

## Message from the Scientific Director

Welcome to the fall issue of our INMD newsletter. The summer months have allowed us to slow our pace at the Institute a bit, with staff taking some well-deserved time off. We have kept active on several fronts, most notably with evaluation reports for CIHR, strategic and operational planning, meetings with stakeholders, and responding to media requests including Statistics Canada's initial release of data from the Canadian Community Health Survey.

In June, we said goodbye to two outgoing members of our Institute Advisory Board,

and welcomed two new voices. Patricia Brubaker, University of Toronto, and Michael McBurney, who has just moved to be Chair of the Department of Nutrition and Food Science at Texas A&M University, have been major contributors to the work of the IAB and they will definitely be missed. We are looking forward, however, to welcoming two new board members, Robert Haché from the Ottawa Research Institute and the Department of Medicine, Biochemistry, Microbiology and Immunology at the University of Ottawa, and Laurie Anderson, Health Scientist from the U.S.

Centers for Disease Control and Prevention.

We have also been busy this summer preparing for participation in the annual conference of the North American Association for the Study of Obesity (NAASO), to be held this year in Vancouver. We have a special event planned for Canadian participants. Have a look at our expanded list of events and conferences on our website for more information.

In this issue of INMD Update we are pleased to profile two of our major partners, the Canadian Diabetes

Association and the Kidney Foundation of Canada. We have worked with these health charities extensively over the past several years, and are pleased to continue working together on initiatives like the KRESCENT training program. In this issue you can also read about some recent Canadian advances in the study of obesity, and catch up on some changes to CIHR policies.

We look forward to your feedback on our newsletter. We will be sending you another one in January. Best wishes for the fall.

Dr. Diane T. Finegood

### RESEARCHERS:

## Mysteries of the hormone leptin pursued at BC lab

The health-related dangers of being obese are increasingly garnering more public attention. And while a debate ensues over what constitutes an unhealthy weight, researchers at the University of British Columbia are quietly delving into the complex world of hormonal regulation of body weight in an attempt to build our understanding rather than our biases.

Dr. Timothy Kieffer heads a team of 15 researchers seeking new approaches to treat diabetes, a disease that frequently afflicts those who are obese. Kieffer believes a possible link between diabetes and obesity could be the hormone leptin, which is produced by fat cells and is responsible for feelings of satiety. Leptin was first described ten years ago, and the importance of its discovery is being acknowledged by a

Gairdner Foundation Award this year (see related story page 2).



Dr. Timothy Kieffer in his lab

Photo: Bayne Stanley

Initial data showed that leptin, when administered to leptin-deficient mice or people, could reverse obesity. A novel discovery made by Kieffer, using leptin-deficient mice, suggested that type 2 diabetes could develop independently of obesity. Without leptin, the mice became twice a normal size, and developed type 2 diabetes. When his team administered leptin, "we could virtually cure the diabetes overnight". Weight loss also occurred, but took much more time. These results suggested that leptin worked in different ways to protect against diabetes, and to protect against obesity.

However, leptin replacement has been ineffective if obesity is due to leptin resistance. And as Kieffer notes, "Most obese humans produce plenty of leptin,

continued next page

**Mysteries of leptin...**

but are resistant to its actions.”

Kieffer’s aims now are to learn how people become resistant to leptin, and how problems with this hormone may disrupt glucose homeostasis and lead to obesity. “If we can figure out how people develop leptin resistance we might understand why they have a great risk of developing diabetes, and ultimately this research could lead to new ways to control body weight and reduce the associated risk for diabetes.”

Kieffer’s team uses animal models and human tissue, and their focus is on leptin receptors on pancreatic beta cells and in liver cells.

Beta cells produce insulin to induce uptake of blood glucose into body cells. Kieffer has shown that in human beta cells, leptin inhibits insulin production and secretion. At the same time, circulating insulin increases release of leptin from fat cells, completing a regulatory feedback loop. Dysregulation of this loop may cause obesity, and lead to changes that cause diabetes.

Studies in animal models support this idea. “Based on the analysis we have conducted so far, we have good evidence that the action of leptin on beta cells is critical for the maintenance of proper glucose homeostasis,” says Kieffer. When leptin action is faulty, excessive insulin is released and this can promote weight gain and insulin resistance. Notably, this effect of leptin appears independent of food intake.

