

# THE LASER

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## The Orderly Social World of Cells

In his inaugural paper as a member of the National Academy of Sciences, PNRI Principal Scientist Senitiroh Hakomori emphasizes what he calls “cell sociology.” It is, he admits to a visitor who has come to gather information for a layperson’s account of his work, a non-scientific phrase. But it summarizes the processes Hakomori has studied for more than 40 years—the processes by which cells recognize and connect with one another, exchanging information that is essential to their growth and development. It is an orderly world, and in explaining it Hakomori urges his visitor to start at the beginning.

### The Basic Principles

Two basic principles govern all organic life. The first principal is that DNA information is the basis of all internal cell function. DNA contains the genetic information that is translated into proteins. These genetically programmed proteins in turn govern the complex processes of cell division and lead to the vast organic diversity of nature. All medical science is based on this principle and, according to Hakomori, it is generally well known.

Much less is known about the second principle, and much less attention is paid to it. It is that cells are social, that they have a social structure. All cells—from the smallest bacteria to the complex higher organisms of plants and animals—require interaction with others cells. All require cell-to-cell recognition and interaction.

Many classes of molecules support this

process of cell-to-cell interaction. One major class of such molecules is the carbohydrate group Hakomori studies, carbohydrates that are bound to the lipids or proteins in the surface membrane of every cell. These specialized carbohydrates are called glycosphingolipids and glycoproteins.

Out on their membrane surfaces, cells are teeming with complex structures. It is there that these carbohydrates do their critical work. The membrane provides the cells’ first contact with the outside world. By means of its various component structures, they learn what’s around them, drawing near to what’s familiar, recoiling from (or attacking) what’s alien. The cell membrane also serves as a communication web, picking up messages from outside and transmitting them to the nucleus, giving the nucleus important instructions for the cell’s own differentiation and proliferation, for movement, even for death.

The importance of the membrane carbohydrates Hakomori studies—and of the cell-to-cell interactions that they regulate—is that they play a critical role in disease. All diseases, he explains, develop from a failure of cell-to-cell interaction. Cancer is just the most striking, the most stark example of this phenomenon.

### Membrane Molecular Assembly and Cancer

If you could actually see the membrane of a cell in three dimensions with the naked



PNRI Scientist Senitiroh Hakomori

### PERSPECTIVES

by R. Paul Robertson, M.D.



## Type 2 Diabetes: a Disease that Demands Respect

One of my pet annoyances guaranteed to push my “on” button is an often-heard contention about people with type 2 or adult-onset diabetes. “It’s their own fault; they eat wrong and are fat.” Yes, it is true that roughly 80% of people with this disease are overweight, and that weight loss will aid in glucose control. Yes, it is true that some people with diabetes eat the wrong kinds of food. But is it true that obesity and wrong foods can cause diabetes? The answer is a resounding “No!” Just consider how many Americans are obese; only 25% of obese individuals have clear-cut diabetes. Just consider how many Americans eat improperly at their favorite fast food venues; most do not have diabetes. It is important to realize that type 2 diabetes is basically a genetic disease. Clearly, it’s not possible to design one’s own genome. So, it’s not “their own fault”; people with this illness are genetically destined to

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## PNRI PRINCIPAL INVESTIGATORS

■ **Peter Dempsey, PhD**

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

■ **William A. Hagopian, MD, PhD**

(Type 1 diabetes mellitus)

■ **Senitiroh Hakomori, MD, PhD**

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

■ **Ingegerd Hellström, MD, PhD**

(Tumor immunology)

■ **Karl Erik Hellström, MD, PhD**

(Tumor immunology)

■ **Michael Kahn, PhD**

(Chemical biology & functional genomics)

■ **Donald Malins, PhD, DSc**

(Breast, ovarian, prostate cancer)

■ **Vincent Poitout, DVM, PhD**

(Pancreatic beta-cell dysfunction in Type 2 diabetes)

■ **Christopher Rhodes, PhD**

(Biochemistry of pancreatic beta cells)

■ **R. Paul Robertson, MD**

(Pancreas and islet transplantation, glucose toxicity of pancreatic beta cells)

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FROM THE EDITOR:

## Science and Society

by Rich Murphy

Tracy Kidder's new book, *Mountains beyond Mountains*, tells the story of Dr. Paul Farmer, the crusading medical anthropologist working to combat HIV and tuberculosis in Haiti, Peru, Russia, Africa, and elsewhere around the world. One of Farmer's inspirations, Kidder shows, is the work of 19th century cell biologist, Rudolf Virchow.

