment will only happen when individuals, families, and communities have access to the information and encouragement that enables them to manage the disease.

For more information about Project REACH, visit <http://www.metrokc.gov/health/reach>.

PNRI is a 501(c)(3) organization and welcomes donations to help support its research in the basic biomedical sciences. All gifts to PNRI are tax deductible as provided by law. The Institute is registered with the Secretary of State, Olympia, Washington.

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Special thanks to the following for their help in preparing and distributing this issue: Salwa Al-Noori, Linda Bonomi, Juanita Garrison, Bridget Haba, Jamie Harmon, Paul Robertson, Dave Rood, Mike Toney, and Barton Wicksteed.

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Barton Wicksteed: "You Only Get One Life"



Dr. Lorna Dickson and Dr. Barton Wicksteed

Dr. Barton Wicksteed is the newest independent investigator at PNRI. With funds from the Juvenile Diabetes Research Foundation and PNRI, he is starting up a laboratory to study alpha cells, the pancreatic islet cells that secrete glucagon.

The functional importance of alpha cells is that they work with beta cells to regulate blood glucose. When the system is operating properly, glucagon and insulin balance one another. When it's not, hyperglycemia or hypoglycemia ensue. If blood glucose is too high, because of too much glucagon and not enough insulin, a person experiences *hyperglycemia*. If blood glucose is too low, because of too much insulin and not enough glucagon, the condition is called *hypoglycemia*.

Both conditions are fraught with problems. Prolonged hyperglycemia brings with it all the secondary complications of diabetes. Hypoglycemia also entails complications. At its most severe, it can cause patients to slip into a coma and even die. A whole battery of body responses exists to keep the profound glucose drop of hypoglycemia from happening. The most important of these responses is the job of the

alpha cell: to produce and secrete glucagon. It is this cell that Barton Wicksteed is intent on understanding.

Courses in endocrinology "leapt out at him," he says, when he was an undergraduate at Australian National University (ANU) in Canberra. But he also studied zoology and botany, chemistry and mathematics. After graduation he worked in a number of biology laboratories at the John Curtin School of Medicine in Canberra, then later at the University of Aberdeen in Scotland.

It was an opportunity to join the ANU field hockey club on a playing tour of the UK that took Barton to Scotland. While traveling on the continent and taking fortuitous summer farming stints in Buckinghamshire, he also interviewed for research jobs, ultimately choosing a position in the lab group of Alistair Brown at Aberdeen. After one year, he had earned an MSc. After four more, a doctorate.

"You only get one life," he says matter-of-factly of the conviction that has driven him to pursue so many interests. (Even as he's studying hypoglycemia at PNRI, he makes time to explore photography, different kinds of film, and the nuances of color and light.) It's this same passionate and wide-ranging curiosity that guides his study of alpha cells.

According to Barton, defective alpha cell function is related to the beta cell failure characteristic of diabetes. The ability of alpha cells to synthesize, store, and secrete glucagon apparently remains strong, but their ability to detect and respond to hypoglycemia is somehow impaired.

Studying this phenomenon systematically, however, is a significant research challenge. In healthy animals, the alpha

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...passionate and wide-ranging curiosity that guides his study of alpha cells.

PNRI Laboratories and Their Major Areas of Research

n Peter Dempsey, PhD

Cellular communication, ErbB ligand trafficking and processing, disintegrin-metalloproteases, ErbB receptor signaling

n William A. Hagopian, MD, PhD

Type I diabetes mellitus

n Senitroh Hakomori, MD, PhD

Aberrant cell recognition and signaling in cancer, based on changes in glycosylation

n Donald Malins, PhD, DSc

Breast, ovarian, prostate cancer

n Vincent Poitout, DVM, PhD

Pancreatic beta-cell dysfunction in Type 2 diabetes

n Christopher Rhodes, PhD

Biochemistry of pancreatic beta cells

n R. Paul Robertson, MD

Pancreas and islet transplantation, glucose toxicity of pancreatic beta cells

n Barton Wicksteed, PhD

Islet alpha cell function

Help Us Keep in Touch!