The liver is also involved in this complex system. The liver has leptin receptors, which when activated appear to increase the organ’s sensitivity to insulin. Kieffer’s recent experiments suggest that a diet high in fat can increase production of intracellular proteins that counteract this effect. Again, dysregulation could lead to obesity, or diabetes, or both.

With funding from CIHR and the Michael Smith Foundation for Health Research, Kieffer and his team will continue their research from his lab in Vancouver.

**Lecture tour and panel discussion will honour recipients of Gairdner awards**

Co-recipients of one of this year’s Gairdner Foundation Awards are one American-born and one Canadian-born researcher, for the discovery of the hormone leptin. Drs Jeffrey M. Friedman and Douglas Coleman will be honoured during a week of lectures in October.

A highlight during the week will be the 5<sup>th</sup> Annual Gairdner Public Lecture, given by Friedman at the MaRS Collaboration Centre October 25 in Toronto. His talk will be followed by a panel discussion, with host Ann Medina, on the topic “Why Are We Obese?” The panel will consist of Dr. Bernard Zinman, Sam and Judy Pencer Chair in Diabetes and Director of Leadership at the Sinai Centre for Diabetes in Toronto, Dr. Diane T. Finegood, Scientific Director of INMD, and Mr. Giles Gherson, Editor, Toronto Star. The evening’s events are co-sponsored by the Gairdner

University in Hamilton October 26, and at the University of Toronto October 27.

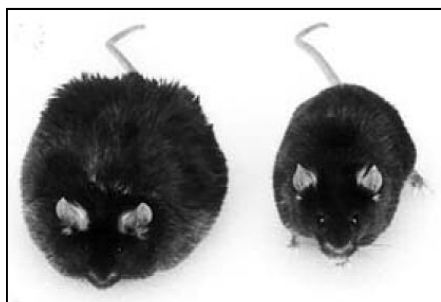
Friedman was born in Orlando, Florida, and received his MD from Albany Medical College of Union University in New York, and his PhD from Rockefeller University in New York. He has been working on the control of body weight for more than 20 years, and is presently situated at the Howard Hughes Medical Institute at Rockefeller University. Coleman was born and raised in Stratford, Ontario, received his BSc from McMaster University, and his PhD from the University of Wisconsin. He is now an emeritus researcher at the Jackson Laboratory in Bar Harbour, Maine.

The two men are being honoured “for contributions to our understanding of obesity and particularly for the discovery of the adipose tissue hormone, leptin”.

Other recipients of this year’s awards include Dr. Craig C. Mello (Howard Hughes Medical Institute) and Dr. Andrew Z. Fire (Stanford University School of Medicine), “for the discovery of RNA interference which initiated a revolution in the study and use of RNA in gene silencing”, and Dr. Brenda Milner (McGill University) and Dr. Endel Tulving (University of Toronto), “for pioneering research in the understanding of human memory, and providing the necessary framework within which findings in neuroanatomy, neurophysiology, and neuropharmacology can be integrated”.

All award recipients will be lecturing across Canada, along with several other well known researchers.

More information on the public lecture and panel discussion can be found at [www.marsdd.com](http://www.marsdd.com), and on the award recipients and the Gairdner Foundation at [www.gairdner.org](http://www.gairdner.org).



Leptin deficient mouse (left) compared to normal mouse (right)  
Photo courtesy J. Friedman Lab

Foundation and CIHR.

Both Friedman and Coleman will be giving lectures across Canada October 24 to 27. Friedman will speak on “Leptin and the Biologic Basis of Obesity” at the BC Cancer Research Centre in Vancouver October 24, and at the University of Toronto October 27.

Coleman will be lecturing on “Mouse Mutants and the Discovery of Leptin” at the John P. Roberts Research Institute in London October 25, at McMaster

## Kidney researchers create unique training ground

An innovative training program designed to address the relative decline in the number of kidney disease researchers in Canada was launched earlier this year. The Kidney Research Scientist Core Education and National Training (KRESCENT) program was the culmination of five years of discussion by all kidney research stakeholders, i.e. the Kidney Foundation of Canada (KFOC), the Canadian Society of Nephrology (CSN), kidney researchers, academic nephrology centres and CIHR.