According to Kidder, Virchow was a key figure in creating the foundations of modern medicine. It was Virchow's special scientific contribution to suggest that self-replicating cells are the fundamental components of organic life. In Virchow's view, disease could only be understood by taking into account changes in the structure and function of cells.

Virchow's importance as a major innovator in the scientific study of cell biology is the reason PNRI's annual award lecture—the Langerhans-Virchow Lecture—is named after him. This year's lecture will be given on April 7 by Dr. Lee Hartwell, winner of the 2001 Nobel Prize in Physiology and Medicine for groundbreaking studies of the ways cells divide and grow in cancer.

But as Kidder's book makes clear, Virchow's legacy is broader than cell biology itself. Virchow's horizon extended beyond the laboratory. He designed urban sewage systems, built nursing schools and hospitals, studied epidemics of malaria and dysentery, and advocated for political and social change in order to address the problems of overcrowding, poor hygiene, and malnutrition among the poor. "Medicine is

a social science," Virchow said. It is this large view of the intersection of society and science that has inspired Paul Farmer in his MacArthur Prize-winning campaign on behalf of global health.

It is this large view that puts the work of PNRI researchers into proper context as well. Senitiroh Hakomori's work on the adhesion and signaling processes of the cell membrane reaches beyond cancer into all the social operations of cells. Bill Hagopian's large-population study of the genetic risks and environmental triggers of type 1 diabetes will help us better understand the onset of this disease. It may also yield new insights that will inform health education and public policy.

The epidemic rise in the incidence of type 2 diabetes, both in the US and abroad, gives added urgency to PNRI's comprehensive type 2 research program. The beta cell studies of the Rhodes laboratory, and the Poitout and Robertson studies of the effects of fatty acids and glucose on insulin production and secretion, are all aimed at the prevention and cure of this intolerable disease.

PNRI is committed to more than understanding. It is dedicated to creating the conditions of change. Its targets are the diseases that beset us all, but in the case of type 2 diabetes particularly, a disease that has grown especially threatening in contemporary society to children, the poor, and persons of color, whose access to health education and health care can be severely limited.

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Special thanks to the following for their help in preparing and distributing this issue: Carolyn Anderson, Steve Anderson, Linda Bonomi, Chris Carney, Cynthia Cousens-Jacobs, Victoria Dobbins, Bridget Haba, Derek Hagman, Senitiroh Hakomori, Jim Norman, Paul Robertson, Aaron Robitaille, Gene Williams, and Casi Zurawski.

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# TRUSTEE PROFILE *profile*

## Jim Norman: Bringing Excitement and Value to PNRI's Board

Jim Norman, of Sage Real Estate Strategies in Seattle, is the newest member of PNRI's Board of Trustees. After a prominent career as one of the city's leaders in commercial real estate, Norman continues to provide strategic real estate advice to health care, higher education, and business clients.

"We create so much value," he says, "it's exciting!" His eyes are alight with the fun of it. It's clear that the pleasure he takes in serving his clients has motivated him throughout his professional life.

In recent years, he has worked with the Fred Hutchinson Cancer Research Center on its capital campaigns and serves on the Visitors' Committee of the University of Washington Medical School. Today, he sees PNRI's cancer research and powerfully integrated diabetes program making an important contribution to public health.

"Diabetes is a critical public issue," Norman says. "And PNRI's laboratories are out in front." His eyes light up again. "It's nice to be a part of that!"