We are now using the ease and economy of the Internet to keep PNRI's friends and family current on news, stories, research, and event announcements. The Institute's website posts the latest press releases and media stories at www.pnri.org/news. Links to on-line versions of the print *Laser* are sent to subscribers whose addresses we have.

So please send us your address today. Subscription is easy. Just visit www.pnri.org/howtohelp/subscribe. When you do, we will be able to keep you even more closely in touch with our work.

In the meantime, we hope you will continue to enjoy *The Laser*. And we hope you will continue to share it with colleagues and friends.

n Year-End Giving

Now is the time to plan ahead so you can make your donation before the end of the year for a 2004 income tax savings. There are many different giving opportunities available at PNRI. Our development staff will work together with you and your advisors to bring to life your vision for your philanthropy. For more information about making a year-end gift to PNRI please visit our website www.pnri.org/howtohelp or contact Development at 206.726.1200

n Personalize Your Gift

Whether you are looking to express congratulations or condolences a Tribute Gift to PNRI is a perfect way to cherish the memory of a loved one or acknowledge special occasions.

When you give in honor or in memory of a loved one, PNRI provides a personalized letter announcing your gift to the family or person you designate. You also receive a confirmation letter that the gift has been received and acknowledged. For "in memory gifts" a fund will be created in the person's name and will grow over time with each additional gift. When the fund reaches \$2,500, the name for whom the gift(s) are given will be permanently inscribed in the Memorials section of the Donor Recognition Wall. You can make a tribute gift online with a secured donation using your credit card at www.pnri.org/howtohelp/ or call Development at 206.726.1200 to request a special tribute gift envelope be sent to you by mail.

An Evening of Wine first flight



Takes Off in a Big Way for PNRI

The first annual fundraiser for the Pacific Northwest Research Institute, *An Evening of Wine—First Flight*, was held at the Golf Club at Newcastle on August 5, 2004. Over 150 people joined PNRI to show their support and bid on wine-themed packages. PNRI exceeded the fundraising goal with over \$100,000 brought in, \$47,200 of which is earmarked for a one-year training fellow-

ship for a post-doctoral fellow in diabetes research.

Guests experienced an unforgettable evening of extraordinary Washington State wines, provided by eight premier Washington wineries. They bid on 15 packages in a live auction and tested their taste buds to "Name That Wine" with wine expert Richard Kinssies, columnist for the Seattle Post-Intelligencer and director of the Seattle Wine School.

The event was sponsored by AWineStore.com, Gene Colin, and B & H Investments. Wine partners included Pepper Bridge Winery, Chandler Reach Vineyards, Three Rivers Winery, Saviah Cellars, Sheridan Vineyard, Dunham Cellars, Owen-Sullivan Winery, and Andrew Will Winery.

Proceeds benefit diabetes research at PNRI, the most comprehensive program of diabetes science in the Northwest. PNRI is dedicated to the prediction, prevention, and treatment of both type 1 and type 2 diabetes.

The Event Committee is forming to begin work on *An Evening of Wine 2005*. If you are interested in helping to plan PNRI's annual fundraising gala please contact Development at 206-726-1200 or email donations@pnri.org.



Thanks to Our Event Volunteers

We extend a very special thank you to those who volunteered to help at *An Evening of Wine – First Flight*.

Carolyn Anderson, Sandy Brewster, Heidi Dellinger, Lisa Gibbon, Cindy Haba, Derek Hagman, Stephanie Kleven, Gordon Lambert, Colleen Mounsey, Jean Pasche, Aaron Robitaille, Bryan Bartley, Chris Carney, Victoria Dobbins, Donna Gordon, Matt Haba, Suzan Hruska, Ron Lamarca, Christopher Mounsey, Chinwe Okeke, Dan Rasmussen, and Mike Toney.

Please visit our website www.pnri.org/howtohelp to learn about volunteer opportunities at PNRI.