Development of the KRESCENT program was prompted by awareness that the incidence of kidney disease in Canada was increasing at a rate that was surpassing the pool of kidney scientists and clinicians, as well as those from allied health disciplines such as nursing, nutrition, pharmacology and social work. Data from the Canadian



Institutes for Health Information showed that the number of patients being treated for end-stage renal disease or kidney failure increased by approximately 20% between 1997 and 2001.<sup>1</sup>

This trend is expected to continue.<sup>2</sup> This increasing incidence is due in part to the rise in diabetes. Type 2 diabetes was the primary cause of kidney failure in 29% of new patients in Canada in 1997, and the number climbed to 33% in 2001.<sup>3</sup> People with kidney failure require long-term dialysis or transplantation to survive. Unfortunately, the number of kidney transplants has remained very low because organ donation is low, and many people with this disease have complicating co-morbidities that preclude transplantation as an option.<sup>4</sup>

According to President of CSN Dr.

Kevin Burns, "Although there have been tremendous therapeutic advances over the past few decades, most kidney diseases still progress to kidney failure. Enhancing research across a broad spectrum is crucial for long-term management of these diseases. One of the great benefits of the KRESCENT program is that it will support research in a variety of areas, from basic biomedical, to clinical, to health services, to population health."



Dr. Kevin Burns  
President, CSN

INMD recently joined the KFOC and the CSN on the KRESCENT program Governing Council, and will help support the program financially. CIHR's Institute for Circulatory and Respiratory Health (ICRH) also contributes financially. Donations from the Branches of the KFOC, and a special contribution from the membership of the CSN have been complemented by support from AMGEN, Baxter Corporation, Merck Frosst Canada Ltd., Ortho Biotech, Shire BioChem Inc., and private donors. Overall, funding available for the program will grow to \$6.5 million total over the next five years.

KRESCENT is unique not only in the breadth of applications considered, but in the structure of training. Trainees complete courses and conduct research in their chosen academic unit. In addition, they complete a core curriculum using web-based modules and attend two workshops each year, which integrate core lectures with transdisciplinary research challenges. These challenges require trainees to address a problem by incorporating several of the four CIHR research themes. For instance, working in

small groups, they are required to examine a disease such as type 2 diabetes, and work their way through scientific studies to understand the mechanisms for progression of kidney disease in people with type 2 diabetes (biomedical), develop a method to better understand individual disease progression rates (clinical), design an intervention strategy to identify signs of early illness (health systems and service), and finally, evaluate the determinants of disease progression with consideration of factors such as socioeconomics, gender, geography and ethnicity (population and public health).

Another important aspect of KRESCENT is provision of mentorship. At a fellowship level, mentorship is provided by research supervisors, and at a faculty level, this role is fulfilled by specifically-chosen mentors who provide one-on-one guidance and support.



The KRESCENT program funds university researchers within the first two years of a faculty appointment, postdoctoral fellowships for MDs and PhDs destined for a career in nephrology research, and graduate students in allied health services. The KFOC, the CSN, ICRH and INMD are proud to invite eligible applicants to apply in the inaugural year of the KRESCENT program. Competition deadline is November 1, 2005. More information on the program can be found at <http://kidney.ca/Krescent/index.asp>.

<sup>1</sup>[http://secure.cihi.ca/cihiweb/dispPage.jsp?cw\\_page=media\\_21jan2004\\_e](http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=media_21jan2004_e)

<sup>2</sup><http://ije.oxfordjournals.org/cgi/reprint/27/2/274>

<sup>3</sup>[http://secure.cihi.ca/cihiweb/dispPage.jsp?cw\\_page=media\\_21jan2004\\_2\\_e#diabetes](http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=media_21jan2004_2_e#diabetes)

<sup>4</sup><http://linkinghub.elsevier.com/retrieve/pii/S0041134503008807>



RESEARCHERS:

## Altered neurological response to food may contribute to obesity

How does the brain process the pleasurable aspects of eating? Finding some answers might provide insight into some of the factors that contribute to obesity in certain individuals, hypothesizes Dr. Beth Tannenbaum. After receiving a three-year grant under the Target Obesity Fellowship program this year, Tannenbaum will be comparing



Researcher Dr. Beth Tannenbaum

activation of brain centres known to respond to pleasurable sensations in non-obese, overweight and obese people. The program is a Heart and Stroke Foundation of Canada initiative, with additional funding from various partners. Tannenbaum's work is being financially supported by the Canadian Diabetes Association, and two CIHR Institutes, the Institute of Cancer Research and INMD.

"To the best of our knowledge, this is the first investigation into how obese individuals may differ from normal weight people in the way that their brains evaluate how rewarding food is to them," she says.