Jim is a 3rd generation Seattleite. The earliest members of his family were dairy farmers in Bellevue, then later in Snoqualmie Valley. After graduation from Central Washington University, Jim followed a career in commercial real estate holding executive positions with such firms as Wright Runstad & Company, the Trammell Crow Company, and most prominently The Norman Company, where he was founder and owner. He played key roles in the development of 1111 Third Avenue and One Bellevue Center, while with Wright Runstad, and in the manage-

ment and sales of major downtown office buildings, including the Bank of California, Park Place, Marsh McLennan and the Columbia Tower, while heading The Norman Company. Now, with a group of very experienced partners at Sage, he is providing important consulting advice to clients throughout the region.

Sage's tag line is "aligning real estate with corporate and institutional goals." Jim explains, "We help our clients create real estate strategies that follow and enhance their business strategy. All too often, we find these entities doing the reverse, which compromises the true viability of their business strategy."

Jim says he hopes he has his mother's genes, especially those for energy and enthusiasm. Late in her life, after a career in life insurance and real estate, she became one of the founders of the Village Theater in Issaquah. She traveled to a remote outpost in Alaska to research the life and times of her pioneering, gold rush grandfather. Then in her early 90's she learned computer word-processing and promptly wrote three books, one about her grandfather. Jim admires both her knowing where she wanted to go and her willingness to take risks, trying out new things, being excited about possibilities.

The latest possibility for Jim Norman is PNRI's mission—the prevention and cure of diabetes and cancer. It's a mission to which he brings personal energy and professional value. Look in his eyes: you can see his excitement.

## New Chair for Development Committee



PNRI Trustee Gene Williams has been elected chair of the Institute's Development Committee. He brings a personal passion for health to PNRI as well as professional expertise that is naturally suited to the Institute's needs.

Gene has worked for more than 30 years helping individual and business clients with their estate liquidity and business succession planning. He is a past president of Seattle Life Underwriters, a past member of the University of Washington Estate Planning Advisory Board, co-founder of the Seattle University Estate Planning Advisory Board, and a member of the Archdiocese of Seattle Gift Planning Committee.

As a specialist in estate planning, Williams has made a career of providing business and estate advice designed to maximize the goals of his clients and minimize their cost. His special interest in philanthropy is essential to this work. "Charitable giving," Gene says, "is not just an afterthought to good estate management. It's a vital part of the process. One of the core processes in effective estate planning is lifetime gifting." The donor gets to enjoy giving the gift. The estate faces fewer taxes, and the whole giving process helps people keep together what they put together.

So it is fitting that Williams should be heading up the committee charged with guiding PNRI's development and fundraising efforts. He is just the person the Institute needs to help its friends learn the pleasures of giving while maximizing the substance and value of their estates. And it makes sense that he should help them do so on behalf of something he believes in so deeply—scientific research dedicated to the prevention and cure of debilitating diseases.

### PNRI BOARD OF TRUSTEES

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*trustees*



## ■ Do You Have An Estate Plan? Become a PNRI Partner in Discovery.

In 2003, PNRI's Board of Trustees announced the formation of Partners in Discovery — an honorary organization for those who have provided for a future gift to PNRI. Partners in Discovery affords PNRI an opportunity to extend warm appreciation to individuals who notify us of their thoughtful gift intentions. If you have named PNRI as a beneficiary of your estate, please let us know so we may recognize you as a Partner in Discovery. Contact Linda Bonomi, Director of Development at 206.716.1203 or by email at [donations@pnri.org](mailto:donations@pnri.org).

## ■ Special Tribute Gifts

With a special gift to PNRI you can create a lasting tribute to a loved one. PNRI offers a way to honor special moments in our lives. Birthdays, weddings, anniversaries, the arrival of a new grandchild or the passing of a dear friend or family member are all times when a gift to research at PNRI to help prevent and cure diabetes and cancer can be very meaningful.

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 at [www.pnri.org/howtohelp/](http://www.pnri.org/howtohelp/) or call Bridget Haba at 206.726.1200 to request that a special tribute gift envelope be sent to you by mail.

