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Inside this edition: Focus on human health and disease

Volume XXVI Number 1 Winter 2011

Research magazine

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A Helping Hand

Look for this link to view SPARK*Air interviews with U of Guelph researchers.

SPARK writer Nicole Yada gets the inside story on a Guelph-developed robotic arm designed to help stroke victims with rehabilitation. See her story on page 23.

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Address correspondence to:
Owen Roberts, Director, Research Communications
Office of Research, room 437, University Centre
University of Guelph, Guelph, ON N1G 2W1
519-824-4120 ext. 58278
inforc@uoguelph.ca

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Cover Photo: Martin Schwalbe | Photo by Kyle Rodriquez

Working together is vital for global health

Prof. Kevin Hall, Vice-President (Research)

You might be surprised to learn that the University of Guelph receives more health-related research funding than any other Canadian university without a medical school. Our long-standing expertise in life sciences got us there, enabling us to address new challenges that arise as problems become more global, and usually more complicated.

Guelph researchers, provincial and federal granting councils, and business and industry are connecting very well, and society is the beneficiary. Working together is vital, as health care costs continue climbing, commanding more and more public support and as health issues become more complex and global in nature.

We're committed to staying on top by looking at health from every possible angle. In the pages of this *Research* magazine, you'll see how Guelph faculty, staff and students bring together a breadth of expertise in linking human health, animal health and environmental health. This is indeed the approach that the World Health Organization has espoused as One Health – One World. And it's a deeply engrained part of the research culture at the University of Guelph.

Driving through campus, the most visible evidence of the one-health approach is the $70-million Pathobiology/Animal Health Laboratory building that supports the growing role of veterinarians and scientists in research and educational initiatives related to public health. This building houses the University's Centre for Public Health and Zoonoses. Climate change, globalization, pollution and ecosystem health all contribute to the one-health equation.

There's much more. Guelph researchers have also received special recognition from Canadian health funding agencies for their work on cancer studies. Teams of geneticists, molecular biologists and pathologists work together to understand every stage of this disease, with the goal of one day having a cancer-free world. We also house one of the largest neuro-science clusters outside of conventional medical schools, and the development of advanced diagnostic and detection systems occurs in four of our colleges. In many countries, including Canada, poor diets are being implicated for their role in epidemics such as obesity and diabetes. In response, University of Guelph researchers are borrowing traditional knowledge and dietary advice from cultures half way across the world. By combining ancient medicinal practices with modern lab techniques, researchers are helping turn food back into a source of sustenance and health.

We are reaching out around the world, working with both academic, industrial and NGO partners in Europe, Asia, Australia and in many marginalized communities across Africa and southeast Asia.

Communities allow us to share places, resources and people. A community's health is determined by the health of the individual people and places that make it up. At Guelph, we're proud to contribute to the health of the global community, and we appreciate the support of those who believe in our work.

SPARK

The University of Guelph *Research* magazine is written and co-ordinated by participants in the Students Promoting Awareness of Research Knowledge (SPARK) program.

Animal science major Carol Moore grew up playing basketball in her hometown of Sussex, New Brunswick. She took a particular interest in research that showed how staying hydrated during sports can improve performance significantly. See page 19 for the full story.

For Joey Sabljic, a third-year English major from Guelph, Ontario, the piano is his main go-to treatment for whatever's ailing him. But if the piano doesn't cut it, he now knows that how Guelph Prof. Praveen Saxena is breeding Eastern medicinal plants as a natural alternative for Western consumers. Read all about it on page 11.

Chatham, Ontario's Johnny Roberts, a fourth-year theatre studies student, has always been interested in new, innovative research, especially that which pertains to human health and disease. So he was excited to learn that researcher Prof. Jim Petrik has come up with some pertinent findings that will help in the fight against ovarian cancer, page 35.

Fourth-year animal science major Maurice Harvey didn't hear much, if anything, about Q fever, growing up in downtown Toronto. So he was surprised to learn of its importance to small ruminant producers. Learn more about zoonotic disease detection and Q fever on page 42.

Growing up in a family of scientists, marketing major Nicole Yada has almost a genetic understanding of the benefits of research and development. Her cover story on Prof. Hussein Abdullah's work involving robots that help rehabilitate stroke victims demonstrates the University of Guelph's involvement in medical research.

Guelph native Robert Fieldhouse is a longtime SPARK contributor and biophysics PhD candidate in the Department of Molecular and Cellular Biology. On page 38, he writes first-hand about his own research in identifying and characterizing protein toxins and the work of his colleagues, who've developed toxin inhibitors that may lead to future treatments.

Adolescent mental health is of particular interest to fourth-year psychology student Vanessa Perkins from Newmarket, Ontario. See page 28 for her story on University of Guelph psychology professors who are researching non-suicidal self-injury and new ways to help adolescents cope with the thought processes that lead to such behaviour.

Research magazine co-ordinator Natalie Osborne loved to spend winters in the snow, on her farm just outside Guelph. Now a third-year biomedical science student, she's learning how important the ice and snow are to the health of Canada's northern communities. See her story on climate change's effects on health, page 26.

This is second-year marketing management Bruce Sargent's first semester with SPARK. In 2010 Bruce started his own business called Farm Boy Productions, creating multi-media marketing material including videos. Now, he's the first SPARK staffer to be specifically dedicated to video production.

The choice between getting a needle or getting sick is tough for some people. Third-year agricultural business student and Guelph native Rebecca Hannam, writes how mathematicians calculate the probability and outcomes of these decisions to develop vaccine strategies for different illnesses, page 39.

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Dysfunctional equality

Dear Editor:

"Equality among citizens is vital for maintaining a functional society." It must be so, because [*Research*] magazine says so. (Winter 2010, p. 23).

Shucks. We've been chasing equality for maybe 50 years, and we have developed into a society in which some teenage girls torture and murder their friends, and bystanders may be killed in gunfights on public streets. I guess that's all part of being "functional."

Imperial China and Japan each lasted for more than 1,000 years, and the Pharaonic culture of Egypt lasted a long time. Even Rome lasted for hundreds of years, and so did many other societies in which 'equality' was reserved for the aristocracy.

To be fair, the only long-term functional societies on Earth (Australian Aborigines and the !Kung of Africa) are egalitarian, but they are also small and uncrowded.

Normally I would ignore even such an obvious gaff as this in a magazine, but [*Research*] represents the University of Guelph and this statement suggests that it may be home to a dangerous level of groupthink.

At the very least, it implies that your magazine desperately needs an editor.

Andy Turnball
sent via email

Houdini hardly a medium

Dear Editor:

I very much enjoy *Research* magazine, but I must point out an error in the otherwise excellent article, "The Magic of Science," by Natalie Osborne from the Volume XXV (1) Winter 2010 issue on page 33. It says that "… many magicians such as Harry Houdini began their careers as mediums …".

Although this statement is true of some others of the period, notably the Davenport Brothers, it is not true of Houdini. Although his advertising posters suggested that he "dematerialized" to affect his miraculous escapes, Houdini never claimed to possess supernatural powers. He spent much of his life debunking and exposing spirit mediums.

Dr. David Colby
Denfield, ON

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Backing off bird flu

SPARK air video

The reappearance of avian flu in Asia and Europe proves that the threat remains. Even with current surveillance methods, the risk of a pandemic still exists.

Avian flu H5N1 virus doesn't spread among humans like other similar influenza infections, such as H1N1 … but it's extremely lethal. Up to half of those infected with the avian influenza virus will die.

A research team from the University of Guelph and elsewhere is trying to develop vaccines for chickens, to stop disease transmission between animals before it gets to humans.

Team leader Prof. Shayan Sharif, Pathobiology, says the group is looking for avian influenza antigens (viral molecules or molecular fragments) that trigger an immune response.

"We want to see if we can contain the viral infection in chickens," says Sharif. "Once it readily spreads among humans it's likely that we could see a severe pandemic, because of the high mortality rate."

Other researchers involved in this project include Dr. Shahriar Behboudi, University College London, UK; Dr. Mansour Haeryfar, University of Western Ontario; Prof. Éva Nagy, and laboratory staff members Dr. Amirul I. Mallick, Hamid Haghighi and Leah Read, University of Guelph.

This research receives support from the Natural Sciences and Engineering Research Council, the Poultry Industry Council, the Canadian Poultry Research Council, the Saskatchewan Chicken Industry Fund and the Ontario Ministry of Agriculture, Food and Rural Affairs.

Shame cycles drive addictions

SPARK air video

Guilt may be an important element in curbing self-destructive behavior, such as compulsive gambling.

Prof. Sunghwan Yi, Marketing and Consumer Studies, says feeling guilt instead of shame may help people break the cycle of addiction. Guilt is when you regret the way you acted or reacted in a situation; feeling shame means interpreting a regretful situation as indicative of your entire self-worth.

For example, guilt exhibits itself when you say *I shouldn't have eaten all of those donuts.* Shame is seen in this response: *I ate all of the donuts, therefore I am a failure.*

"To break the pattern induced by a patient's feelings of shame, they must learn to recover a healthy sense of self and to find ways of avoiding making mistakes, such as keeping away from situations in which they may feel tempted," says Yi.

His recent research was funded by the Ontario Problem Gambling Research Centre. Yi has an academic paper in press, and another paper under review, both of which are based on survey datasets he collected in 2008-2009.

Better nutrition and health for seniors

SPARK air video

Many older adults living in long-term care facilities are unsatisfied with their culinary experiences, due to poor-tasting, nutritionally inferior foods on the menu, according to Prof. Heather Keller, Department of Family Relations and Applied Nutrition. She has been interviewing and observing older adults to track what they're eating, so she can determine what nutrients are missing from their diets.

Prof. Heather Keller

She's found that many items on the menu – particularly meat and vegetable purees – go uneaten because they are plagued by unappealing tastes and textures.

"We have to find a way to make food products better quality and more appealing to the elderly," says Keller.

Also involved are Profs. Alison Duncan, Department of Human Health and Nutritional Science; Lisa Duizer, Department of Food Science; and Ken Stark from the University of Waterloo.

Keller's work receives funding from the Social Sciences and Humanities Research Council and the Alzheimer Society of Canada, as well as support from the Murray Alzheimer Research and Education Program at the University of Waterloo.

Photo by (clockwise from top) iStock, Martin Schwalbe and Nicole Yada |

Prof. John Dutcher

Natural nanoparticles ideal for drug delivery

SPARK air video

Pilot trials are under way at the Guelph Food Technology Centre to test a revolutionary advancement in materials science called PHYTOSPHERIC™ nanoparticles. A startup company, Mirexus Biotechnologies Inc., has formed to guide the development of this new platform technology.

The tiny particles (one billionth of a metre in length) are unique because they're all natural and safe for human use. The body contains enzymes to break them down, which makes them ideal for biomedical applications such as drug delivery.

"They can serve as non-toxic, biodegradable replacements for current synthetic nanoparticles," says physics Prof. John Dutcher, one of the particles' discoverers. "It's about being imaginative with what kind of molecules you can attach to the particles' outside surface to get the function you want."

Funding for this research is provided by the Advanced Foods and Materials Network.

Eating to beat allergens

A Guelph researcher has developed egg-derived peptides that may someday allow children to slowly eat their egg allergies into submission.

Physicians normally advise parents to eliminate from their child's diet any foods causing allergic reactions. However, that approach can be costly, time-consuming and ultimately affect a child's nutritional well-being.

Food science Prof. Yoshinori Mine and PhD student Marie Yang isolated the exact amino acid sequence responsible for triggering an allergic reaction to egg. This sequence, contained in the peptides, was fed to mice born with egg allergies.

After six weeks of ingesting the egg peptides, up to 80 per cent of the mice were able to consume the complete protein without experiencing any allergic reactions. The rest only experienced mild symptoms.

Mine is collaborating with medical schools in France and Japan, as well as Canadian medical institutes.

Funding is provided by the Natural Sciences and Engineering Research Council.

Prof. Yoshinori Mine

Sleeping problems and obesity clearly connected

SPARK air video

High rates of obesity and sleeping problems are clearly connected, say University of Guelph researchers. A great deal of research has been done separately on obesity and sleeping problems, but the existence of a possible relationship between the two issues has, until recently, been unexplored.

Filling this knowledge gap is applied nutrition Prof. Paula Brauer at the University of Guelph and graduate student Tamara Marsden, who have found a clear connection between sleep quality and quantity in people trying to lose or maintain weight.

"Obesity and sleep problems are connected," says Brauer. "We're aiming to understand the connection between the two in the community."

This study is co-authored by Tracy Hussey of the Hamilton Family Health Team.

Brauer's research was funded by Canadian Foundation for Dietetic Research.

| Photos by Martin Schwalbe

Where's the evidence?

SPARK air video

BY CAROL MOORE AND TERESA PITMAN

Researchers wonder if evidence-based medicine results in better patient care.

Evidence-based medicine is based on clinical research (or "evidence") that guides health-care decisions for practitioners and policy-makers. Through generalized results, procedures and policies are created for a broad spectrum of the population. It's considered by some to be a cost-effective way of dealing with a wide range of people.

Until the 1980s, physicians and other health-care practitioners tended to rely on what they'd learned in medical school, and their own experiences and habits in providing care to patients. Then along came the proponents of evidence-based medicine, who wanted to make physicians aware of ongoing research and encouraged them to apply it in deciding how to diagnose and treat their patients.

But given that the population consists of a group of unique individuals, what is the likelihood that evidence-based medicine truly reflects the specific experience of most patients? The challenge comes in extrapolating clinical information to patients in the real world.

"The promoters of evidence-based medicine have not reflected on how difficult it is to apply the research to real individual people," says Prof. Maya Goldenberg, Department of Philosophy. "I question how we claim to know what we know, and at what point a belief becomes a piece of knowledge that we can become confident in," she says.

Prof. Maya Goldenberg

By asking these questions, Goldenberg hopes to encourage discussion and debate between the supporters of evidence-based medicine and their critics, all of whom share the common goal of improved patient care.

"It's hard to evaluate claims that evidence-based medicine actually results in better outcomes for patients than the more intuitive, experiential type of care that came before," says Goldenberg. To her, a generalized clinical result from thousands of test subjects has a role to play in health care, but it shouldn't displace a personal understanding of an individual's needs. R

Photo by Perry Hagerman, Guelph General Hospital |

Prof. Praveen Saxena is selecting plants with the maximum amount of medicinal value.

Eastern medicinal plants for western health woes

SPARK air video

BY JOEY SABLJIC

The natural medicine industry has bloomed from a small, niche market two decades ago, to a multi-billion dollar industry today. Yet, despite plant-based supplements and medicines becoming increasingly mainstream, relatively little is known about their effects on human health – or, for that matter, how to safely cultivate and reap their medicinal rewards.

University of Guelph Prof. Praveen Saxena, Plant Agriculture, wants to change all that. In his Guelph lab, he and his research team are combining cloning, tissue culture and controlled environment greenhouses to grow and mass-produce medicinal plants that are renowned in different cultures and traditions around the world, starting with ayurveda.

Ayurveda is a traditional medicine system native to India. It uses botanical and medicinal knowledge to help its practitioners select the most effective plants to treat and prevent sickness and disease. Saxena says ayurveda offers people natural ways to fight signs of aging, boost their immune systems, reduce stress, combat depression and even prevent the progression of other related neurological disorders.

"If Canadians start growing [ayurveda] plants, which then became part of a regular diet, it could be really positive," he says. "People's enthusiasm for a holistic lifestyle is increasing rapidly and they are starting to wake up to medicinal plants."