Working at the Montreal Neurological Institute at McGill University, in collaboration with researchers at Yale University in Connecticut, Tannenbaum will be using functional magnetic resonance imaging (fMRI) to examine blood flow (an indication of activation) in areas of the brain that respond to pleasurable stimuli. One

neurotransmitter, dopamine, is known to be released in these areas under various pleasurable conditions. What Tannenbaum wants to know is if these dopamine centres respond differently in obese individuals when a pleasant food stimulus (i.e. a food "reward") is delivered. If the neural response to this pleasurable stimulus is heightened, this could make an individual susceptible to overeating and weight gain.

Tannenbaum's work involves asking people to rate the pleasantness of different solutions that vary in their fat and sugar content, as she monitors brain blood flow. Her hypothesis is that obese individuals find calorie-dense foods (such as cream and sugar) more rewarding and pleasurable than normal weight individuals and, as such, the brain response of obese people will be markedly different. She will be controlling for possible confounding effects of motivational state, that is, whether her subjects are feeling hungry or satiated, as well as considering their general mood.

Tannenbaum's research could also reveal something about what lies behind this hypothetical differential processing. The amygdala is a brain centre that "codes" responses to environmental stimuli, such as the appearance or taste of food.<sup>1</sup> A "hedonistic" amygdala could respond with heightened sensitivity in some people, creating a code that increases the expectation of, and response to, a pleasurable reward.

Research has already shown that processing of information about food can be different in obese people. Some obese people have reduced numbers of receptors available to bind dopamine in the striatum.<sup>2</sup> This reduction in receptors is associated with disruptions in dopamine activity in brain areas that are involved with impulse control and compulsive behaviors. This can in turn alter the reinforcing and rewarding properties

of foods, and might contribute to an addictive-like state.

"It is important to think about how perception and subjective experience of food and eating may impact on neurochemistry and in turn, promote overeating," summarizes Tannenbaum. "Obese individuals may process food and cues about food in a dramatically different way and this may contribute to their developing obesity."

Tannenbaum's work could lead to better ways of treating obesity. A clearer understanding of how reward cues are processed in the brains of obese people could allow development of drugs that work more effectively and with fewer side effects compared to the pharmaceutical products currently available.

<sup>1</sup>Ahn S. et al, *Neuroscience* (2003) ; 116 : 295-305

<sup>2</sup>Wang G.J. et al, *Lancet* (2001); 357: 354-357

### News from CIHR about funding and form changes

New funding opportunities, and changes to application procedures, have recently been posted to the CIHR website:

Information on newly launched funding opportunities is available at <http://www.cihr-irsc.gc.ca/e/28761.html>.

Training module applications forms, which must be submitted for doctoral research awards, fellowships and phase 1 clinician scientist (new and renewal) awards, have been updated since July 2005. CIHR will no longer process older application forms. For more information visit <http://www.cihr-irsc.gc.ca/e/28773.html> and to access the form go to <http://www.cihr-irsc.gc.ca/e/797.html>.

## The value of partnerships:

### A profile of the relationship between the Canadian Diabetes Association and INMD

Consultation with stakeholders to identify shared priorities, research gaps, and strategies to optimize resources and research dollars has always been a high priority for INMD. Establishing partnerships with a wide range of organizations is a major strategy towards realizing these goals. Partnerships involve sharing knowledge, or resources, or both, and often bring together several groups to work toward a common goal.

The Canadian Diabetes Association (CDA) was one of INMD's first partners. CDA received its charter in 1953, and now has a presence in more than 150 communities across Canada. Their mission is "to promote the health of Canadians through diabetes research, education, services, and advocacy".

To accomplish this, they work with various governmental and non-governmental organizations, and benefit from the efforts of nearly 35,000 volunteers. CDA became involved with INMD soon after its inception, supporting various nominations to the Advisory Board.

"We've been involved since day one," confirms Donna Lillie, Vice President of Research and Professional Education at CDA. Lillie speaks enthusiastically about the relationship between CDA and INMD. CDA was quick to realize the potential of collaborating, she explains, because they rely heavily on donor dollars and volunteer commitment, and are always

struggling to meet the demands of their community.

"The reality is that there just isn't enough money to fund all the research opportunities we are presented with in our organizations."

The Chronic Disease New Emerging Team program was one of the first partnerships conceived and initiated within this new research environment, Lillie says, "even ahead of clear formats and protocols for such innovative partnerships. But all the partners worked it through together and learned a lot from the process."

This program is supported by several organizations, and provides funding and support to research teams investigating a variety of chronic diseases. The program was assessed by CIHR after three years, and a positive evaluation encouraged CDA's continued involvement. Transparency and accountability is important to organizations such as CDA, that rely on donor dollars.