# PNRI Receives Seattle Foundation Grant

The Seattle Foundation has awarded PNRI a grant of \$50,000 for the development of a new Confocal Microscopy Cell Imaging Core Laboratory. The funds will be used toward the purchase of equipment essential to its research into the mechanisms of disease, particularly diabetes. The total cost to develop the Core Laboratory is nearly \$300,000, and PNRI welcomes additional donor support to help finance the project.

"This is an important supplement to PNRI's regular NIH funding," according to Paul Robertson. "We are fortunate to have the Seattle Foundation fostering and facilitating philanthropy in our community. PNRI is a grateful beneficiary of their important work. The new grant will help us maintain and grow the high quality of our diabetes and cancer research."

The new laboratory at PNRI will feature an Olympus confocal microscope, and it will employ state of the art digital imaging technology to study real-time protein and genetic interactions within cells. Such new technology will be especially helpful to those research programs focused on pancreatic beta-cell physiology. The confocal

instruments will allow for three-dimensional resolution and live-cell imaging, which will enable Institute researchers to analyze more closely the cell structures and signal pathways critical to type 1 and type 2 diabetes.

Robertson points out that PNRI's diabetes research groups are unique in the region. "We have established expertise in beta-cell physiology and a strong team of researchers working to cure diabetes. Such a cure," he explains, "requires us to understand how beta-cell mass is regulated, how insulin secretion is controlled, and how beta-cell function is impaired."

The confocal microscope, its imaging software, and a perfusion chamber for live-cell imaging will be the only such lab in the region devoted especially to the work of an integrated diabetes research program. According to Dr. Peter Dempsey, the new laboratory's director, "this facility will permit us to accelerate and deepen our study of some of the key problems of beta-cell development and function. Problems that must be solved if we want to prevent and cure diabetes."

## PNRI Tribute Gifts

October through December 2003 (Tribute name is listed in bold)

### MEMORIALS

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### HONORS

**Mr. and Mrs. Mark Clippinger**

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**R. Paul Robertson, M.D.**

Ms. Megan Robertson

# An Evening of Wine first flight



PNRI is premiering its first annual fundraiser, *An Evening of Wine – First Flight*, on Thursday, August 5, at The Golf Club at Newcastle. This wine-themed evening will offer a blind-tasting contest for all our guests to “Name That Grape.” The tasting features a flight of eight of Washington State’s finest wine varietals, facilitated by a very special guest sommelier. Following the tasting our guests will have time to visit each winery station for some additional samplings of both wines and delicious paired appetizers. A short program that highlights the important work being done at PNRI precedes a ten- item live auction where some spirited

bidding will raise money to benefit diabetes research at PNRI.

The distinguished Honorary Committee for this inaugural event includes: Ryan Allison, Founder and Owner, AWineStore.com; Juanita Garrison, Community Volunteer; Carol Heimkes, Community Volunteer; Richard Kinssies, Wine Columnist for the Seattle Post-Intelligencer and Director, Seattle Wine School; Bill Lewis, President and CEO, Lease Crutcher Lewis; Laurie Nichols, Partner, SeaCap Investment Advisors; Pennie Pickering, Vice President, Executive Producer, and Owner, Palazzo Intercreative; Richard Roberts, President and Owner, Palazzo Intercreative; Robert M. Williams, Vice President, Washington Mutual Bank.

The artwork for the save-the-date card and invitation shown here is an original watercolor titled “Columbia Valley Wine Country 2003,” by Patrick White. It was created especially for *An Evening of Wine – First Flight* by Mr. White, who is the Principal at St. Thomas More Parish School. The framed watercolor will be one of the items featured in the live auction.

Tickets are \$150 per person or \$1,500 for a table of 10. Attire for the event is elegant casual. To reserve your seat or table, contact Linda Bonomi, Director of Development. 206.726.1203 or [lbonomi@pnri.org](mailto:lbonomi@pnri.org).