One such plant being cultivated by Saxena is tulsi, or holy basil, a plant that has been used for thousands of years in sacred cultural and spiritual practices. Tulsi (*Ocimum sanctum*) is consumed on a daily basis as tea, as a powder, and as a food additive in Southeast Asia, where it's highly regarded for its reported antibiotic, antiviral and antifungal properties. Research has shown that tulsi, along with many other ayurvedic plants popularly referred to as "brain tonics," can help improve certain brain functions and possibly delay the onset of some neurological diseases.

Saxena says a plant's medicinal content is drawn mostly from the phytochemicals it releases to repel insects and other predators, and to adapt to harsh climates. But in a natural field setting, no two plants are chemically identical, meaning that the amount of desirable medicinal compounds in them can vary widely.

That's where Saxena comes in. Through cloning and tissue culture growth in controlled environment chambers and in his greenhouse, he's able to select plants with the highest amounts of medicinal compounds. Then, using tissue culture from the plants' roots or leaves, he can generate thousands of genetically identical plants – all featuring the same medicinal content – in a safe and contamination-free greenhouse environment.

And thanks to the rich literature on ayurvedic medicine, the best time to harvest, process, and eat certain plants for the ideal results has already been made widely available.

"Plant medicines are a big business today and introducing safe and reliable products from medicinal plants commonly consumed by growing ethnic populations can be profitable for the Canadian economy," says Saxena. "The key lies in the fact that we need to introduce novel plants that have been proven safe and effective over a period of time in many cultures and populations with proven benefits."

Other plants being investigated in the Saxena lab include St. John's wort (also known as "nature's Prozac" for its contents' reported effect on depression) and ginseng, which is reported to have anti-diabetic and anti-cancer properties.

This research receives funding from the Natural Sciences and Engineering Research Council, the Ontario Research Fund and the Gosling Foundation.

| Photo by Joey Sabljic

Sexuality is a wei issue, researcher

BY JOEY SABLJIC

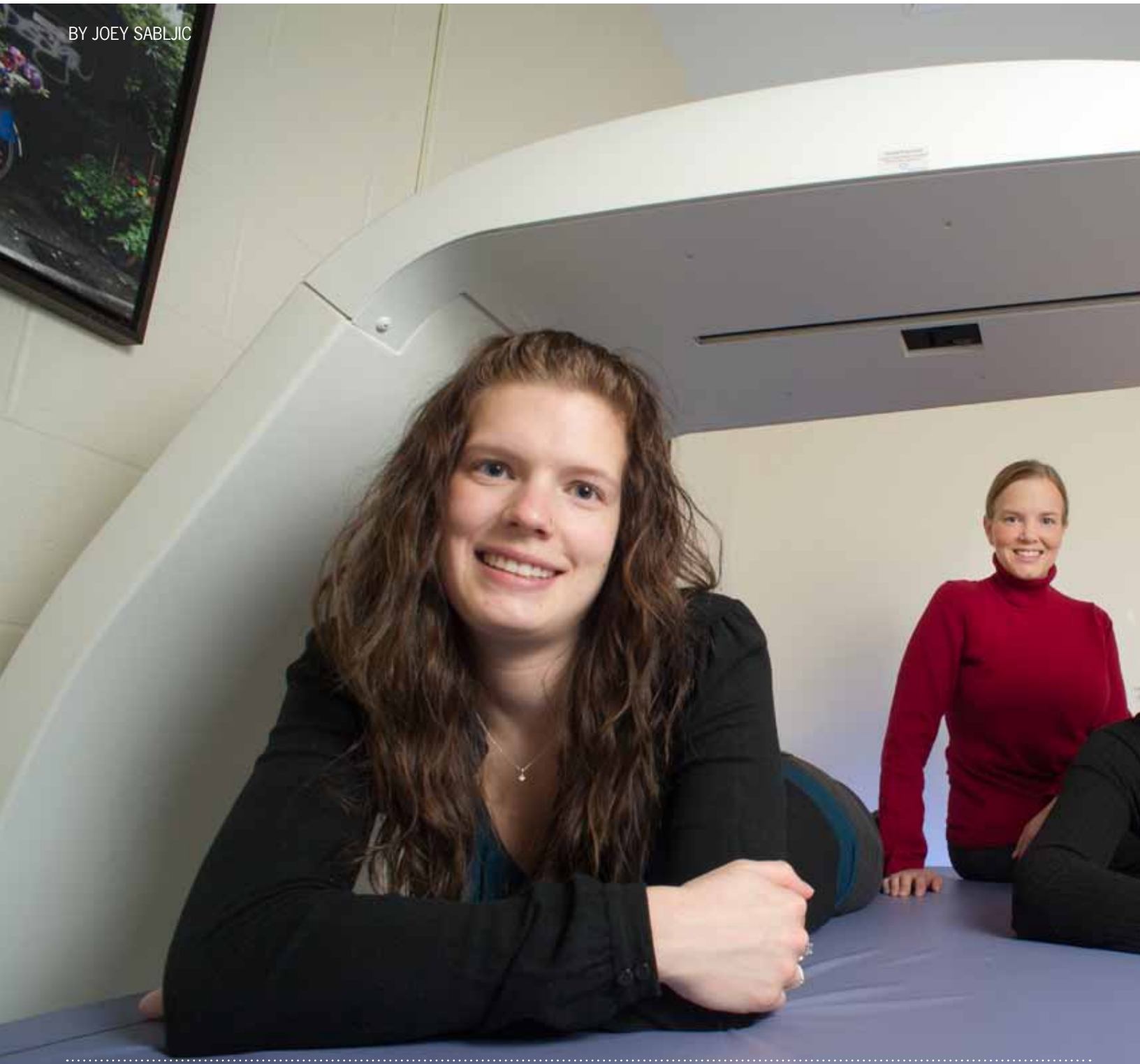


Photo by Martin Schwalbe |

ghty s say

Profs. Andrea Buchholz (right) and Robin Milhausen, and graduate student Emily Opperman (left), collected measurements such as participants' total body fat in the university's Body Composition and Metabolism Lab.

When it comes to sex, two Guelph researchers say size matters – but not in the way you might think.

Their study, *Sex, Health and YOU!*, has already received an outpouring of interest at the national level, ranking third out of more than 70 Research Development Initiative proposals submitted to the Social Sciences and Humanities Research Council. In this unprecedented and groundbreaking work, a dietitian and a sexuality researcher join forces to answer questions about the connection between body physique and sexuality.

Led by Prof. Andrea Buchholz, a registered dietitian and expert in body composition, and Prof. Robin Milhausen, a sexuality researcher, both from the Department of Family Relations and Applied Nutrition, the study's early results show that men and women with higher weights and body fat tend to have a poorer perception of their own bodies. They also experience lower sexual functioning and satisfaction.

The researchers recruited and surveyed close to 200 men and women between the ages of 18 and 25 involved in romantic, heterosexual relationships. First, they categorized participants by their body mass index (BMI) as healthy weight, overweight or obese. Then, they measured the participants' total body fat at the Body Composition and Metabolism Laboratory on campus, using a dual energy X-ray absorptiometer, or DXA, machine.

"Our goal was to have as wide a representation of as many different body types as possible," says Buchholz. "So we recruited people who fell into the normal weight range, as well as those who were overweight or obese."

Participants reported on many aspects of their lives, such as their health and sexual behaviours and their feelings about their bodies. They also responded to questions regarding their current romantic relationships.

Buchholz and Milhausen are using this information to assess the associations between body composition, body image, relationship quality and sexual well-being. Milhausen says sexual functioning and satisfaction are highly connected with how people view their own bodies, regardless of how much they actually weigh.

Another major piece of the weight-sex puzzle, say the researchers, is how a person's romantic relationship can affect their body image and sexual functioning. To get a sense of relationship quality, they asked participants to rate factors such as satisfaction, openness, communication, intimacy and acceptance within their own relationships.

The researchers hypothesized that people who are involved in the most supportive relationships may not be as impacted by sexual problems related to body composition or body image. Analyses to test these hypotheses are under way. However, their preliminary data suggest that higher weights lead to greater sexual dissatisfaction in women. The same can also be said for men with higher BMIs and trunk (abdominal) fat.

The researchers also found that women who had negative thoughts about their appearance – particularly during intimate, sexual moments – experienced poorer sexual functioning despite their relationship satisfaction, relationship length and their actual amount of body fat.

These results show that the consequences of greater body weight extend far beyond chronic disease risks such as Type 2 diabetes or cardiovascular disease. Rather, clinicians need to seriously consider patients' thoughts about their bodies when treating sexual problems for men and women of all body sizes.

"What we're finding so far is that everything is extremely interconnected," says Milhausen. "How you feel about yourself can impact your life and relationships in many ways."

In the future, the researchers hope to branch out their study to explore whether and how ethnicity, sexual orientation, menopausal status, aging and chronic diseases may influence the relationship between body composition and sexual functioning. They believe their study will give them and other professionals the ability to tackle both the psychological and physical problems behind sexual dysfunction.

"We can intervene to help people get more fit and reduce body fat, which might improve their sexual satisfaction," says Milhausen. "But we can also try to help them feel better about themselves and we might see gains in their sexual functioning and satisfaction even if they haven't changed a thing about their body weight."

Masters students Emily Opperman and Lindsay Benson are also involved in this research.

This study receives funding from the Social Sciences and Humanities Research Council.

Similar soy, better taste

That distinctive beaniness could be a thing of soy's past

BY JOHNNY ROBERTS

Soy milk is produced by combining a stable concoction of soybean oil, protein and water. However, the product sometimes carries a taste that many consumers don't enjoy – even when it's masked with chocolate or vanilla flavouring. A University of Guelph researcher is devising a way to reduce the "beany" aftertaste that consumers often detect in soy milk.

Plant scientist Prof. Peter Pauls, Plant Agriculture, says the taste occurs when the lipoxygenase enzymes normally found in soybeans act on high levels of linolenic acid that are also present in normal soybeans used for soy milk production.

To counter the effect, he and his research team have developed a soybean variety that has almost 75 per cent less linolenic acid, and none of the lipoxygenases that are responsible for the oxidization reactions.

The team is further identifying which varieties possess the non-beany taste trait when crossed with popular high-yielding soybean varieties. They believe this will have commercial applications for the agri-food industry.

"We have identified which genes in this variety give you the low linolenic acid and lipoxygenase null traits," says Pauls. "We have also developed genetic markers that can be used by soybean breeders to select new varieties with low linolenic acid levels and no lipoxygenase activities."

Pauls is working with Prof. Istvan Rajcan, a colleague in the plant agriculture department, as well as Agriculture and Agri-Food Canada research scientist Vaino Poysa. The work was conducted by research associate Yarmilla Reinprecht and graduate student Shunyan Luk-Labbey. The late Gary Ablett was also central to this research.

Improving soybeans' taste could increase their consumption, says Prof. Peter Pauls.

Research funding was provided by the Ontario Soybean Growers and the Hannam Soybean Utilization Fund.

Healthier starches for everyday diets

BY JOEY SABLJIC

The way to a healthier population is through its stomach. And for many, that journey starts with starch, an essential carbohydrate that comprises about 75 per cent of peoples' daily calorific food intake.

It's also the reason why Profs. Michael Emes and Ian Tetlow, Molecular and Cellular Biology, are looking at how to manipulate and modify plant genes and enzymes to produce healthier starches that can be incorporated into people's everyday diets, through foods such as baked goods.

These healthier starches are called resistant starches. Unlike regular starches, resistant starches aren't broken down in the small intestine – they "resist" the digestion process. That means their sugars aren't absorbed as rapidly into the body.

As a result, they help to reduce the risk of Type 2 diabetes (because less sugar is released into the bloodstream) and they act as a dietary fibre source, which prevents colon cancer.

"We're trying to change starches in ways that are much more useful," says Emes.

This research is funded through the Ontario Ministry of Agriculture, Food and Rural Affairs- University of Guelph Partnership.

So-called "resistant" starches could be used in staple food items, such as bread, or even in baked goods.

Photo by Nicole Yada (top), Bruce Sargent (bottom) |

Boosting nutrient uptake for cancer prevention

SPARK air video

Researchers aim to make anthocyanins more available to the body

BY JOEY SABLJIC

You can't get too much of a good thing, especially when it comes to anthocyanins (a type of polyphenol, an antioxidant). Anthocyanins fight cancer and give foods such as blueberries, strawberries, apples and sour cherries their vibrant colours. Anthocyanins can also be found in processed products, such as juices.

But getting them into your bloodstream is not easy.

It seems that no matter how much or how many antioxidant-rich foods people eat, less than one per cent of the active ingredient is actually absorbed into the blood plasma.

University of Guelph plant agriculture Prof. Gopi Paliyath, along with several other researchers, is trying to change that. Paliyath thinks the answer lies in finding ways to increase the body's uptake of these beneficial polyphenols.

"Getting more anthocyanins into the blood plasma is all about cancer prevention," says Paliyath. "And that's why we have to find a way to increase polyphenol uptake."

Paliyath and his team have found that anthocyanins generally appear in two forms within a fruit's cell structure: on their own as "free" molecules, and as a "bonded" molecule that's blended with carbohydrates or lipids.

At this stage in their research, Paliyath and his colleagues aren't sure which of these two forms allows for maximum anthocyanin absorption, and they are currently conducting studies to find out.

Paliyath and his team are working with living cells and circulatory systems in animal models to see how they metabolize anthocyanins and whether the free or bonded antioxidant molecules are more effectively absorbed.

Paliyath hopes this understanding could give the food industry the ability to create functionally enhanced foods that increase the bioavailability of antioxidants. In the long term, consumption of such foods as a part of normal diet could prevent tumour cell development as the cancer cells are preferentially killed in the presence of these compounds.

"We want to develop methods to enhance and design foods that allow for the most possible antioxidant uptake," he says.

Other research collaborators include Profs. Alan Sullivan and Jay Subramanian, Department of Plant Agriculture; Prof. Milena Corredig, Department of Food Science; and Prof. Ming Fan, Department of Animal and Poultry Science.

This study receives funding from the Ontario Ministry of Agriculture, Food and Rural Affairs.

(front to back) Research technician Renu Chandra, doctoral student Julieta Correa and Prof. Gopi Paliyath are investigating ways to increase humans' uptake of cancer-preventing polyphenols from fruits such as Ontario berries.

| Photo by Martin Schwalbe

Slow down the sodium

Through processed foods at restaurants and supermarkets, Canadians are eating more than twice their recommended daily salt allowance. This constant sodium overload brings the increased risk of hypertension, serious heart disease and stroke. However, Guelph researchers say that most people won't give up their favourite salty foods overnight.

Reduced-salt foods need to be able to satisfy people's craving for the same salty taste. And that's where food science Prof. Lisa Duizer, along with master's student Matt Rietberg and undergraduate student Derek Vella, are laying the groundwork. Together, they form part of a multi-disciplinary, multi-institutional research team led by Ryerson food scientist Dérick Rousseau, which is developing new approaches to reducing salt consumption.

One such approach is to use emulsions, for a more gradual, controlled salt release. In this way, consumers' taste buds will sense saltiness over a longer period and beat the urge to reach for the salt shaker for an extra shake.

But will this approach satisfy the public's salt cravings? That's what Duizer's sensory lab will find out by studying different salt tastes and concentrations.

"Everyone has a different relationship to salty tastes," says Duizer. "Some people can find a lot of saltiness appealing while others could find it repulsive."