Lisa's Story

Lisa Gibbon, a courageous and lovely young mother from the Tri-Cities area, spoke to the guests at An Evening of Wine to encourage them to make a gift to the Fund-A-Need appeal to support a post-doctoral scientist in diabetes research for one year at PNRI. Here are excerpts from what she said:

I was first diagnosed with type 1 diabetes at ten years old. From the time I was a teenager till after I got married I was told, like so many other girls my age with diabetes, that I probably couldn't have children. When my husband and I talked about marriage, it was a difficult conversation to have with him. In the end we beat the odds. Because of medical advancements, we were able to have two healthy boys who are now 4 and 5.

Do I worry about learning someday that my children will have type 1 diabetes? Of course, I do, every day. But I do believe there's hope for the future. And much of that hope is because of research occurring in the field, especially at PNRI.

PNRI brought me into their family two years ago when I applied and was selected to have an islet transplant through the Human Islet Transplantation program in Seattle known as HITS, a program coordinated by Dr. Paul Robertson. HITS is a collaboration involving PNRI, Puget Sound Blood Center, Virginia Mason Medical Center, Swedish Medical Center, and the University of

Washington Medical Center.

In 2002 I became Seattle's third islet transplant patient.

For those of you who might not be familiar with islet transplantation it's a procedure where islets from a donor pancreas were put into my body, into my liver, by a simple surgical procedure. The islets in a person with type 1 diabetes are no longer capable of producing insulin. The newly transplanted islets begin to produce insulin right away and in the best of scenarios, I would not need to give myself insulin shots ever again.

I know firsthand what it *might* feel like to be cured — my transplant worked for a few months. That was truly wonderful — it was what the scientists were looking for. Unfortunately, the good effects didn't last. For me, the anti-rejection drugs became a problem and pushed my white blood cell count to a dangerous low so that I was constantly vulnerable to any illness.

Was I disappointed? Sure.

Did I lose hope? Absolutely not!

I consider myself one of the lucky ones to be selected to participate in this research. It was all worth it. Because of my transplant the scientists know they need different and better immune anti-rejection drugs.

Being part of the protocol has given me hope for the future of people everywhere with diabetes.

My dream is that in my lifetime there will be a cure!

Fund-A-Need had a goal of \$30,000. After Lisa spoke the audience responded pledging gifts totaling over \$47,000.

A Charitable Bequest: the "Gift of Choice"

Why are charitable bequests so appealing when it comes to using accumulated assets to support Pacific Northwest Research Institute? Consider these features:

n Take your pick! – Through your will or living trust, you can name PNRI to receive a fixed sum of money, a particular asset, or a certain percentage of your residual estate. You can also make the Institute a contingent beneficiary by indicating your bequest will take effect only under specific circumstances: e.g., "If my spouse does not survive me . . ."

n Flexibility – As your financial picture changes, a bequest can be altered, so long as applicable legal requirements are met.

n We love them! – And we love donors who – in the course of planning for friends and others who are dear to them – make arrangements that ultimately lead to the prevention and cure of diabetes.

n The legacy you leave – On behalf of those you help by furthering diabetes research, we strive to recognize and thank you. That's why not only bequest donors but those who make other types of planned gifts to PNRI are honored as Partners in Discovery.

In determining how to structure a bequest or related gift, we urge you to work with your own legal and financial advisors. If you or they would like to know more about what's possible, then PNRI's Director of Development, Linda Bonomi, is the person to contact at 206.726.1200 or by e-mail at donations@pnri.org.

PNRI Tribute Gifts

June through September 2004 (Tribute name is listed in bold)

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Barton Wicksteed

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cells are so awash in the insulin environment of the pancreas that they cannot be studied independent of the beta cell. In diabetic animals a different challenge presents itself. No successful way has been found to re-introduce active healthy beta cells in order to study their changing effect on alpha cell function.