## Help PNRI Prevent and Cure Diabetes

### Donor Recognition Wall of Honor

The PNRI Board of Trustees is pleased to announce the addition of a Donor Recognition Wall to our building lobby. The Wall, designed by Callison Architecture, Inc., who also designed the PNRI building, was completed last fall and honors donors who give generously to support PNRI research. The Wall features: a Memorial listing for gifts made in memory of a loved one; a Lifetime listing, honoring cumulative gifts made over a lifetime; an Endowment listing; and Partners in Discovery, a listing of donors who have named PNRI in their will. For more information about the Donor Wall, or if you would like an opportunity to see the wall and tour PNRI, please contact Linda Bonomi, Director of Development, at 206.726.1203 or by email [lbonomi@pnri.org](mailto:lbonomi@pnri.org).

**PNRI**

### Your Help Is Needed

While grants finance the majority of our science, we must build a base of private funding to provide for important needs that traditional sources typically do not support. These needs include scientific equipment, new technology, faculty, and facilities. To show our appreciation for private gifts, we offer a variety of naming and other recognition opportunities.

We must obtain private support for the following immediate needs:

- An advanced Confocal microscope to provide scientists with sophisticated imaging technology to view cellular activity
- Renovation of two laboratory floors
- Start-up support to attract the brightest and most talented scientists
- Funding for pilot projects for promising new directions in research
- Training fellowships to support post doctoral fellows — young scientists still in training
- Interim funding support for existing research awaiting the approval of a grant renewal application

For more information on how to provide support for any of these needs, please contact Linda Bonomi, Director of Development, at 206.726.1203 or at [lbonomi@pnri.org](mailto:lbonomi@pnri.org).



## Collecting email addresses—send us yours!

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](http://www.pnri.org/news). The inaugural issues of the *e-Laser* were distributed this past September and January, and links to on-line versions of the print *Laser* are sent to subscribers whose addresses we have.

So we need yours.

Please send it today. Subscription is easy. Just visit [www.pnri.org/howtohelp/subscribe](http://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* in all its forms. And we hope you will continue to share it with colleagues and friends.

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PACIFIC NORTHWEST  
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LANGERHANS-VIRCHOW  
LECTURE  
DR. LEE HARTWELL

GLASER AUDITORIUM,  
SWEDISH HOSPITAL, SEATTLE  
APRIL 7, 2004, 3:30-4:30 PM

Reception following the lecture, at PNRI.  
The public is cordially invited to attend.

## PROFILE *profile* Steve Anderson

Since 1987, Steve Anderson has been the key administrative coordinator of the cancer/cell biology research laboratory directed by Dr. Senitiroh Hakomori. It is a position that gives him enormous responsibilities. It makes use of his broad experience as a teacher, writer, editor, and PhD, and it provides him with considerable satisfactions.

Hakomori is one of the world's leading scientists in cell membrane biochemistry. His research has pioneered the study of the role of glycosphingolipids in the progression and prevention of cancer. Previously at the Biomembrane Institute, and now at PNRI, Steve Anderson is the lab's interface with the "outside world," both scientific and non-scientific. He has edited nearly 350 papers from the Hakomori lab. "Every sentence," Steve says, making precise the extent of his responsibility. All the grant applications, progress reports, manuscript reviews, and other scientific documents likewise pass through his hands. Scientists from around the world correspond with Hakomori. Steve manages that correspondence, responding to inquiries, writing on Hakomori's behalf to researchers seeking information or scientific counsel. These interactions with correspondents from Japan, Taiwan, Italy, Belgium, Brazil, Argentina, France and China are a regular part of Steve's day, and give him a fascinating glimpse of their different cultures.

In addition to this scientific work, Steve also manages the day-to-day administrative operations of the Hakomori lab, one of the largest groups at PNRI. He tracks budget and purchasing, facilitates visas for visiting foreign scientists, and coordinates equipment repair on behalf of the lab scientists. He is modest in his account of this role. "I'm not qualified to guide or direct them," he says. "I don't understand their projects in depth. They don't need me to interact between them and Hakomori." At the same time, Steve often provides just that link, and he does so with great effectiveness, thanks in large part to a varied and accomplished past.