According to Duizer, one type of emulsion doesn't fit all foods – an acceptable level of

How sweet it is

Guelph researcher developing vaccines that recognize sugar coating on intestinal bacteria

BY JOEY SABLJIC

Many intestinal pathogens have developed protective sugar coatings to avoid detection by our immune system. The chemical make-up of these shells must be determined in order for Prof. Mario Monteiro, pictured here, to develop effective vaccines against them.

Sugar-based vaccines for troublesome intestinal bacteria – which will someday make their way to doctors and consumers – are currently being developed and tested, as part of the latest work from a University of Guelph chemist, who specializes in what he calls "sugar chemistry."

Prof. Mario Monteiro is leading research efforts at Guelph to develop sugar-based vaccines for two common-yet-dangerous intestinal bugs, *Campylobacter jejuni* and *Clostridium difficile*. These bacteria infect millions of people worldwide each year, and treating them is a constant challenge.

"People have become very interested in vaccine research,

Photo by Joey Sabljic |

The Guelph Food Technology Centre's sensory lab allowed Prof. Lisa Duizer (left) to improve the emulsions' tastes and textures. Along with students Matt Rietberg (right) and undergraduate student Derek Vella, she ran sensory trials where panellists were located in individual booths to evaluate the emulsions.

Studying salt behaviour a first step to reducing intake

BY JOEY SABLJIC

saltiness for one product may not be acceptable for another. That's why the researchers are trying to determine the role salt plays and how it behaves as a structural component within a variety of different foods, such as soups, breads and cheeses. This way, team members in Rousseau's lab will be able re-engineer and tailor their emulsions as needed depending on their use.

Another major part of their work involves studying how salt interacts and is broken down by people's saliva and received by their taste buds. For this, the researchers are using a specially trained salt-tasting panel to determine the right combination between taste and viscosity so that the emulsions can deliver the most appealing and functional taste and texture.

Reducing salt doesn't just affect taste. Sodium plays an important role in many foods as a preservative or as a structural component that lends certain foods (such as bread) an appealing, edible texture. Duizer's future work will determine how the taste, texture and structure of various liquid and solid foods respond to altered salt content.

"It's not strictly a taste issue," says Duizer. "Salt is also a safety component, so we need to find that fine balance with the emulsions between function and acceptable tastes."

This research is funded by the Advanced Foods and Materials Network of Canada.

because antibiotics are expensive and overused," says Monteiro. "That's where we come in and play the prevention game."

In his most advanced vaccine, Monteiro and his United States-based collaborators are preparing for human clinical trials to test a vaccine they developed against *Campylobacter jejuni*, the bacterium responsible for traveller's diarrhea. Millions of travellers feel *Campylobacter's* wrath each year. However many more people are afflicted in underdeveloped nations, through contaminated food and water. In addition, both *Campylobacter jejuni* and *Clostridium difficile* bacteria affect animals as well.

Next in Monteiro's sights is the more dangerous *Clostridium difficile* – or *C. difficile.* Disease outbreaks involving this bacterium most often occur in hospitals and nursing homes, where patients with weakened immune systems are more susceptible to infection. It can cause significant diarrhea and severe colitis that can be fatal, especially among elderly patients.

Monteiro develops vaccines known as glycoconjugates, or a sugar joined to a protein. Both *Campylobacter* and *C. difficile* bugs have adapted genetically over time to create their own unique sugar-based protective shell, to try to avoid being detected and destroyed by the patient's immune system.

For these vaccines to be most effective, Monteiro must first crack the chemical makeup of each of these bugs' protective shells. Only once he's deciphered this crucial chemical formula is he able to design the vaccines.

Monteiro says that sugar-based vaccines only stimulate the patient's B memory cells – that is, cells which produce antibodies and act only as a short-term response against infection or threats to the body's immune system. So he and his team have coupled their sugar vaccines to a protein, which will also stimulate a patient's T-cells (they fight infection longer).

This approach offers long-lasting immunity over several years, which Monteiro says could change the way these intestinal infections are treated – especially for infants and the elderly, who would benefit from long-term immunity to these bacteria, without experiencing any negative side effects from vaccination.

Although human trials with the *Campylobacter* vaccine are approaching, it could take another 10 years before the vaccines make their way to consumers, due to the long and demanding regulatory approval process required for any new pharmaceutical product.

"It's a deeply involved process, but we're very excited about it," says Monteiro.

David Hobson of the University of Guelph Business Development Office says a multinational pharmaceutical company is now collaborating with Monteiro to bring the *C. difficile* vaccine to market.

Blue Dog beats bites

BY JOHNNY ROBERTS

Children constantly want to interact with their surroundings, including the family dog. Unfortunately, this can have disastrous results. A University of Guelph researcher believes that an interactive video game called *Blue Dog* may reduce the risk of injuries in the home by teaching children how to behave around their pets.

Prof. Barbara Morrongiello, Psychology, has teamed up with researchers in Belgium to develop and evaluate the *Blue Dog* software program. It's designed to help children understand a dog's behaviour, and recognize when it's friendly and wants to play or when it wants to be left alone.

According to Morrongiello, who is also the director of the University of Guelph's Child Development Research Unit, many dog bites occur in the home and often result from an interaction initiated by the child.

"Dog bites are considered a major issue because, when they do happen to children, they tend to be severe," she says. "Young children are similar in size to dogs, so when a dog bites, it often bites on the face or neck. Despite this, there is little out there in terms of effective educational tools to prevent dog bites."

To teach children how to behave around their dog, the video game provides the players with different scenarios, such as a dog eating, playing with its favourite toy or hiding under a table.

The child is then asked to choose how to respond to the dog's behaviour. If the child makes an unsafe decision, the video dog shows its teeth and growls, allowing the child to identify and understand that this was the wrong decision.

"We're trying to make the child aware of the dog's behaviour and, based on that, whether it's a good time to interact with the dog," said Morrongiello. "Children assume their own dog won't hurt them, but a dog is still an animal and it can behave unpredictably. They need to know how to 'read' their dog because a dog can communicate only through behaviour."

Children are also taught not to play with their dog's toys or to hold treats above their head because, depending on the dog's weight and size, their pet might jump at them, knocking them down.

"The video game is an effective tool because each child has to decide how to respond and, with repeated playing, we can see improvements in the child's understanding. Video games are also a great teaching tool because they are fun, familiar and highly appealing to children – making it all the easier for us to get children to learn about important safety information," she says.

Morrongiello says that if the *Blue Dog* game proves effective, it will be distributed on a national scale by Safe Kids Canada to children through daycares, schools and other community sources.

Funding was provided by the Canadian Institutes of Health Research.

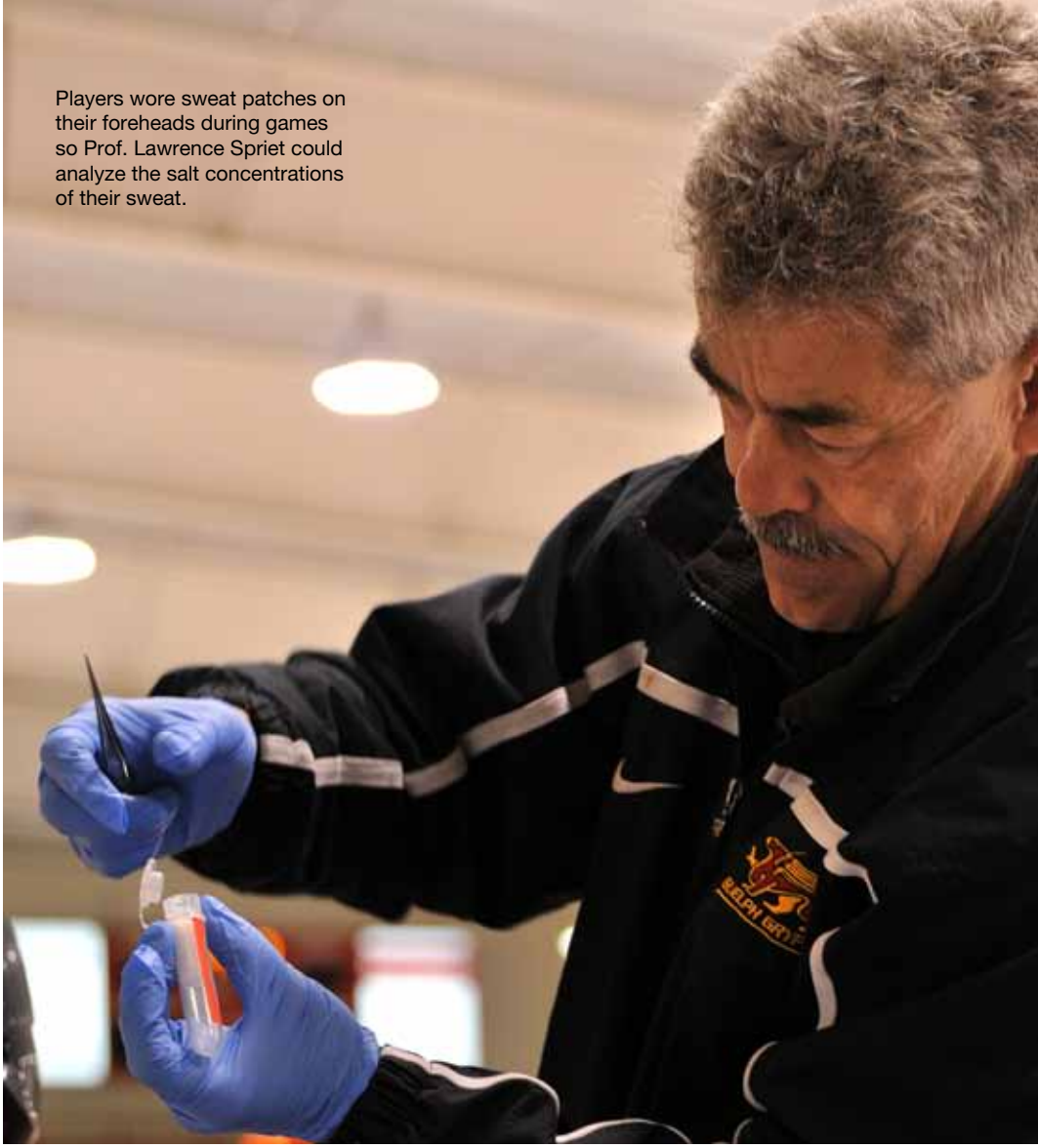
Photo by istock |

Top up your tank

SPARK air video

Prevent dehydration by all means, researcher advises athletes

BY CAROL MOORE



Players wore sweat patches on their foreheads during games so Prof. Lawrence Spriet could analyze the salt concentrations of their sweat.

Athletes such as hockey and basketball players can often push themselves so much that they sweat to the point of becoming fatigued, resulting in decreased performance in the late stages of a game.

Prof. Lawrence Spriet, Human Health and Nutritional Sciences, is researching the effects of mild dehydration on athletes playing sports involving decision-making, such as hockey, basketball and football. Spriet and his research team are measuring the difference in performance between a group of hockey players that are kept hydrated during scrimmage, and those who are not. He hopes he can use these results to show the importance of hydration during intense exercise.

"What we are trying to do is to educate the athletes that they need to prevent dehydration," says Spriet. "If an athlete loses two to three per cent body mass from sweating, they enter the danger zone, where peak performance becomes difficult to maintain. And anything from five to six per cent can be detrimental to their health."

Spriet and M.Sc. graduate student Mark Linseman tested 18 hockey players over a period of eight weeks. The participants were separated into two teams of nine: one team with fluids withheld during the scrimmage, and another that drank enough to maintain their body mass.

Spriet found the drinking group lost no body mass, while the non-drinking group lost an average of 1.8 per cent body mass, which is close to the danger zone.

The researchers also found that in the dehydrated group there were higher heart rates, higher core temperatures and their ratings of perceived exertion were worst.

During their scrimmages, the players were filmed to monitor their on-ice performance. Spriet and his team are now working to digitize the movements of each player. They expect to find that in the dehydrated group, the players covered less ice over time or covered the same amount more slowly.

Spriet had problems persuading some players that drinking a sport drink during the game would keep their performance at top level. With this research, he's generating the science behind the claims made by sport drink companies.

"I always ask the hockey players who among them would go on the ice with skates that aren't sharpened the way they like them, or a stick they don't like, or pants that are too baggy," says Spriet. "So why would they let themselves get dehydrated? Staying hydrated won't make you a better hockey player, but it will keep you at the best you can be."

Others involved in this project are PhD candidates Matt Palmer and Heather Logan, and undergraduate students Stephanie Dykes, Carla D'Angelo and Sandra McCubbin.

Funding for this project is provided by the Gatorade Sports Science Institute Canada and the Natural Sciences and Engineering Research Council.

| Photo by Gatorade Canada

Building a better brain

BY VANESSA PERKINS

Whether it's trying to lose some weight, kick a bad habit, improve memory for an exam or increase work efficiency, the key to success lies in our understanding of the brain, as well as how we develop and look after this precious organ. A University of Guelph neuroscientist is working with a variety of individuals – ranging from the highly successful to those struggling to get ahead – to investigate how the brain's attention, emotion and motivation systems contribute to healthy functioning, and how each of us can obtain what he has called a "Winner's Brain."

The underlying concept is that the specific ways in which we engage our brains can help to increase its performance in daily undertakings. In developing this concept, Prof. Mark Fenske, Psychology, has interviewed people from all over the world, including leading scientists and those he calls winners (who achieve extraordinary success in a particular aspect of life that they greatly value) to understand the neuroscience behind success.

Prof. Mark Fenske

While uncovering traits that can make an individual particularly successful, Fenske also recognizes the importance of finding ways to use this information to help those who struggle with challenges such as depression, substance dependence or compulsive gambling.

Fenske and his lab combine behavioural tests of cognitive abilities with functional Magnetic Resonance Imaging (fMRI) scans – a common tool in cognitive neuroscience that measures changes in neural activity through corresponding fluctuations in levels of blood oxygenation within regions of the brain – to understand which parts of the brain are important contributors to successful task performance, and how they can be used most efficiently.

"Despite common belief, the brain's capacity is *not* hardwired past adolescence," Fenske explains. "Our thoughts, emotions and experiences shape the way our brain operates, and it is possible to strategically engage ourselves in specific activities that can fine-tune our brains to function more effectively as we pursue our personal objectives in life."

In Fenske's book *The Winner's Brain: 8 Strategies Great Minds Use to Achieve Success*, written with Harvard cognitive-behavioural psychologist Jeff Brown, the drivers of London's famous black cabs provide real-life proof of this concept. These cab drivers spend around three years studying more than 25,000 streets, learning more than 400 routes and memorizing thousands of tourist stops, to achieve a mental map of the area.

As a result, not only are they faster than anyone else trying to get around London, but brain scans show that these individuals also have literally built themselves larger brain areas. Key regions within the hippocampus – an area of the brain associated with memory and spatial navigation – become thicker than those possessed by most people.

Other research has shown that the simple act of exercise can significantly improve an individual's mental capacity. Ongoing studies have shown that not only does exercise improve physical health, but the augmented flow of oxygen and glucose to the brain during exercise, as well as the release of brain-cell growth factors, can result in increased focus, improved memory and learning, lower stress levels, and an

increase in the volume of important structures in the brain, such as the hippocampus.

In fact, exercise has been shown to be one of the few activities that can actually promote new neuron growth in this critical region.