"It's important to know that we have checkpoints, and that we can show accountability to all our stakeholders," says Lillie.

CDA also partners with INMD in Target Obesity, a program initiated by the Heart and Stroke Foundation of Canada. Target Obesity is a collaborative effort of these three organizations, and the goal of the program is to train investigators and

fund research in the study of obesity.

Previously, INMD and CDA worked together to fund six doctoral students undertaking diabetes research.

As well as direct partnerships, CDA and INMD have had a long-standing relationship as members of larger discussion groups related to diabetes research, such as the National Diabetes Surveillance System and the National Diabetes Strategy. The National Diabetes Strategy brings together experts, researchers, representatives from all levels of government, and representatives from non-governmental organizations, in the best interest of addressing a full complement of diabetes issues for Canadians.

Another important aspect of working together that Lillie appreciates is the opportunity for CDA to learn from INMD. "The expertise and willingness to share that knowledge is an important contribution."

CDA has grown as an organization because of this type of mentorship, she says. "INMD expanded the opportunity for CDA to go more places, to do more, and to have more leverage with our research activity."

One indication that INMD has influenced the Association in this way is that Lillie says CDA's new strategic research plan will be focusing on innovative and unique partnerships more than it has previously.

## HOW TO GET IN TOUCH WITH US:

### Institute of Nutrition, Metabolism and Diabetes

Room WMC2805, Simon Fraser University, 8888 University Drive, Burnaby, BC, V5A 1S6  
Tel: 604-268-6707; Fax: 604-291-3055  
<http://www.cihr-irsc.gc.ca/e/12043.html>

Newsletter: [inmd\\_communications@sfu.ca](mailto:inmd_communications@sfu.ca) (Nola Erhardt)  
General Information: [inmd3@sfu.ca](mailto:inmd3@sfu.ca) (Meena Bagri)

### CIHR Corporate Headquarters

160 Elgin Street,  
Room 97,  
Address locator: 4809A  
Ottawa, ON  
K1A 0W9  
<http://www.cihr-irsc.gc.ca/e/9833.html>



## MEETINGS AND CONFERENCES:

Canadian Public Health Association 96th Annual Conference and the Statistics Canada's Health Statistics Data Conference Ottawa, ON, Canada	Sept. 18 - 21, 2005
Health Management Research Conference: From Cure to Prevention: Bringing Together the Partners for Change Banff, AB, Canada	Sept. 29 - Oct. 1, 2005
North American Association for the Study of Obesity: Annual Scientific Meeting Vancouver, BC, Canada	Oct. 15 - 19, 2005
The Canadian Association of Paediatric Health Centres Annual Meeting: Healthy Bodies, Healthy Minds for Canada's Children and Youth St. John's, NL, Canada	Oct. 16 - 19, 2005
4th International Symposium on Obesity and Hypertension Berlin, Germany	Oct. 27 - 29, 2005
Third Annual World Congress on the Insulin Resistance Syndrome San Francisco, CA, USA	Nov. 17 - 19, 2005
Obesity, Lifestyle, and Cardiovascular Disease Symposium Washington, DC, USA	Jan. 18 - 20, 2006
Sixth International Conference on Dietary Assessment Methods Copenhagen, Denmark	April 26 - 29, 2006

Please visit our website at <http://www.cihr-irsc.gc.ca/e/13521.html> for constantly changing information about conferences and meetings.

## INMD FUNDING OPPORTUNITIES:

We are happy to report that funding is now available for "Workshop Support – Research Development and Knowledge Exchange". The closing date for applications is October 15, 2005. More information is available at <http://www.cihr-irsc.gc.ca/e/28719.html>.

### Opportunity available for Canadians to impact Framework Program

The European Union's newest Framework Program (FP7) model contracts and rules for participation are currently being developed. An open consultation of the Rules of Participation is underway. More information is available at: [http://europa.eu.int/comm/research/consultations/list\\_en.html](http://europa.eu.int/comm/research/consultations/list_en.html).

In addition, through diplomatic channels, there is an

opportunity for Canada to try to influence these documents with the interests of Canadians in mind. If you or your organization have FP6 experiences or FP7 suggestions you would like to contribute, regarding special clauses for third-country researchers who do not receive funding from the FPs, please contact: [paola.de-rose@international.gc.ca](mailto:paola.de-rose@international.gc.ca) as soon as possible.