So Barton is working on an entirely new approach with his colleague, Dr. Lorna Dickson (also his spouse; the two met at Aberdeen). They are separating the cells, marking them, sorting and culturing them. Also, with the help of PNRI principal scientist Dr. Peter Dempsey, they are creating new lines of isolated alpha cells for study. Once the technology of separating and culturing them successfully is available, the analysis of alpha cell functions can be studied under controlled conditions.

It's too early for a hunch, Barton says patiently, but the causes of alpha cell dysfunction are most likely related to subtle dynamics within the whole pancreatic islet environment, not just to single signals between beta and alpha cells. It is, he says, "a complex web of interactions." But it is a critical part of the central biochemical operation of diabetes. And understanding its complex dynamics will have potentially huge benefits for diabetes patients everywhere. This is the goal for which Barton is designing his new scientific investigation. And if you only get one life, it is an exhilarating—and keenly important—challenge to undertake.



TRUSTEE PROFILE profile

Juanita Garrison: Bringing the Personal and Political Together

After serving for a year on PNRI's Development Committee, Juanita Garrison joined the Board of Trustees this past July. She explains her desire to serve the Institute simply: "It's family history," she says. "The connections between PNRI and my family go back to the beginning. This is a way for me to contribute to that relationship and to enhance that legacy."

Garrison's first link to PNRI was to Dr. Bill Hutchinson, the Institute's founder. "His family and ours were close friends. I always admired Dr. Hutchinson's goals and the things he accomplished—in both his practice as a physician and surgeon, and in his public works to advance health." Garrison's father, Senator Warren G. Magnuson, also admired Hutchinson's energy and achievement and worked closely with him in the early years of PNRI to secure government funding and to personally help start the Fred Hutchinson Cancer Research Center.

Garrison is also motivated by her father's experience fighting diabetes. "He was a real trooper," she says of the aging Senator, who ultimately died of the complications of diabetes. "To see such a vital, active person stricken like that," Garrison says, "it was painful to watch." But she never stopped admiring his resiliency and

strength. "He never complained. He always surprised us. Against ulcerations that wouldn't heal, against amputations and heart attacks, he always struggled back. He was always getting back on his feet. He was incredible."

In his memory, Garrison and her mother, Jermaine Magnuson, have established a fund for research and medical education at the University of Washington. Substantial scholarships are given to a select number of students each year to help complete their research and graduate work. Now Garrison sees a further opportunity to put her admiration for her father to work: by focusing her energy on advancing diabetes research at PNRI.

As the daughter of a six-term United States Senator, Garrison was educated in Seattle, worked for KIRO TV and Senator Brock Adams, and was appointed to the Washington State Gambling Commission. She later campaigned herself for statewide political office as a candidate for Secretary of State.

"I grew up in politics," she says. "I believe in the grassroots approach to getting things done." There was always a rule in the Magnuson house—take it to the public. "If you need help, if you want to effect change," she says with conviction, "the best thing is to take it to people on the street. If they trust who you are and understand the need, they will respond."

Garrison's goal now is to make PNRI more well known, to broaden awareness of its efforts to transform the prevention and treatment of diabetes. "I want PNRI to be the premier diabetes research center in the region," Garrison says. "I want it to be a household name. And I know from my experience of politics, that when we get this message to ordinary people—people with families, people with neighbors or children or fathers with diabetes—they will help."

PNRI BOARD OF TRUSTEES

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Type 2 Diabetes

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ences in the presence of chronic high glucose diminishes its capacity to produce the insulin needed to bring the glucose levels down. The result? A downward spiral in islet function of increasingly serious proportions.

Like glucose toxicity itself, beta cell damage has been recognized by doctors and researchers before now. But Robertson proposes that the traditional explanation for this damage is incorrect. Conventionally, drug failure has been blamed for beta cell defects. The Robertson lab has shown, however, that this problem is independent of drug failure, and that in fact, even with drug function that is effective, beta cell damage continues its inexorable course in the presence of chronic hyperglycemia.