Fenske says these findings show that concrete changes in the brain can be made through conscious effort, and he believes it bestows optimism on anyone hoping to make positive changes in important aspects of their lives. For example, it takes the average smoker eight tries to quit, but each time they make an attempt leads to changes within the brain and a corresponding increase in the likelihood that the individual will subsequently be able to resist cravings for a cigarette.

Fenske's research examines other ways in which developing specific cognitive abilities can help with such acts of self-regulation. Such work has shown that simply ignoring something can help to reduce its ability to control behaviour. Developing better attentional control may therefore be vital in resisting the temptation of certain maladaptive actions.

"A plate of Oreos is assigned great value when placed in front of someone who is trying to diet," Fenske explains. "The brain gives more attention to things that are valued and that elicit an emotional response. If you can help the individual guide their attention elsewhere, then the Oreos become less salient and less likely to interfere with the long-term goals of the dieter."

A related focus in the work of Fenske's team of researchers is to understand how such attention, emotion, and motivation-related functions are affected in those who struggle with problem gambling or substance abuse and how to address the impairments faced by these individuals.

The next step is developing more useful interventions to reduce temptation, and reduce how rewarding the stimuli associated with these maladaptive habits can be.

"We spend thousands of dollars on research, and are learning a tremendous amount about how the human brain functions. But a rewarding and critical step is getting the results of the work we do out to the public," says Fenske. "We're learning how to build a better brain, neuron by neuron, and hope to help people improve their lives through what we are learning."

This research was done in collaboration with York University, University of Waterloo, Massachusetts General Hospital, Bangor University, Yale University and Harvard University.

Funding for this research was provided by Natural Sciences and Engineering Research Council, the Canada Foundation for Innovation, the Ontario Problem Gambling Research Centre and the Wales Institute of Cognitive Neuroscience.

These magnetic resonance images reveal the structure of Prof. Mark Fenske's brain

Selective hearing aids offer focused listening

BY CAROL MOORE

A big problem with hearing aids is that they pick up *everything.* They're not selective in the sounds they amplify, which can make background noise just as prominent as whatever the listener is trying to focus on.

It's a problem that's increasingly pertinent. More than a million Canadians have hearing problems, and more than 30 per cent are over the age of 65. With an aging population – and with the iPod generation, whose members risk harming themselves by playing personal listening devices too loud – that number is increasing.

Against that backdrop, a University of Guelph researcher is looking at how to improve hearing aid technology by making it more adaptive to the way the human brain works.

Prof. Robert Dony in the School of Engineering is combining computer chip technology and computational intelligence to improve how hearing aids adapt to different environments, such as a restaurant, office or car.

Advanced hearing aids may soon have an environmental classification mechanism that can automatically change the incoming sounds, depending on the environment.

"One of the classic problems with hearing aids is that they amplify everything – not just the speech but also the background noise," says Dony. "So we need to figure out a way to get rid of some of that noise, improve the amplification of speech and keep people from turning off their hearing aids."

Dony is using neural networks architecture in pursuit of his goal. Neural networks mimic the brain's auditory processing networks. They analyze the incoming analog sounds (as does the temporal lobe in the cerebral cortex of the brain), assess these sounds for environmental factors, digitize the noise and then process it into sounds with improved quality.

The neural networks will automatically adjust the sound parameters based on the environment, so that the individual doesn't need to switch back and forth between settings. The hearing aid user will be able to enjoy a conversation at a restaurant without having all of the extra background noise amplified.

"This process will make hearing aids a lot more useful and adaptive to what our brain is doing in terms of neural networks," says Dony.

Other collaborators involved with this project include Prof. Shawki Areibi of the University of Guelph School of Engineering and ON Semiconductor.

Funding for this project is provided by a Natural Sciences and Engineering Research Council Collaborative Research and Development Grant and ON Semiconductor.

Photo by iStock |

Robots help stroke victims recover

SPARK air video

Guelph is home to automated technology that enhances physiotherapy

BY NICOLE YADA

A robotics system designed to help rebuild strength in post-stroke patients is being developed at the University of Guelph.

Robots that simulate physiotherapist-guided exercises have been created by Prof. Hussein Abdullah, director of the School of Engineering. These robots are designed to work with physiotherapists and aim to improve upper limb range of motion in patients.

"Given the biological and life sciences focus at Guelph, I want to use our robots to make a difference to peoples' lives," says Abdullah. "This differentiates us from other universities who mainly use robots for industrial purposes."

Abdullah began his work on robots for therapeutic uses in 2001 and, starting in late 2007, conducted clinical trials with 19 patients over two years at the Chedoke Stroke Rehabilitation Unit at Hamilton Health Sciences . The patients had undergone a stroke assessment using the Chedoke McMaster Stroke Assessment (CMSA) and scored between stages 1 and 3 (a healthy patient scores a seven). The patients were in the early stages of recovery, having suffered strokes only two weeks prior to being part of the robotics trials.

The clinical trial compared a physiotherapist's conventional treatment with therapy using the robot exclusively.

The results showed that patients who received only the robotic treatment for their arm did as well as those receiving conventional treatment.

The robots mimic daily activities such as picking up items. They begin the treatment process with two stages. The first is the passive stage where the robots performs all movements for the patients, guiding their limbs.

In the second "active assisted" stage, the robots assists patients only if they detect no movement.

With continued treatment, patients increase their level of independence and the robots rebuild the patients' strength by applying resistance to build muscle. The robots can be programmed to a physiotherapist's specifications to individualize the treatment.

Throughout the various stages, the robots record data on the patients' movement, which can then be analyzed by the physiotherapist to monitor progress.

Ultimately, Abdullah hopes stroke patients will be able to use the robots at home so they can work on their own schedule between physiotherapy appointments to speed up the recovery process. His intent is to enhance physiotherapists' work, to ease their workload and the physical strain that can be caused by their job.

Abdullah performed his clinical trial with Hamilton Health Sciences physiotherapists Susan Barreca and Cynthia Lambert and research assistant Cole Tarry. He is seeking funding for larger clinical trials, which would allow the robots to be marketed for therapeutic use. The robots are currently approved by Health Canada to be sold for research purposes only. R

Stroke patients using Prof. Hussein Abdullah's robotic arm system recovered just as well as patients receiving conventional physiotherapy.

| Photo by Grant Martin

Bacteria can't beat Roboguts

BY CAROL MOORE

People with Inflammatory Bowel Disease may have different gut bacterial communities than healthy people. The simulated human intestinal tract allows Prof. Emma Allen-Vercoe to grow and profile these various bacterial colonies.

One in every 160 Canadians suffers from Inflammatory Bowel Disease (IBD), a chronic, debilitating disease that affects the digestive system and causes symptoms including inflammation, abdominal pain, cramping and fatigue. Canada also has among the highest incidence of IBD in the world, costing the economy approximately $1.8 billion annually.

Now, a simulated human intestinal tract called Roboguts has been developed by University of Guelph researchers to mimic gut conditions in people who suffer from IBD. The researchers' goal is to profile gut bacterial communities and better understand the relationship between gut bacteria and IBD.

The research team, led by Prof. Emma Allen-Vercoe, Department of Molecular and Cellular Biology, is comparing distal (lower gut) bacterial profiles from healthy donors to those from patients suffering from IBD. She's using the Roboguts to grow the bacterial communities found in fecal samples in an anaerobic environment, and then profiling the stability of these bacterial communities.

Allen-Vercoe has found patients suffering from IBD have reduced diversity in their colon bacteria. She reasons that the decline in bacterial diversity impairs the patient's ability to combat different types of stress, whether it's physical or mental.

"Healthy guts have a very diverse colon microflora population and that can absorb a lot of stress," says Allen-Vercoe. "But IBD patients have reduced diversity and can't absorb the stress, which leads to all sorts of health problems."

The researchers are using the Roboguts to monitor what happens when stress is added to the system, and then comparing the stress response in IBD and healthy patients.

The specific stress response currently being examined is to norepinephrine, an acute stress hormone that affects the attention and responding actions in the brain and the flight-or-fight response. Norepinephrine is known to cause changes in gene regulation in some pathogens, such as *E.coli* O157:H7.

Photo by Martin Schwalbe |

So far, Allen-Vercoe has observed that the gut bacterial profiles from healthy people respond to norepinephrine, and she is currently testing whether the changes seen are greater in bacterial communities from patients with IBD compared to healthy people. She believes that the lack of diversity of gut bacteria in IBD patients would skew the gut micro-ecology, and contribute to an imbalance within the gut that then predisposes an individual to a flare-up of their disease.

She wants to find out the mechanism behind the imbalance.

"We know that IBD is the smoking gun and stress is the trigger," says Allen-Vercoe. "Now, we need to figure out what the bullet is."

Once the mechanism is found behind the imbalance, Allen-Vercoe wants to be able to research how therapeutic treatment with a pre- or probiotic might help to restore the gut bacteria population to normal. She hopes this will prevent or reduce relapses in IBD patients, increasing the quality of life for individuals affected with IBD.

The research is applicable not only to IBD, but also to other diseases that are increasingly being connected to disturbances in the ecology of the gut microflora, including obesity, *Clostridium difficile*-associated disease, irritable bowel syndrome, and regressive autism.

Collaborators on these research efforts include Dr. Sydney Finegold, University of California at Los Angeles; Dr. Derrick MacFabe, University of Western Ontario; Dr. Elaine Petrof, Queen's University; and Dr. Cezar Khursigara, University of Guelph.

Funding for this project is provided by the Crohn's and Colitis Foundation of Canada, Canada Foundation for Innovation, the National Institutes of Health, the Ontario Ministry of Agriculture, Food and Rural Affairs, the Canadian Institutes of Health Research and the Ontario Ministry of Innovation.

Horses go green

BY JACKIE BELLAMY

Horse owners are playing their part in contributing to a healthy environment. As the number of horse owners increase, so does the need for stewardship of the equine environment. Equine Guelph has responded to this need with new and innovative initiatives.

The *Stewardship of the Equine Environment* course, winner of Horse Journals' Green Horse Award (featured in the Equine Consumers' Guide 2010), promotes awareness and strategies for landowners to develop plans benefiting the health of horses while protecting land and water resources.

This course was born from a need identified by Equine Guelph's Healthy Lands for Healthy Horses program committee. The program offers popular weekend workshops, teaching landowners to make environmentally friendly improvements on horse farms.

Equine Guelph believed that even greater knowledge and awareness could be developed through the creation of the *Stewardship of the Equine Environment* course, which includes an action plan for reducing the environmental hoofprint by protecting wells from contamination, properly managing nutrient waste, reducing energy use, and preserving habitats, wildlife and plant life.

Active participation is an important part of the course to create healthy lands for horses and their human counterparts.

Says Prof. Stew Hilts, program advisor: "Thousands of landowners have now participated in stewardship programs across Canada, learning the best way to care for their own land, or contributing to stewardship of public land and waters. Horse owners and their horses can benefit directly by taking this course to learn about stewardship practices that enhance equine operations."

Storytelling links climate change and health

Students at the Northern Lights Academy in Rigolet, Nunatsiavut participate in a digital media workshop.

Researchers, Inuit community collaborate on digital storytelling project

BY NATALIE OSBORNE

For centuries, Inuit knowledge, culture and history have been passed down from one generation to the next through storytelling. Now, researchers are using digital media to document stories that are first-hand accounts of how climate change is affecting the lives and health of Inuit people in Canada.

This unique project, led by the Rigolet Inuit Community Government in Nunatsiavut, Labrador, with support from University of Guelph researchers, is the first of its kind and is funded by Health Canada's First Nations and Inuit Health Branch.

Dr. Victoria Edge, a senior epidemiologist with the Public Health Agency of Canada and an adjunct professor with Guelph's Department of Population Medicine, and PhD candidates Sherilee Harper, Population Medicine, and Ashlee Cunsolo Willox, Rural Studies, have partnered with Rigolet community leaders, including town manager Sarah Blake and AngajukKâk (mayor) Charlotte Wolfrey. Through the process of digital storytelling, community members are given the opportunity to create their own three- to five-minute first-person narratives, highlighting the impacts of climate change on the physical, mental, emotional and spiritual health and well-being of community members.

"The digital stories are much better than a series of numbers that don't have a context – they really give a better understanding of what health means to Inuit people," says Edge.

Since November 2009, more than 20 adults and youth have participated in week-long digital storytelling workshops, creating 25 digital stories. These workshops are led by Rigolet community members, who received training in this technique from the Centre

Community members Dina Wolfrey (left) and Tanya Pottle were trained to promote participation and co-ordinate workshops, in addition to creating their own digital stories.

for Digital Storytelling. In addition, Rigolet has also created the 'My Word': Storytelling and Digital Media Lab, the first Northern centre dedicated to using community-based digital media to promote Inuit culture, oral wisdom and stories. These stories can be screened in community centres and shared online (view stories at www.rigolet.ca).

Researchers will also collect information using more traditional qualitative methods, such as interviews, focus groups and questionnaires. But the digital stories serve as the initial data collection, and provide important aural and visual narratives about life in the North.

"Video allows community members to tell their stories free from outside intervention, unlike an interview where questions can frame the discussion or introduce researcher bias," says Cunsolo Willox. "The voices and faces you see are Inuit people, not southern researchers." Adds Harper: "It's an emerging process, not an extracting process. So you're not extracting information from people but allowing it to emerge naturally from what they consider to be important. It's a very different way to initiate the collection of health data, and it should give us a much richer picture of what health means to the community."

The project hires and trains community members, including Tanya Pottle, Dina Wolfrey, Ashley Flowers, Marilyn Baikie, Inez Shiwak and Joelene Pardy, to co-ordinate the workshops and facilitate communication and participation in the project. All community workers also created their own stories and participated in the study.

For example, Pottle's story, titled *Will we even exist?* talks about how climate change affects the ice and snow that she and her community members rely on for transportation and hunting. Delayed and insufficient ice formation prevents access to caribou, their main source of healthy, fresh food in the winter. Baikie's story discusses the ways in which changes in the weather and on the land are affecting Inuit culture, traditional activities, and food harvesting, and she wonders what these changes will mean for her children.

"The land is our healer," says Rigolet AngajukKâk (mayor) Wolfrey. "We rely on the ice to go out on the land, but with the changing climate, we can no longer trust our traditional knowledge of which ice paths are safe to travel."

Normally, Rigolet residents can go out on the ice from December to May. But last year, they were only able to spend two months on the ice. Community members used the My Word lab digital stories to record this unusual winter, which Wolfrey believes will be useful for comparing to future seasons.

She also believes the stories could be used to preserve Inuit heritage, culture and language, and would be a good learning tool for use in northern schools. This summer, the Rigolet My Word team organized an elder and youth storytelling and culture-sharing summer camp, which brought together youth and elders from all the Inuit communities of Nunatsiavut (Nain, Hopedale, Postville and Makkovik) for a week of storytelling, hunting, fishing, culture-sharing and climate change discussions.

The community of Rigolet is continuing to run digital storytelling workshops, and through the My Word lab can travel to other communities to run workshops, and look forward to collaborating with researchers and policy-makers interested in using digital storytelling to gather community-based narratives.

"The ultimate goal is for Rigolet to become the leader in the North for digital storytelling," says Wolfrey. "We can use the talent and capabilities we have locally to spread the word and show other communities how to start these projects."

The Rigolet stories have been screened at community gatherings and story nights, as well as posted to the Rigolet town website (www.rigolet.ca), YouTube (www.youtube.com/UKausitga), Facebook ('My Word': Storytelling and Digital Media Lab), and burned to a DVD given free to all community members in Rigolet.