After a childhood in Berkeley,



California, that included a year in Ecuador—his mother was an anthropology graduate student researching Inca pottery—Steve attended Harvard College where he majored in Biology. His graduate studies at the University of Southern California led to a doctoral dissertation focused on tropical ecology of mammals in Costa Rica. When he first came to Seattle, Steve taught anatomy and physiology at Seattle Central and North Seattle Community College. He edited nine books on osteopathy and craniosacral therapy (mostly translations from French) for Eastland Press. In the mid-1980s, Steve worked at Virginia Mason Medical Center and the Fred Hutchinson Cancer Research Center, editing and managing scientific documents. It was this experience that brought him to the newly-founded Biomembrane Institute in 1987 as a "manuscript editor." But he brought more than editing skill with him.

"I save Hakomori a tremendous amount of time," Steve says. "There are so many projects going on, and so much communication with 'outside people,' that things are always hectic around here. His research is so important, and he needs to maximize the time and attention given to that, rather than peripheral things. I understand him, and his thought processes, better than most people. It helps that I also understand science."

It's an extraordinary combination. And it gives Steve real rewards. As he puts it, "I like the challenge and variety of the work. It's exciting being part of an active community of scientists from around the world. And I like the chance to work with folks—here at PNRI and abroad—on the frontier of discovery."

*...on the frontier of discovery*

# The Social World

continued from page 1

eye, its structural components would enthral. Hakomori's papers—more than 500 of them by now—are full of figures that illustrate segments of its intricate surface. Look at Figure 1 below, for instance, from *Proceedings of the National Academy of Sciences*. It shows what looks like a vegetable garden, complete with carrots and herbs popping up from a richly composted bed with potatoes still buried in the soil.

In fact, what this schematic figure illustrates is the way that large carbohydrates can be clustered together in the cell membrane, anchored there, and sometimes organized with other components. Hakomori explains that there are many molecules that make up the cell membrane, and that from cell to cell these molecules can be very similar. What is essential to their distinctive function—and to their dysfunction in cancer—is the way they are assembled. It is the membrane's molecular assembly that is so critical to cancer development.

In studying both the structures and functions of these membrane groups, Hakomori and his colleagues have delineated two critical ways they can affect cancer growth.

First, they can promote cell adhesion. When tumor cells adhere to endothelial cells in blood, Hakomori says, they begin the process of metastasis by which cancer travels from the site of the primary tumor to remote tissues and organs in the body. The second key contribution of membrane carbohydrates is their induction of cell signaling. Cell signaling can enhance the motility of cancer cells and their destructive invasiveness in nearby tissues. Both of these

processes involve cell-to-cell interaction, and both are theoretically capable of being blocked once their mechanisms are fully understood.

This is Hakomori's goal. By deepening our understanding of the structures and functions of these carbohydrate groups in the cell membrane, he hopes to be able to inhibit the cell behavior that leads to the growth and spread of cancer. "The better you understand their structure," Hakomori says, "the better you can interrupt or affect their signals."

## Cell Sociology

As sharply focused as he is on the structures of membranes and the mechanisms of cancer, Hakomori sees them in a bigger context. "No cells can live alone," he tells his visitor, at the small round wooden table in his laboratory office. "They are always together, always dependent on others. They adhere to one another. They communicate." They have a "social structure."

This view applies to all living cells, and it describes in very general terms one of the fundamental features of organic life. "My focus is on cancer," Hakomori explains, "but it doesn't need to be. All organisms use these organizational processes. Cancer is just one instance of their application."

You can hear the wonder of life in his voice. It's not just disease that is at stake. Brain development, learned human behavior, imagination, language, the invention of political institutions, the arts—all the phenomena of organic life, Hakomori says, depend fundamentally on the intricate sociology of cells. There at the edges of their membranes, cells interact. There, in their interactions, and in the complex carbohydrate and protein structures that make those interactions possible, are some of the most important mechanisms of life.

# Perspectives

continued from page 1

have it, albeit in various degrees of severity.