"It's like a death spiral," Robertson says. High blood sugar damages the beta cell itself, thus causing the natural regulation of hyperglycemia to be further disabled. This in turn causes the levels of glucose in the blood to further increase, which leads to further damage to the beta cell's function. But now that this mutually reinforcing mechanism is becoming clear, Robertson believes that there may be a way to block its action and avert its grim results.

Oxidative Stress and the Hope of Antioxidants

The hope lies in the possibility that antioxidants may be able to interrupt the glucose toxicity cycle.

A review article published by Robertson in the October 8, 2004 issue of the *Journal of Biological Chemistry* (JBC) summarizes the major mechanisms and pathways of glucose toxicity. There are many different ways that glucose works its damaging effects on the beta cell. All of these have one element in common: chronic oxidative stress brought on by the formation of what are

known as "reactive oxygen species" (ROS).

When glucose accumulates in the blood, it causes the creation of a number of different chemical substances that in excess amounts interfere with the production and secretion of insulin. The most serious of these, hydroxyl radicals, can penetrate the cell nucleus and cause mutations of the cell's DNA. But several other reactive oxygen species can also affect insulin gene expression and lead to decreases in insulin content and insulin secretion. More than this, ROS also can lead to beta cell death.

Many other cells in the body have built-in protection against ROS. They produce special enzymes that help limit the ravages of oxidative stress. But beta cells are especially vulnerable to this damage because they have so little antioxidant enzyme protection. Robertson and his colleagues have demonstrated that this intrinsic beta cell weakness can be compensated for by introducing genes into the beta cell that increase antioxidant enzyme levels.

So the new understanding of glucose toxicity brings with it an unexpected hope.

A number of antioxidant drugs have been lab-tested by the Robertson group. Their initial success in impeding oxidative stress in rodents suggests that antioxidant therapy might effectively augment other forms of treatment for type 2 diabetes in people.

Antioxidants by themselves can't stop hyperglycemia. That's a fundamental condition of type 2 diabetes. But the effects of hyperglycemia may be controlled. And the inexorable secondary consequences of the disease may be able to be forestalled. Thanks to this new understanding of the effects of chronic high glucose on beta cell function, patients with diabetes may be able to use antioxidants to effectively keep the complications of this disease from getting worse.

Perspectives

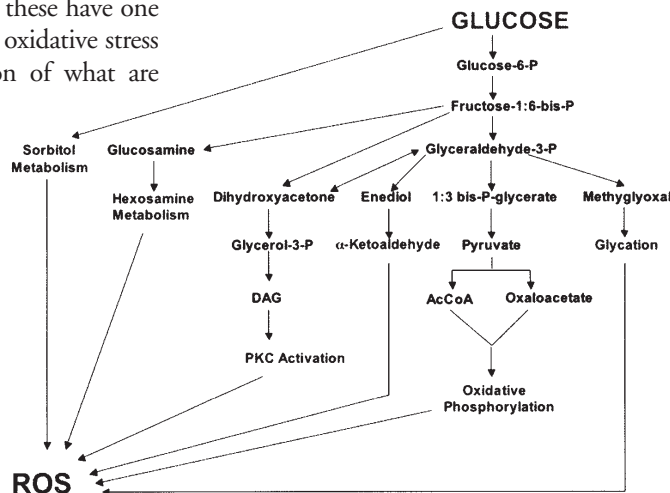
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diabetes. 17% of all persons living to age 80 will develop it. In Washington State, in just three years, between 1996 and 1999, the prevalence of diabetes increased 44%. Nationally, some ethnic and racial communities are more severely impacted than others. 7.8% of non-Hispanic whites have diabetes. 10.2% of Hispanic-Latino persons develop the disease. 13% of non-Hispanic blacks and 15.1% of Native-Americans have diabetes. And over the past five years, there has been an estimated 10-fold increase in the incidence of type 2 diabetes in the young. This is why PNRI's Board of Trustees and its scientific leadership are committed to marshalling our resources to address the public health challenge of diabetes.