Funding for the project was provided by Health Canada's Climate Change and Health Adaptation in Northern First Nations and Inuit Communities Program and the Nasivvik Centre for Inuit Health and Changing Environments. R

| Photos by My Word: Storytelling and Digital Media Lab

Helping teens avoid depression and self-injury

BY VANESSA PERKINS

Years of research on mental health are being co-ordinated by two University of Guelph researchers to collectively understand the risk factors associated with depression and non-suicidal self-injury (NSSI).

Psychology Profs. Margaret Lumley and Stephen Lewis want to generate intervention strategies aimed at helping to prevent mood problems and NSSI in at-risk youth. They're constructing an engaging online program for people affected by these mental health issues or interested in improving their emotional well-being.

Over the past 15 years, NSSI has become recognized as a significant issue in young people. It occurs when someone hurts their own body, resulting in body tissue damage without the intent to end his or her life.

The most common form of NSSI is cutting the skin.

Rates of NSSI consistently range from 14 to 24 per cent in teens and university students. The behaviour is often associated with mental health difficulties.

Lewis has found many young people who self-injure would prefer to obtain help for NSSI on the Internet, rather than from somewhere else.

"Teens use the Internet more than any other age group, which makes online intervention programs not only innovative, but relevant," he says.

For her part, Lumley has been studying how to more effectively identify people experiencing depression in its early stages during the transition to adolescence. She estimates about one-fifth of adolescents experience an episode of major depression prior to adulthood. And those who experience depression as youth are more vulnerable to experience a more serious course of the illness in their lifetime, underlining the need for creating better coping mechanisms for teens.

Prof. Margaret Lumley

To help illuminate what leads to depression and NSSI, the researchers are employing unique lab-based computer tasks that indirectly assess people's responses to stimuli related to depression and NSSI.

Furthermore, they're finding core beliefs are more important in predicting depression than previously believed.

"So much research has focused on the associations between negative beliefs, depression and thoughts of suicide," says Lumley. "Our research also focuses on positive self-views and how these relate to mental illness and emotional resilience."

New evaluation and intervention methods are particularly important because many of those who self-injure do not seek professional help, and some never tell anyone about it. Lumley and Lewis see the enormous potential that the Internet can provide as a research tool for understanding troubled youth who do not seek professional help.

And that potential is driving their efforts towards interactive website development.

"The Internet is available in the daily lives of most teens. They can access the Internet from home, school, and at any time on their cell phones," says Lewis. "At the same time, the nature of content accessed is not always accurate and in some cases, it may be harmful."

Lewis and other researchers have found a particularly troubling increase in self-injury-related themes in the media. Over the past five years, there's been a significant increase in the number of message boards, websites and videos about NSSI posted on the Internet. Many of these do not have overt statements against NSSI, and researchers have suggested that this material – which is often portrayed in an artistic manner – may trigger the behaviour in those who access it. ("Triggering" is a new phenomenon, whereby viewing or reading NSSI content may increase thoughts and urges to self-injure, and perhaps self-injury itself).

To better understand NSSI, Lewis is examining it on the Internet. He's also involved in research examining cognitions among those who self-injure – how they cope with stress, why they self-injure, and what their family experiences have been (an

Prof. Stephen Lewis (right) and grad students Shaina Rosenrot (left) and Jill St. Denis are developing an online intervention program for at-risk teens.

important factor involved in self-injury is difficulty coping with negative emotions.)

In an effort to help youth build their emotional resilience, Lumley and Lewis are developing an online program to explain research-supported techniques on how to cope more positively with stress. Included are tasks that help individuals recognize their moods, challenge their regular thinking mechanisms and build on positive thought processes.

The program, which is currently in development, will be personalized for each user. Visitors will be able to write in a diary and provide themselves with reminders to use the online material.

"We will be able to track their usage and interview certain individuals to gain an even deeper understanding of their behaviour," says Lumley. "We're confident the website will be a step in the right direction towards reaching out to those who are in need."

Funding for this research was provided in part by the Ontario Mental Health Foundation New Investigator Fellowship.

Collaborators include Drs. Heidi Bailey, David Dozois, Karl Hennig, Nancy Heath, E. David Klonsky and Karen Rodham, and graduate students Lindsey Keyfitz, Ashley Marsh, Alexis Arbuthnott, Michele Davis, Shaina Rosenrot and Jill St Denis. R

| Photos by Natalie Osborne

Stress that helps you grow and learn

BY REBECCA HANNAM

SPARK air video

Feeling valued and supported by your employer can help turn negative workplace stress into a positive opportunity for growth, says Prof. Gloria Gonzales-Morales.

Workplace stress research has traditionally focused on the health challenges associated with job-related pressures. But according to University of Guelph researchers, experiencing stress at work isn't always negative.

Prof. M. Gloria Gonzalez-Morales, Department of Psychology, is leading research on the positive aspects of stress in the workplace. She is trying to determine what causes people to perceive stress positively, and what organizations can do to lessen negative stress on employees.

"Stressful tasks at work can hinder your health and emotional state," she says, "but they can also be perceived as challenges that can help you grow and learn in a positive way."

Stress sources are usually considered positive when workers feel dedicated to their job, and when the opportunity for personal growth is clear.

Past research has fingered physical and emotional exhaustion as outcomes of perceiving stress negatively. But more recent studies have determined that perceiving stress in a positive manner leads to workplace engagement.

With that in mind, Gonzales-Morales is now focused on determining what types of company resources and individual coping mechanisms motivate positive stress perception.

In the workplace, she's found that workers who feel valued and supported by their organization are more likely to see job pressures as positive challenges, rather than obstacles.

Preliminary results indicate that an effective strategy for companies to boost employee support involves supervisors communicating their support directly to individual employees. Genuinely listening to employee concerns and providing assistance with job-related tasks is a leading example of this support, she says.

"We are finding that employees are more engaged when they feel they are being treated as a person and not just another number within the company," says Gonzalez-Morales.

The effectiveness of an individual's coping mechanisms may also contribute to how stress is perceived. Previous research led by Gonzalez-Morales showed coping mechanisms are matched with gender in the workplace. That means some types of coping strategies are more effective for men than women, and vice versa.

For example, direct action coping – that is, dealing directly with the source of pressure through planning and management – is most beneficial for men. On the other hand, looking to other people for instrumental and emotional support, an approach called social support seeking, is more beneficial to women.

The stress perception study was conducted by questioning social service workers and their supervisors about workplace experiences. This method allowed researchers to analyze overall perceptions of job-related stress, and to examine how direct relationships between supervisors and employees relate to the perception of stress and to their experiences of work engagement and exhaustion.

This research is funded by Valencian Community Government, Conselleria d'Empresa, Universitat i Ciència, Spain; U.S. Army Research Institute for the Social and Behavioral Sciences; Foundation for Science and Technology; and the Ministry of Science, Technology and Education, Portugal.

Photo by Nicole Yada |

This "anti-cancer" agent is no wonder drug

BY CAROL MOORE

A popular agent thought to have cancer-fighting abilities may not be as effective as its advocates suggest.

Dicholoro acetate (DCA) is widely publicized as being a safe anti-cancer reagent, which has led to its unofficial use by cancer patients, often without their physician's knowledge.

Some studies show DCA has an ability to reduce the growth of experimental tumours and possibly some types of human cancer as well.

But researchers at the University of Guelph have discovered an unexpected twist involving DCA and the cancer cells it's supposed to be killing: it doesn't always work and could make things worse.

Prof. Brenda Coomber, Biomedical Sciences, and her research team found that not all cancer cells treated with DCA were killed. Rather, when the cells were exposed to low oxygen conditions in addition to DCA, the cancer cells were actually protected.

The researchers studied the tumour's ischemic regions – areas that are not well supplied with oxygen and nutrients due to abnormal blood flow – to see how the cells there reacted to different therapies. Then they compared the results to see which therapies were more effective at killing the cancer cells or keeping them alive.

"Anything that keeps the cancer cells in ischemic areas of tumours alive is not good and will contribute to tumour progression," says Coomber.

DCA is thought to selectively kill cancer cells because it forces them to use the mitochondrial pathway rather than the lactate pathway within the cell to metabolize glucose when there is oxygen present. This generates oxygen radicals that are toxic to cells.

Normally, cells will use the lactate pathway for glucose metabolism when they're oxygen deprived. Cancer cells act differently; they push glucose towards the lactate pathway within the cell even in the presence of oxygen, perhaps to avoid generating oxygen radicals that can cause cellular damage.

Coomber and her team originally thought that because the tumour's ischemic regions have fluctuating oxygen levels, they could treat the tumour with DCA and force the cancer cells there to use the mitochondrial pathway, generate oxygen radicals, and die.

But that was not the case. Human colon cancer cells grown in culture that were exposed to DCA had twice as much cell death than untreated cancer cells. But when the cells were treated with DCA in low oxygen, they survived better.

The research team then artificially grew tumours in animal models. They tested two colon cancer cell lines, with one showing no therapeutic benefit between DCA treated and untreated tumours, and the other demonstrating the same results as the culture studies. The DCA treated tumours grew larger because the DCA and low oxygen combination was protecting cancer cells rather than killing them.

Coomber and her team have yet to come up with a clear reason why some cells in ischemic regions are protected from DCA. But they believe it's associated with metabolic pathways combined with the ways that cancer cells can avoid things that trigger cell death.

The finding that some cancer cells respond so differently to DCA than others means such a compound may show variable usefulness, depending on the type of tumour.

"The bottom line is that there is no magic bullet to cure cancer, because every cancer has some unique features and if we don't take that into account we may make decisions about treatment that are not be the best for an individual," says Coomber. "There are people out there buying this drug off the Internet and taking it as a self treatment and who knows what's going on in their tumour; they could actually be making it worse."

Members of Coomber's research team were research associate Siranoush Shahrzad; master's student Kristen Lacombe; PhD student Una Adamic; and research technician Kanwal Minhas.

Funding for this project was provided by the Canadian Cancer Society's Research Institute and the Natural Sciences and Engineering Research Council.

This work has recently been published in the journal Cancer Letters. R

| Photo by Nicole Yada

Why drugs fail

SPARK air video

BY NICOLE YADA

Exciting advances are being made in understanding why cancers often fail to respond to chemotherapy drugs, a process known as multi-drug resistance.

Prof. Frances Sharom, a molecular and cellular biologist at the University of Guelph, is excited about a recent scientific paper describing the structure of P-glycoprotein (Pgp), which is responsible for pumping chemotherapy drugs out of tumours. In cancer research circles, this is considered a major advance.

"Now that we know what this protein molecule looks like, there's enough work on this project to keep us busy for another 20 years," says Sharom, whose research on Pgp is funded by the Canadian Cancer Society for the next three years.

Pgp has a flexible binding pocket that accommodates many different chemicals in varying orientations, and then uses cellular energy to pump them out of cells.

When it was initially presented in the 1970s by cancer research pioneer Dr. Victor Ling as a possible reason for chemotherapy ineffectiveness, the scientific community was highly skeptical. At that time, scientists only knew about transporter proteins bringing substances into cells, not kicking them out as Ling was suggesting.

But Sharom (who was a graduate student at the time) thought Ling could be onto a breakthrough and that maybe the scientific community needed to expand its beliefs about the capabilities of transporters. Years later, she went to work in his lab while on a sabbatical leave from the University of Guelph, and has been studying Pgp and its drug interactions ever since.

Here's the problem: Cancer patients are usually treated with several anti-cancer drugs at once, which compete for a spot in the Pgp pocket. Sharom is researching the different ways Pgp interacts with hundreds or thousands of chemical compounds, and how to work around this to achieve successful cancer treatment.

The implications of these proteins are not limited to cancer patients. The Food and Drug Administration now requires that all new drugs be tested to see if they are pumped by Pgp. This mandate came about due to the ongoing identification of dangerous drug interactions caused by combining various supplements such as St John's wort, or even grapefruit or pomegranate juice, with prescription drugs that are normally pumped out of the body by Pgp.

Natural chemicals found in some herbal supplements or fruit juice can compete with these medications, greatly altering their effectiveness, and endangering the patient.

"This research isn't only important for cancer patients but for anyone taking prescription drugs," says Sharom.

Currently, cancer researchers are trying to deal with the Pgp problem by blocking the protein pump with compounds called modulators that bind tightly to the pocket, preventing the chemotherapy drugs from being pumped out of the tumour.

However, because the purpose of Pgp in the body is to pump out toxins taken in from food and the environment, blocking this protein pump means that the body will retain not only the chemotherapy drugs, but also potentially damaging toxins as well.

Sharom is working on Pgp with research associates Joseph Chu and Peihua Lu, and graduate students David Ward and Adam Clay. R

Stopping t cells in the

BY NATALIE OSBORNE

By the time many women are diagnosed with breast cancer, tumour cells are already circulating throughout their bodies. Even when the primary tumour in the mammary tissue is removed, cancer cells may have spread to more life threatening regions, such as the lungs, bones and brain. Some of these cancer cells will re-grow to cause metastatic breast cancer, the form of the disease responsible for a patient's mortality. That's why University of Guelph researchers are using a unique cell culture system to discover how tumour cells move throughout the body and how they can survive to form a tumour in distant sites.

Biomedical sciences Prof. Alicia Viloria-Petit and graduate students Geordon Avery-Cooper and Divya Karsanji study metastasis, the process by which cancerous cells spread from the original tumour site to distant organs.

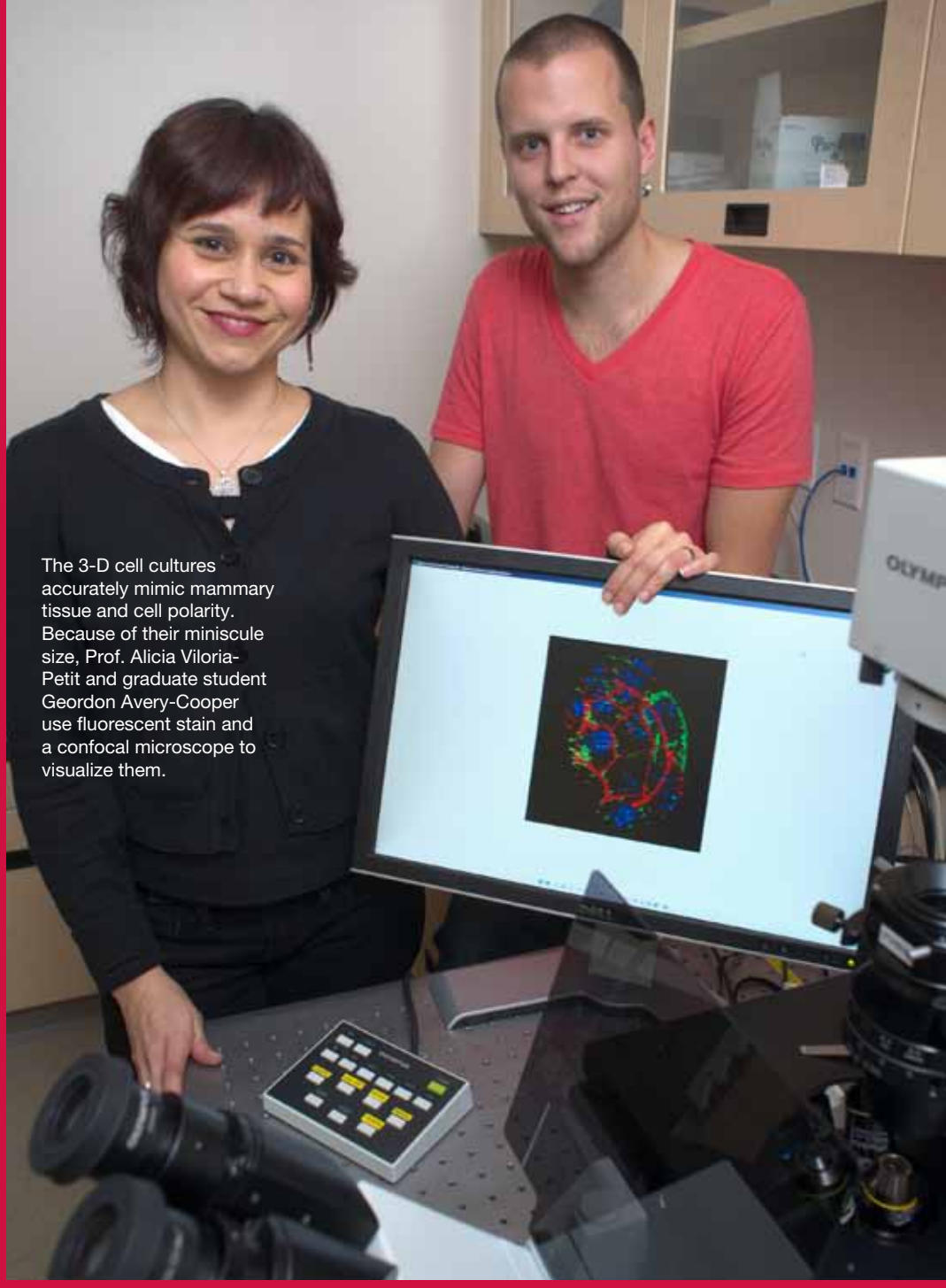
To metastasize, a cell must detach from its neighbours, survive a tumultuous journey through the bloodstream and establish itself in a foreign environment. Viloria-Petit is interested in the cellular signalling pathways that allow cells to accomplish and survive this dangerous voyage.