There. I feel better. The real issue to focus on is the astonishing and alarming rate with which the diagnosis of type 2 diabetes is being made. Current estimates for clear-cut type 2 diabetes in the United States exceed 10% of the population, with another 20% diagnosable as pre-diabetic cases. The latter group are very likely to develop this disease in later years, especially if they become obese or eat improper diets. Even more alarming is the greatly increased incidence of this disease in children. Historically, children developed type 1 diabetes, a totally different disease in which an autoimmune process kills the beta cells in the islets of Langerhans so that no more insulin can be produced by the pancreas. Today's cultural factors of carbohydrate-rich fast foods, lack of physical activity, and resultant obesity in our children have hastened the development of diabetes in genetically prone individuals by 30 or so years. This has huge implications for the future health of this country because these individuals will have 30 more years to develop the chronic complications of diabetes, such as blindness, kidney failure, heart disease, and nerve dysfunction. Not a pretty picture.

Diabetes, whether type 1 or 2, is serious business and needs to be taken seriously by all of us. Over 30% of us currently are destined to develop pre-diabetes or frank diabetes. Yes, we need to avoid obesity and improper foods. But we also need to realize that our understanding of the mechanisms that cause diabetes is still embryonic. People often dream of prevention and cures. There will be none, however, until research in this area provides a full understanding of the nature of this disease. Just as we can't fix a broken down automobile until we know what's wrong with it, we cannot design maximally effective prevention or therapy of diabetes until we understand what's wrong with the dead or dysfunctional islets that are the hallmark of diabetes. And that's just what many of us at PNRI are doing all day long and into the evening—trying to figure out how individual genomes program some of us to be susceptible to this very serious disease that demands our full respect.

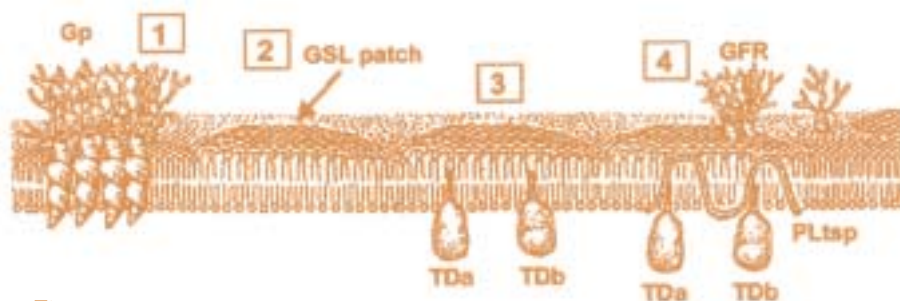


Figure 1

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*Dr. Lee Hartwell*

## Hartwell to Deliver Fifth Annual Langerhans-Virchow Lecture

On April 7, 2004, Dr. Lee Hartwell will deliver PNRI's fifth annual Langerhans-Virchow lecture. The topic of his lecture will be "Technology Development and Curing Cancer."

Hartwell received the 2001 Nobel Prize in Physiology and Medicine for his pioneering discoveries of the mechanisms of cell division. Using the budding yeast that is essential for brewing beer and baking bread, Hartwell identified many genes that control cell division. These same genes that operate in yeast have been found subsequently to control cell division in humans and to play key roles in the development of cancer. In his studies of yeast, Hartwell also discovered a new class of gene: "checkpoint" genes. These genes notice when mistakes have been made during cellular reproduction and halt cell division so that repair can take place.

Hartwell was educated at the

California Institute of Technology and the Massachusetts Institute of Technology. He has held research appointments at the Salk Institute and at the University of California, Irvine, and he has been a professor of genome sciences at the University of Washington since 1973. In 1997, he became the President and Director of the Fred Hutchinson Cancer Research Center in Seattle.

In addition to the Nobel Prize, Hartwell has received many other national and international scientific awards, including the Albert Lasker Basic Medical Research Award, the Gairdner Foundation International Award, and the Alfred P. Sloan Award in cancer research. He is a member of the National Academy of Sciences.

The public is invited to the Langerhans-Virchow Lecture at Glaser Auditorium, Swedish Hospital, Seattle, 3:30-4:30, and to the reception following the lecture, at PNRI, 720 Broadway.