The leading focus of the Institute's work will be to advance the prevention and cure of diabetes, to understand its causes and complications through basic and clinical research, to educate communities to help prevent and manage the disease, and to train new scientists for the future. To achieve this mission, we are actively recruiting more diabetes investigators so that we can increase our research capacity. New grants have been written and our scientists are re-tooling their laboratories to supplement our already vigorous programs in type 1 diabetes prediction and prevention, islet and pancreas transplantation, beta cell biology, and glucose and lipid toxicity.

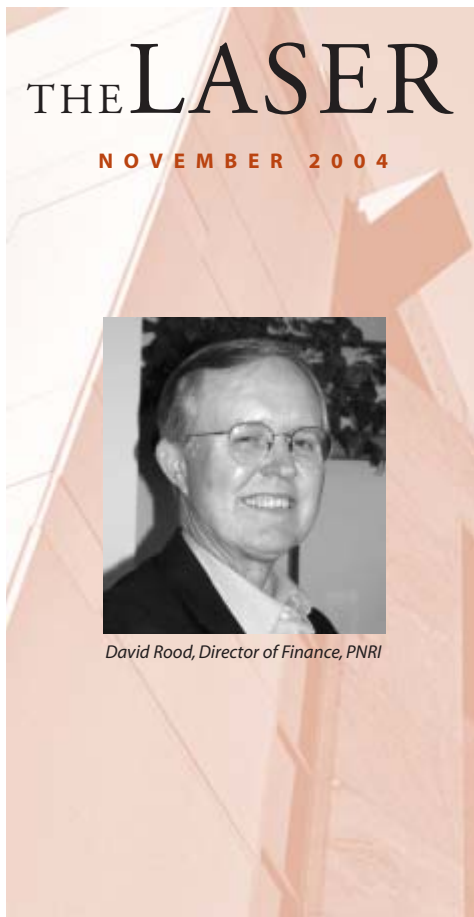
It is an ambitious quest, we realize, but the need is great and the opportunity timely. We are dedicated to becoming *the* comprehensive diabetes research center in the Northwest. We are working to create a future where diabetes is history. We have the scientific talent and passion to do it. We invite you to join us.

PNRI



Schematic illustration from Journal of Biological Chemistry. Through many different pathways, excess blood glucose causes the formation of destructive reactive oxygen species (ROS).

ADDRESS SERVICE REQUESTED



David Rood, Director of Finance, PNRI

PROFILE *profile* **David Rood: Focused on a Mission**

Eclecticism is the first thing you think when you hear David Rood's story—that, and the genial warmth of his welcome. Marine, Naval Flight Officer on an F4 Phantom, private pilot with commercial and instrument ratings, CPA, Trustee for a private college—this is a mix of experience that has shuttled him between LA and Seattle for thirty years.

But the new Director of Finance at PNRI is not here by accident. His family provides some of the motivation. His brother, he says, has type 1 diabetes, has had it “all his life, it seems.” Then there's the value system that's threaded through Rood's professional career. “I want to work for an organization that's trying to better humankind,” he explains, recounting the chief responsibilities he's undertaken.

After the Marine Corps, Rood put his accounting expertise to work for Mission Aviation Fellowship (MAF), an organization supporting faith-based and humanitarian organizations in Africa, Asia, Eurasia, and Latin America. “I thought I'd be flying

planes for humanitarian purposes,” he says now, “but I ended up running the numbers.” For six years, he served as MAF's Chief Financial Officer.

Here in Seattle, after working for public accounting firm Hagen, Kurth, Perman, and Company, Rood became CFO for the Alliance, fostering higher academic achievement by all children in the Seattle Public Schools. Rood was responsible for shepherding the organization's financial resources from grants, private foundations, and individual donors, channeling them to programs designed to help all students achieve.

Now he's at PNRI, a basic science cell-biology laboratory devoted to preventing and curing diabetes. “It fits perfectly,” Rood says, invoking an idea he heard his first week on the job from PNRI Trustee Gene Williams. “If there are three ways to serve humanity—in faith work, in education, or in health—then it's time for me to put my talents to work in health.”

This isn't eclecticism. It's a mission.