"If we can identify and understand these pathways in both normal and tumour cells, then we can eventually design ways to target and block them to reduce metastasis," says Viloria-Petit.

The researchers use three-dimensional cell cultures that mimic a minute part of the mammary gland: the acinus, the minimal milk-secreting unit. The tiny structures generated in this culture system are shaped like a cup, with a lumen in the centre, which resembles the milk duct of a normal mammary gland. In fact, if stimulated with the correct hormones, these cell cultures produce milk.

Photo by istock |

tumour
eir tracks



The 3-D cell cultures accurately mimic mammary tissue and cell polarity. Because of their miniscule size, Prof. Alicia Viloria-Petit and graduate student Geordon Avery-Cooper use fluorescent stain and a confocal microscope to visualize them.

Mammary cells, like epithelial cells in many other tissues, have a defined spatial orientation, with their bottom, lateral and top surfaces expressing different molecules and performing different functions. The three-dimensional cell cultures are able to accurately re-create this "cell polarity," so researchers can see the effects different cell signalling events have on this important cellular characteristic.

Here's the key: Loss of normal cell polarity is associated with tumour formation, invasiveness and metastastatic ability.

Polarity is partly defined by cellular connections, called junctions that are distributed in specific patterns along the cell's sides. These junctions help keep the cells anchored to one another. In order to metastasize, a cell must break these adhesive connections.

One of the mechanisms that allow cancer cells to break their connections with one another involves cellular responses to a protein known as transforming growth factor beta (TGFβ), which is present in the tumour microenvironment. TGFβ is essential for development and maintenance of various tissues. One of TGFβ's primary roles is to act as a "tumour suppressor," because in healthy cells it limits growth and initiates cell death when appropriate. However, when cancer causing genes are turned on, the beneficial actions of TGFβ are turned off, and it switches to promoting metastasis.

TGFβ modifies a cell junction protein called Par6, which leads to a series of chemical reactions referred to as the TGFβ-Par6 polarity pathway, initially discovered in Dr. Jeffrey Wrana's laboratory at Mount Sinai Hospital, Toronto. Activation of this pathway disrupts cell polarity, degrades cell junctions, and promotes the formation of cellular protrusions, which allows the cancer cell to detach from the tumour and facilitates its migration.

"We have evidence to suggest the TGFβ-Par6 polarity pathway is also affecting the cells' connection to their surroundings, -specifically the extracellular matrix," says Viloria-Petit. "It does this by changing the way the cell communicates with the extracellular environment, which is essential for the maintenance of polarity, and for cellular survival.

Changes in cell polarity help cancer cells to become invasive, and migrate. The researchers are examining how the pathway contributes to the invasive property of tumours by making molecular alterations to the three-dimensional cultures and observing how it affects their structure. When they blocked the TGFβ-Par6 polarity pathway in cell cultures of metastatic breast cancer cells, they reduced the cells' ability to form invasive protrusions and restored features of normal cell polarity.

Viloria-Petit and her lab will continue to investigate the pathway's role in cancer cells, including tumour cell survival in the bloodstream and in distant tissues.

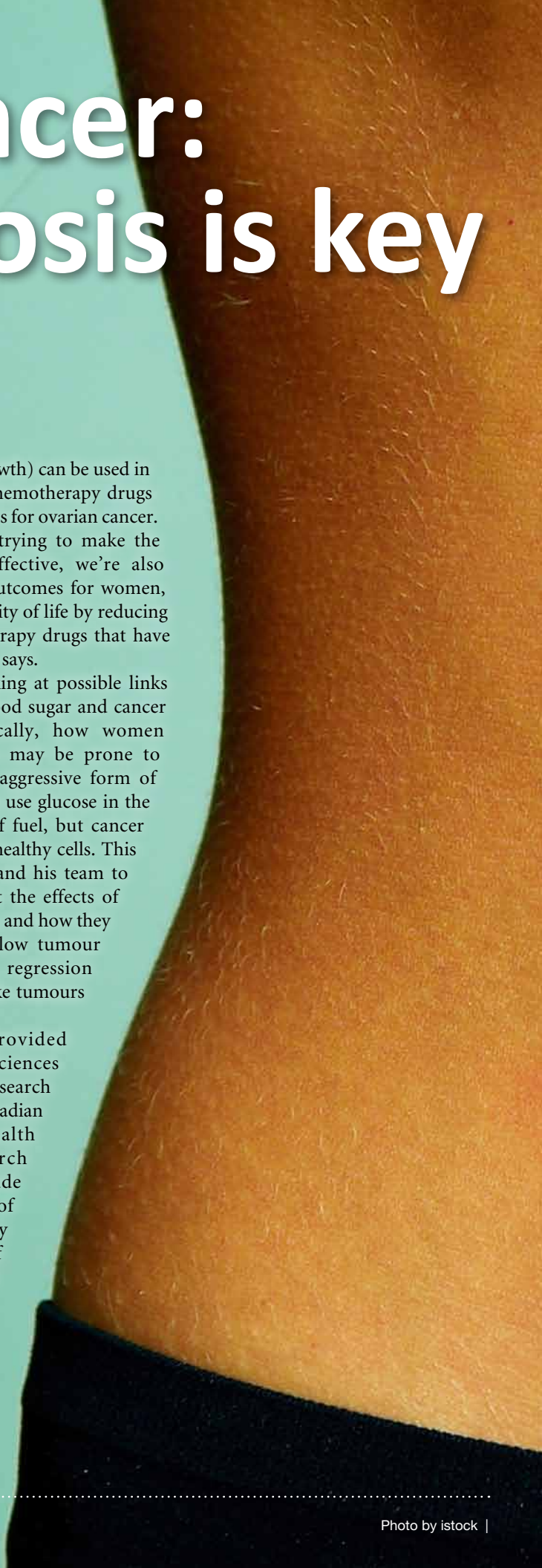
"The TGFβ-Par6 polarity pathway may also be important for later stages when the tumour has already spread and the cancer cells are growing in different organs," says Viloria-Petit. "If it is involved, then we can also take advantage of blocking it at this stage."

Funding for this research is provided by the Banting Research Foundation and the University of Guelph.

| Photo by Martin Schwalbe

Ovarian cancer: early diagnosis is key

BY JOHNNY ROBERTS



Every year, 2,300 Canadian women face ovarian cancer. Considering symptoms can be attributed to a number of diseases, this silent killer often goes undetected until it's too advanced, significantly limiting odds of survival. A University of Guelph researcher has discovered a protein expressed by ovarian cancer cells that may act as an identifying marker at the early onset of the disease.

Prof. Jim Petrik, Biomedical Sciences, and his team of researchers have discovered a way to detect early ovarian cancer in mice. The identified proteins contribute to new blood vessel formation and are expressed almost immediately after the cancer cells interact with the ovary. Petrik says it's the key component in developing a reliable early screening test, which could be as simple as a blood test. However, with current detection techniques, ovarian cancer is not detected until late stages and Petrik has been working on ways to treat the disease when it is established, by attempting to alter the blood vessels that feed the tumour.

Here's what happens. When tumours form, they have the ability to stimulate the growth of new blood vessels. However, when tumours grow blood vessels too rapidly, malformations occur. Thrombospondin is a naturally secreted protein and is partially responsible for killing abnormal blood vessels in the body. This process led to Petrik's interest in thrombospondin, and he has spent considerable time in characterizing its effect in normal physiologic processes and in cancer. Petrik's team has shown that thrombospondin can enhance delivery of chemotherapy drugs to the tumour, significantly enhancing their effectiveness and causing dramatic tumour regression.

Petrik says that the creation of an optimal combination therapy – one that combines the protein with other treatments to induce tumour regression – will signal when they're ready for human trials.

The research team is also investigating how anti-angiogenic therapies (those that target blood vessels that feed tumour growth) can be used in combination with chemotherapy drugs to improve treatments for ovarian cancer.

"We're not only trying to make the treatments more effective, we're also trying to improve outcomes for women, improving their quality of life by reducing the use of chemotherapy drugs that have toxic side effects," he says.

Petrik is also looking at possible links between elevated blood sugar and cancer and, more specifically, how women with hyperglycemia may be prone to developing a more aggressive form of ovarian cancer. Cells use glucose in the blood as a source of fuel, but cancer cells use more than healthy cells. This has inspired Petrik and his team to look more closely at the effects of hyperglycemic drugs, and how they might be used to slow tumour growth, encourage regression and maybe even make tumours disappear entirely.

Funding is provided by the Natural Sciences and Engineering Research Council and the Canadian Institutes of Health Research. Research collaborators include Prof. Jack Lawler of Harvard University and Jack Henkin of Abbott Labs: Global Health Care and Medical Research in Illinois.

Photo by istock |

The connection between diet and breast cancer

BY JOEY SABLJIC

Most women are more than 40 years old when they're diagnosed with breast cancer. But researchers still don't really know when the original genetic changes and mutations occur that initiate breast cancer, nor do they know the conditions within the mammary gland that promote tumour development.

University of Guelph Prof. Roger Moorehead, Biomedical Sciences, wants to find out if the genetic alterations that eventually give rise to breast tumours occur at earlier ages, and whether soy-based diets can reduce breast cancer risk.

Moorehead says that most of the mammary gland's development happens during puberty. During that time, there is a tremendous increase in hormones, along with cell proliferation, which make young mammary glands especially sensitive and vulnerable to the early stages of tumour formation.

"The state of the mammary gland appears to determine how susceptible it will be to genetic mutations and tumour development," says Moorehead. "What we're trying to figure out is whether it's because of cell proliferation or because of the hormonal environment."

Certain cell receptors – proteins found on the cell surface that recognize specific molecules – interact in causing mammary tumours. One particular receptor, the type I insulin-like growth factor (IGF-IR), has been found to be a major factor in breast cancer development.

Moorehead's preliminary findings suggest that when this insulin-like growth factor receptor is overexpressed in pubertal mammary glands, tumours form much more rapidly than in adult mammary glands.

Moorehead and his research team have designed a transgenic animal model that allows them to transplant tissue from a young mouse's mammary gland to an older mouse's mammary gland (and vice versa) to study whether there is a difference in mammary tumour development at different ages and hormonal environments as caused by the IGF-IR.

The researchers are trying to determine whether adding soy protein to diets can help to prevent tumour growth. Moorehead points out that within East Asian cultures, where high soy diets are common, significantly lower breast cancer incidence and mortality rates occur than in Western countries. He says high soy-based diets may be able to cause rapidly developing pubertal mammary glands to behave more similarly to stable, mature mammary glands, where the cells are more developed and less susceptible to tumour formation.

"What our research suggests is that if we get the mammary gland to a more mature state, that it's less susceptible to tumorgenesis," says Moorehead. "Now we're trying to manipulate the mammary glands through a dietary change to trick them into thinking they're more of an adult mammary gland."

He and his team hope that their ongoing research will reveal whether the hormonal environment or increased cell proliferation associated with puberty influences breast cancer risk, as well as whether a high soy diet can decrease a woman's risk of developing breast cancer.

Also involved is Prof. James Petrik, Department of Biomedical Sciences.

This research receives funding from the Canadian Institutes of Health Research.

| Photo by istock

Birthing preferences vary widely

BY NICOLE YADA

Economic status seems to influence women's birthing preferences in Canada, with more affluent women exploring alternative choices while those with limited resources often opt for medical intervention.

The international medical community is trying to provide as many women as possible with access to medical care during the birthing process, yet a growing trend is emerging of women avoiding traditional medical involvement during labour and delivery. University of Guelph political science Prof. Candace Johnson wants to know why.

Johnson is working on a major comparative study of maternal health preferences in countries that take significantly different approaches: Canada, the United States, Honduras and Cuba. She wants to discover why women have such a range of birthing preferences, from having as much medical intervention as possible to having a completely natural birth.

"Women often feel alienated from the birthing experience and as if they must be passive during the process," says Johnson. "They're often not encouraged to participate, and don't feel like there are options available to them."

Johnson, a political theorist interested in public health care policies, is comparing preferences by country, as well as delving more deeply into individual countries' approaches.

For example, she developed a research partnership with Immigration Services of Guelph-Wellington and hired eight researchers who interviewed 120 Canadian women. So far, she's seen a great deal of variation in these women's birthing preferences within Canada, particularly between marginalized and affluent women. Those with limited resources want as much medical intervention as possible, while those with access to resources (financial, educational, etc.) may feel more comfortable exploring choices and having a backup plan, such as going to the hospital, if they experience problems during a home birth.

Other countries are taking different approaches. In Honduras, Johnson has a partnership with the Canadian Red Cross, which, in an attempt to lower the maternal death rate, has set up a clinic where women are encouraged to go to deliver their babies. Over the past 10 years, the CRC has been able to increase attendance at the clinic, from nine per cent of women giving birth in the intervention area to 40 per cent. But many still resist going to the clinic. The Red Cross is trying to determine why.

In Cuba, all pregnant women are required to go to doctor's appointments, to be tested for sexually transmitted diseases and to give birth in hospital with a medical doctor and an obstetrician. Johnson found that women are only allowed to have pain medication if they have a caesarean section. She plans to interview medical professionals to see if this is a resource issue, or if they are worried that the pain medication will be transferred to the baby.

While this birthing experience may seem mechanized, Cuba's infant mortality rate is lower than in the U.S., a huge source of pride for the Cuban government.

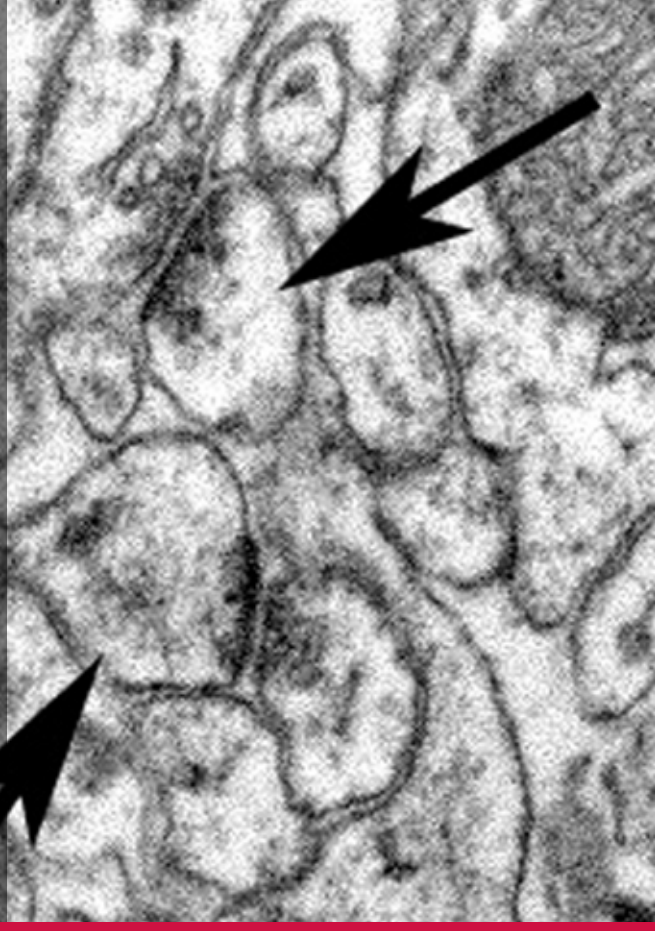
Partnerships with Immigration Services and the Canadian Red Cross were made possible with help from the College of Social and Applied Human Sciences. Funding for this study is from the Social Sciences and Humanities Research Council. R

| Photo by istock

Mental block

BPA can impair the brain

BY NATALIE OSBORNE



Arrows point to neural connections called synapses, pictured here in an electron micrograph.

A chemical present in plastics and flame-retardant products could interfere with cognitive processes such as learning and memory.

University of Guelph researchers have found that Bisphenol-A, also known as BPA, the now-infamous ingredient in plastic water bottles, can impair neural plasticity, the brain's ability to alter its structure and function throughout adult life.

Prof. Neil MacLusky, Biomedical Science, is collaborating with Csaba Leranth of Yale University to understand how BPA interacts with the brain. Studies involving laboratory animals have shown that exposure to BPA below supposedly "safe" levels impairs neurochemical connections called synapses.

"We make synapses whenever we learn something ... the brain is constantly exploring new neural pathways, laying down new synaptic connections," says MacLusky. "If a neurochemical pathway is laid down that you start to use, you'll tend to keep it there. At least in part, that's believed to be the basis of learning and memory."

However, BPA can block this process and prevent new synapses from being formed or old ones from being replaced. This impedes the brain's ability to acquire, analyze and store new information.

Synapse formation is also associated with mood. When people are clinically depressed, their rate of synapse renewal decreases. BPA causes a similar decrease in synapse turnover, and could be linked to mood disorders.

One of the hormones that help maintain synapses and neural plasticity is estradiol. Although traditionally considered a female sex hormone, estradiol is also produced in both female and male brains to promote synaptic turnover. MacLusky found that synapse formation in animals treated with this hormone was blocked by BPA. But exactly how BPA interacts with estradiol is still a mystery.

And so is the so-called "safe" level of BPA. The United States Environmental Protection Agency defines the safe dose of BPA to be 50 micrograms per kilogram per day. Safe levels are usually calculated as 1/1000 of the lowest dose to cause adverse effects. However, many researchers have treated animals with BPA doses at and below this supposed safe level and observed significant effects.

MacLusky and Leranth's ongoing studies were among hundreds that convinced the Canadian government to be the first country in the world to ban plastics containing BPA. Although few people were ever exposed to levels as high as the safe dose, when it comes to chemicals in food products, a generous safety margin is essential. "Even if you completely take BPA out of food containers, the human exposure level is not going to be zero," says MacLusky, "because it is in so many household products, including fire-retardant chemicals used on fabrics as well as many commonly used hard plastics."

MacLusky identified the need to design animal studies that truly reflect human exposure to BPA in North America. Because traces of BPA have been found in placentas, this exposure likely starts in the womb and continues at low levels throughout life. Researchers are concerned that exposure during development could be particularly damaging, especially to tissues like the brain that are formed through long and complex developmental processes.

MacLusky and Leranth will continue to examine BPA's interaction within the brain, particularly which areas it acts on and whether or not it interferes with other hormones vital to healthy brain function. "We don't know if this is something that happens only within certain brain regions or throughout the entire brain," says MacLusky. "There are also many hormones that contribute to synapse formation—if BPA is interfering with these factors, we need to know about it."

Funding for this project is provided by the U.S. National Institutes of Health and the Natural Sciences and Engineering Research Council.

Photo by Neil MacLusky |

A healthy equation

Researchers use mathematical models to find global disease solutions

BY REBECCA HANNAM

Mathematical models developed at the University of Guelph were instrumental in analyzing national vaccine policies for human papillomavirus (HPV) screening in 2007. Now, researchers are using these same models to study other human diseases, and are helping underdeveloped countries better understand treatment options.

Prof. Chris Bauch, Mathematics and Statistics, uses mathematical research models – specifically, differential equations and computer simulations – to study how diseases are transmitted and to determine the effectiveness of disease interventions.

"These help us learn about infectious diseases and vaccination policies by modelling human transmission and demonstrating how interventions impact disease prevalence," says Bauch.

Following the HPV project, Bauch began using these models to study the effectiveness of vaccinations for measles. Currently, he's working to determine the optimal frequency for routine measles vaccinations in low-income countries such as Cambodia, Ghana, India and Uganda.

This work involves applying something called game theory, a model used to analyze group interactions, to determine the most effective strategy for measles vaccination in the given country.

Game theory assumes that individuals make choices with the goal of maximizing their benefits. This theory can be applied whenever the payoff of a person's action is dependent on what other people choose, creating a strategic interaction or essentially a game, says Bauch.

For example, an individual's decision to be vaccinated impacts their entire community, because more vaccinations mean less disease transmission. Consequently, people who chose not to be vaccinated are less likely to get infected because of other people's decisions.

This assumption can be used to predict how the perceived probability of infection influences people's intervention decisions.

Bauch's work also incorporates demographic, environmental and disease exposure factors in predicting how successful vaccinations will be given specific population data.

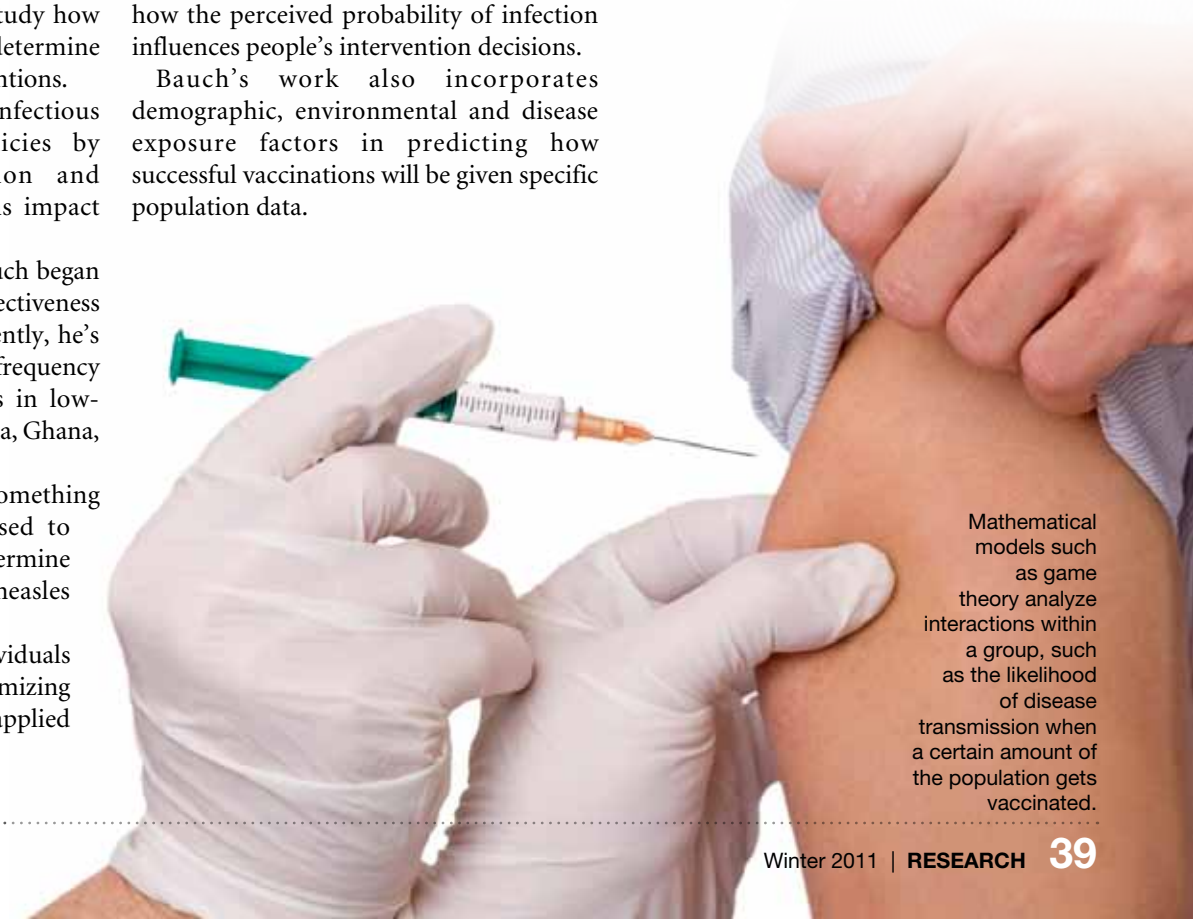
The results of these model studies are shared with government policy-makers and can impact national health recommendations. This research also provides the basis for cost and benefit analysis studies.

"Mathematical modelling is important in this context because low-income countries need to look at the predicted costs and predicted effectiveness associated with different possible vaccination strategies, according to how much healthcare budget is available," says Bauch.

Bauch has also studied other infectious diseases including chickenpox and Hepatitis A and their prevalence in Canada and other developing countries.

Other research collaborators include Alya Dabbagh at the World Health Organization and Louis Garrison at the University of Washington.

Funding sources include the Ontario Ministry of Research and Innovation, Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council, GlaxoSmithKline, World Health Organization, and Bill and Melinda Gates Foundation.



Mathematical models such as game theory analyze interactions within a group, such as the likelihood of disease transmission when a certain amount of the population gets vaccinated.

| Photo by istock

The DNA repair team

Researchers examine body's natural fix-it mechanisms

BY NATALIE OSBORNE

Prof. Mark Baker, head research assistant Alissa Magwood and graduate students Maureen Mundia and Sal Desai (from left to right) developed a test that allows them to examine the early steps of homologous recombination, an important mechanism of genetic repair.

DNA holds the life plan for every cell in the human body. And that's why protecting these molecules and the information they contain is vital to all living organisms. What's more, damaged DNA can lead to cell death or life-threatening diseases, such as cancer.

University of Guelph researchers are studying how cells naturally repair and maintain genetic material.

Molecular and cellular biology Prof. Mark Baker and his team, including graduate students Maureen Mundia, Iulia Cealic, Vatsal Desai and head research assistant Alissa Magwood, have received a major renewal grant from the Canadian Institutes of Health Research for their work on a DNA repair mechanism called homologous recombination.

Baker and his colleagues developed a novel test that can detect homologous recombination's early steps. The assay gives researchers an unprecedented look at the beginning steps of the long and complicated repair mechanism.

"There are so many intermediate steps and products involved in the process, and usually all you can see is the end result," says Baker. "But if you have a test that allows you to look right at the beginning of the repair process, then you can have a glimpse at how the proteins involved are working, and also determine how and why things go wrong."

During cell division, nuclear DNA, in the form of chromosomes, is duplicated. Roughly "X" shaped, each chromosome is made up of two chromatids, forming each side of the "X". These two structures, known as sister chromatids, contain exactly the same genetic information.

When a strand of DNA is broken, the molecule can be degraded around the break site resulting in a loss of genetic information. Homologous recombination uses an undamaged strand, usually found on the sister chromatid, as a "template" or set of instructions, to rebuild the damaged strand. It adds components in the order specified by the template, and "synthesizes" a new DNA segment to match the sister chromatid.

Baker's new test can detect an early intermediate product of the repair mechanism, namely the new DNA synthesis that occurs at the break site. The intermediate's formation requires the participation of many proteins.

Researchers found that when a break occurs in a double-stranded DNA molecule, some of the loose ends are coated with a protein called RAD51. This protein allows the broken end to search out a comparable or "homologous" template that can be used to rebuild the strand.

RAD51 is loaded onto the loose DNA ends by another protein called BRCA2. BRCA2 stands for the breast cancer susceptibility 2 protein. Individuals carrying a mutant allele of BRCA2 (or a related protein called BRCA1), are genetically predisposed to the development of breast, ovarian and other cancers. About 80 per cent of these individuals will develop cancers during their lifetime, and their tumours are characterized by the loss of both normal *BRCA2* (or *BRCA1*) genes. Researchers believe that mutated *BRCA2* genes produce malfunctioning BRCA2 proteins that are unable to perform their loading job. As a result, the cell can't repair damaged DNA, and this may lead to genetic instability that can result in cancer.

However, the *BRCA2* gene can be mutated in hundreds of different ways and doctors don't necessarily know if and how the mutation will affect DNA repair or lead to cancer.

"We're hoping that our test might be used for detecting mutations in breast cancer, because there are over 1,800 catalogued mutations in the *BRCA2* gene, and the vast majority of them are not understood," says Baker. "We need to know exactly what these mutations do in order to provide predictive power for doctors diagnosing cases of breast cancer."

Funding for this research is provided by the Canadian Institutes of Health Research.

Photo by Natalie Osborne |

Uncovering the multiple sclerosis protein

BY NICOLE YADA

SPARK air video

A white-matter component called myelin basic protein (MBP) has long been known to be implicated in the formation of multiple sclerosis. But exactly how it functions remains largely a mystery.

To help address the matter, physics Prof. Vladimir Ladizhansky and molecular and cellular biology Prof. George Harauz are working together to identify the structure of MBP, one of the proteins that make up a large portion of the myelin sheath.

The myelin sheath is responsible for causing rapid nerve conduction in higher vertebrates. In fact, myelinated axons transmit nerve impulses 100 times faster than non-myelinated axons.

In MS sufferers, the sheath loses myelin. This degeneration causes nerve transmission to slow, negatively affecting the brain's ability to communicate with the spinal cord. As a result, neurologically based co-ordination problems become apparent.

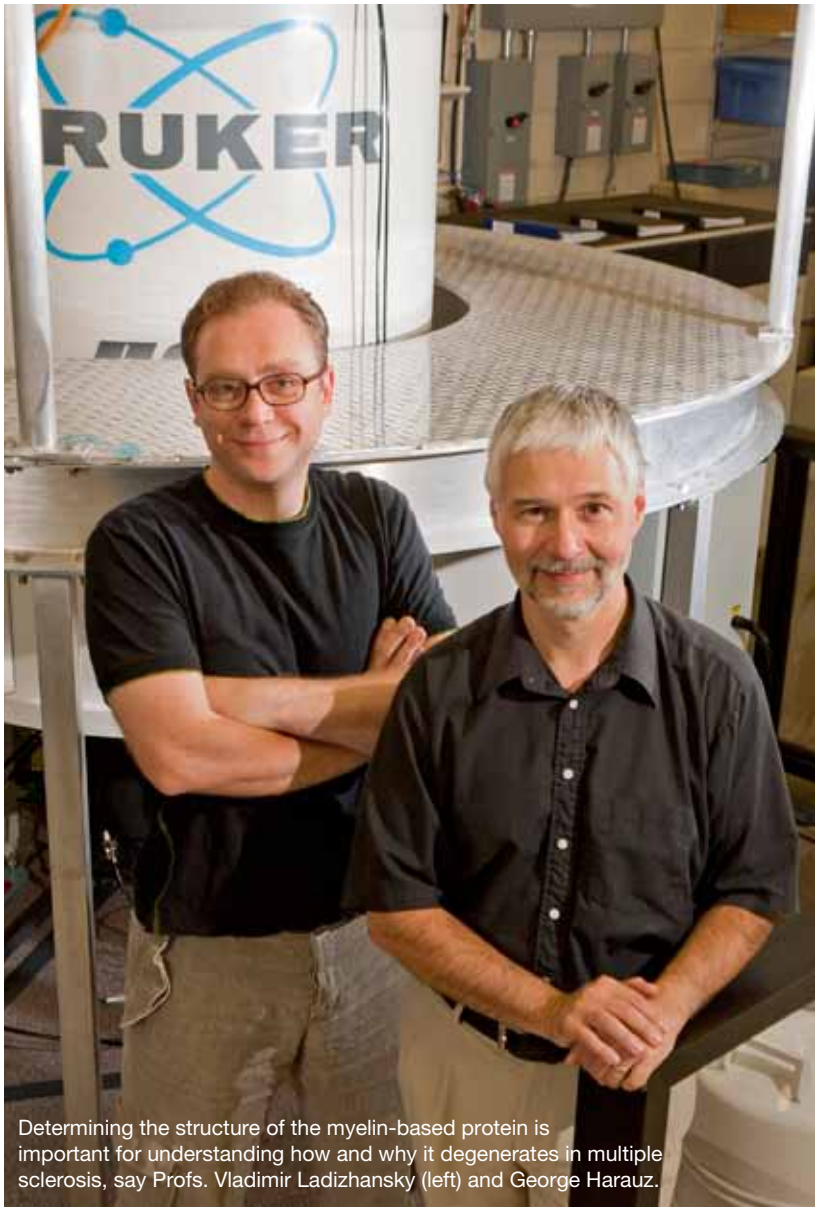
"If you want to look at intelligent design for MS drugs, you'll want to know the molecular basis of this protein," says Ladizhansky.

About one-third of the body's proteins cannot be crystallized, including MBP. So Harauz and Ladizhansky are using solid-state nuclear magnetic resonance spectroscopy to gain a better understanding of MBP at its atomic level.

MBP is "floppy" by nature, with the appearance of a folded string. When the MBP sample is placed in the magnetic field, the nuclei (which behave like small magnets) align, and the strength of interaction between the nuclei is measured. A strong signal means there's a short distance between those segments of the protein. The many distance measurements can then be converted into a structure.

What causes the degeneration of MBP (and consequent development of MS) remains unknown. After age 20, the amount of myelin in a healthy person's body is normally consistent throughout the rest of their lives. However, until age 20, myelin development remains vulnerable to irregular activity in the enzymes responsible for protein processing and modification.

While this much is known, it is necessary to identify the MBP structure to establish how and why the protein degenerates. Knowing the MBP structure will enable researchers to understand key facts, such as how myelin damage spreads and what the genetic component is for MS.



Determining the structure of the myelin-based protein is important for understanding how and why it degenerates in multiple sclerosis, say Profs. Vladimir Ladizhansky (left) and George Harauz.

"By the time MS is diagnosed, a significant portion of the MBP has already been lost," says Harauz. An in-depth understanding of this protein means a method for replacing lost myelin will come closer to being a reality.

This research is funded by Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council.

| Photo by Kyle Rodriguez

On-farm study targets Q fever risk

BY MAURICE HARVEY

Graduate student Shannon Meadows collects blood samples from goats and sheep to test for the presence of antibodies to C. burnetti—the bacteria responsible for Q fever.

For a disease that can have a drastic and detrimental effect on animal production – and can also make humans ill – little is known about Q fever's prevalence in Ontario's small ruminant farms. The causative bacteria Coxiella burnetii can infect any species of animal, including mammals, birds and insects, but sheep, goats and cats appear to express disease most commonly, usually as abortion and stillbirth. Farm workers usually contract the disease when caring for animals during the birthing process. Signs of the disease in humans include fever, headaches and pneumonia. Although most infected people don't become ill or experience mild illness, some become severely ill and may require hospitalization.

Researchers at the Ontario Veterinary College are trying to find out more about this disease. Profs. Paula Menzies and Andria Jones, Population Medicine, are working with Dr. Jocelyn Jansen of the Ontario Ministry of Agriculture, Food and Rural Affairs and master's student Shannon Meadows to learn how many small ruminant operations in Ontario are infected with Q fever, the effects of that infection on animal health, and the risk factors that influence Q fever's spread to humans.

"This is the first time our research has directly involved human disease, and we're very excited about it," says Jones. "Once we have an understanding of how much risk is associated with Q fever in Ontario's sheep, goats and human farm workers, as well as the factors that put us at risk, we'll be able to take a proactive stance to keep our province healthy."

For her part, Menzies has seen first-hand how this disease can affect farm families and the animals they care for. "We believe that this research will give an excellent grounding on understanding the risks in order to make sound recommendations on the control of Q fever," she says.

The risks associated with Q fever are illustrated by the events in the Netherlands in 2009. There, a Q fever outbreak led to thousands of cases of the disease in humans – including several deaths – as well as the culling of more than 60,000 pregnant goats from infected dairy herds. In addition, lifetime breeding bans were levied against infected herds and vaccination against the disease became mandatory.

In Ontario, researchers will determine how many infected sheep and goats exist in the province's livestock and dairy farms by collecting and testing blood samples, looking for antibodies to C. burnetii. In total, 150 farms throughout southern Ontario have been randomly selected, with more than 5,000 animals included in the test.

As well, each participating farm will have up to four workers randomly selected for blood testing and participation in a survey about factors that predispose people to contracting the disease, such as their overall health, lifestyle, and the amount of time they spend on a farm.

This research is funded by the University of Guelph's Animal Health Laboratory, the Ontario Sheep Marketing Agency, the Ontario Ministry of Health and Long-Term Care and the Ontario Agency for Health Protection and Promotion.

New test reveals disease prevalence

BY NATALIE OSBORNE

SPARK air video

Coxiella burnetii, the causative agent of Q fever, can cause spontaneous abortions in pregnant sheep and goats, which is costly for small ruminant producers. A new and highly sensitive test is giving University of Guelph researchers a clearer picture of the disease's prevalence in Ontario and its effect.

Dr. Hugh Cai, Dr. Murray Hazlett and other collaborators at the Animal Health Laboratory investigated the number of C. burnetii in tissues from small ruminant abortions stemming from various causes, using a technique called real time polymerase chain reaction (rtPCR). This technique amplifies the bacteria's genetic material to give an accurate measure of the number of organisms present.

Samples from local farms were analyzed using both the new test and traditional measures. A pathologist determined whether C. burnetii caused the abortion, and researchers compared the levels of C. burnetii in the tissue to the pathologist's diagnosis.

They found that levels above one million C. burnetii per microgram of tissue were significant enough to cause abortion. In some samples, they found as many as one billion C. burnetii per microgram. Overall, they found that Q fever accounted for 21 per cent of abortions in goats and about eight per cent in sheep.

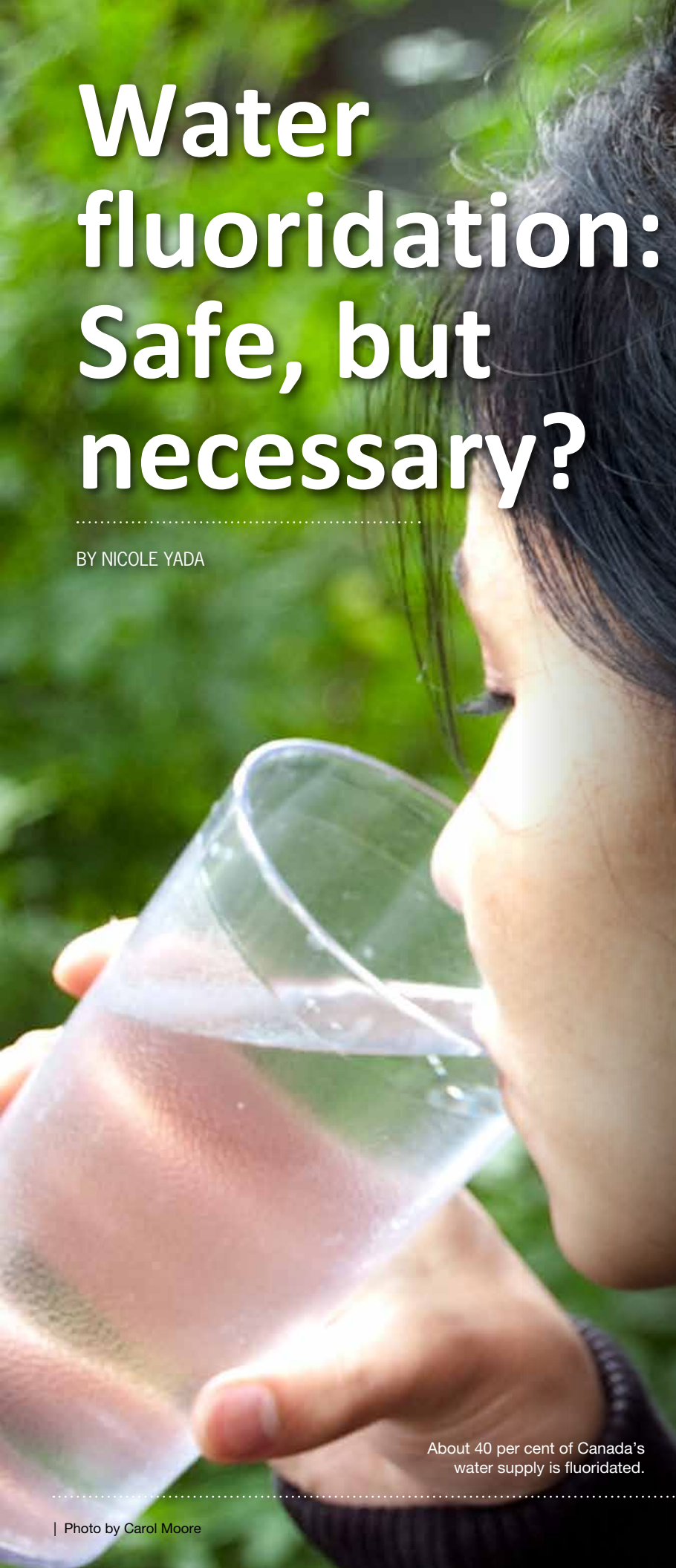
"We will soon provide this as a routine test to practicing veterinarians and pathologists," says Cai. "The findings of this study will help interpretation of the test results and give better understanding of the causes of small ruminant abortion," adds Hazlett.

Funding was provided by the Ontario Ministry of Food, Agriculture and Rural Affairs through the Animal Health Laboratory Animal Health Strategic Investment program.

Photo by University of Guelph |

Water fluoridation: Safe, but necessary?

BY NICOLE YADA



About 40 per cent of Canada's water supply is fluoridated.

Sixty-five years after fluoride was first added to municipal water supplies, it continues to be a contentious issue. Even though adding fluoride to the water supply reduces cavities, University of Guelph history Prof. Catherine Carstairs is examining why water fluoridation never achieved universal acceptance.

Carstairs began her work on fluoridation unintentionally, when researching the history of health food stores. Health food store owners and consumers would become some of the leading opponents of fluoride.

In the 1950s and 1960s, before the use of fluoridated toothpastes was widespread, water fluoridation was a logical and comparatively cheap way to manage public health, says Carstairs. Water fluoridation advocates argued that it would substantially reduce the amount of cavities in children, which was very high at the time.

But anti-communist alarmist groups sprung up claiming water fluoridation was a plot to control the population. They believed fluoride could be used by governments to poison entire communities, or that fluoride would make people docile and more susceptible to a communist takeover.

These conspiracy theories were dismissed, but then came lasting concerns that some people were allergic to water fluoridation, and that it would leader to heart disease, kidney troubles or cancer.

Consequently, only about 40 per cent of Canada's water supply is fluoridated. Montreal, Vancouver and Guelph have never had fluoridated water while Toronto and Waterloo have. However, in October 2010, Waterloo residents voted in a civic election to remove fluoride from their water supply.

Tooth decay rates have dropped significantly since water fluoridation was introduced. However, it has become increasingly difficult to measure the effectiveness of water fluoridation, because people living in non-fluoridated communities often consume beverages bottled in areas where the water is fluoridated. As well, greater health care has increased hygiene over time, and there is greater availability of products such as fluoridated toothpaste and mouthwash.

Looking ahead, Carstairs will examine the scientific debate that took place between the dental and nutritional communities at the time of fluoride's inception. Nutritionists ultimately endorsed fluoridation, because they became convinced of its proven health benefits. "I too believe fluoride is relatively safe," says Carstairs. "As for whether it's a necessary health measure, I'm unsure."

Carstairs' research has led her to municipal and provincial archives in Vancouver, Calgary, Winnipeg and Montreal, in addition to the archives of the American Medical Association.

Her research on the anti-fluoridation movement was funded by the Social Sciences and Humanities Research Council.

| Photo by Carol Moore

Unit adds substance and science to health claims

BY NICOLE YADA

The abundance of health products on the market has prompted tougher legislation regarding allowable health claims. That's increased the importance of product testing, and, along with it, the role of the Human Nutraceutical Research Centre at the University of Guelph. It serves both campus and industry partners as the go-to service for a variety of nutrition-related clinical trials.

Prof. Amanda Wright is the director of the HNRU, which serves as a business and research depot and as an educational unit within the Department of Human Health and Nutritional Sciences. She liaises with her home department and promotes the unit to other departments, to undergraduate and graduate students, and to food companies. Wright is enthusiastic about the practical opportunities the unit offers students, with 10 to 15 undergraduate students and 12 to 15 graduate students working there during the year.

The research unit conducts clinical trials to substantiate health claims for foods or to allow a company to obtain a natural product number, which is now required for all 'natural health products' (i.e., vitamins, minerals, herbals, supplements, etc.) sold in Canada.

"Strategically, we're well positioned to advance the research and science being pursued here at Guelph," says Wright.

Typically, the HRNU is involved in several research projects at a time, all of which are in collaboration with industry partners, other departments or other universities.

Wright collaborates with Profs. Alison Duncan, David Mutch and William Bettger, and Hilary Tulk.

The research unit is located between the Food Science building and the Guelph Food Technology Centre.

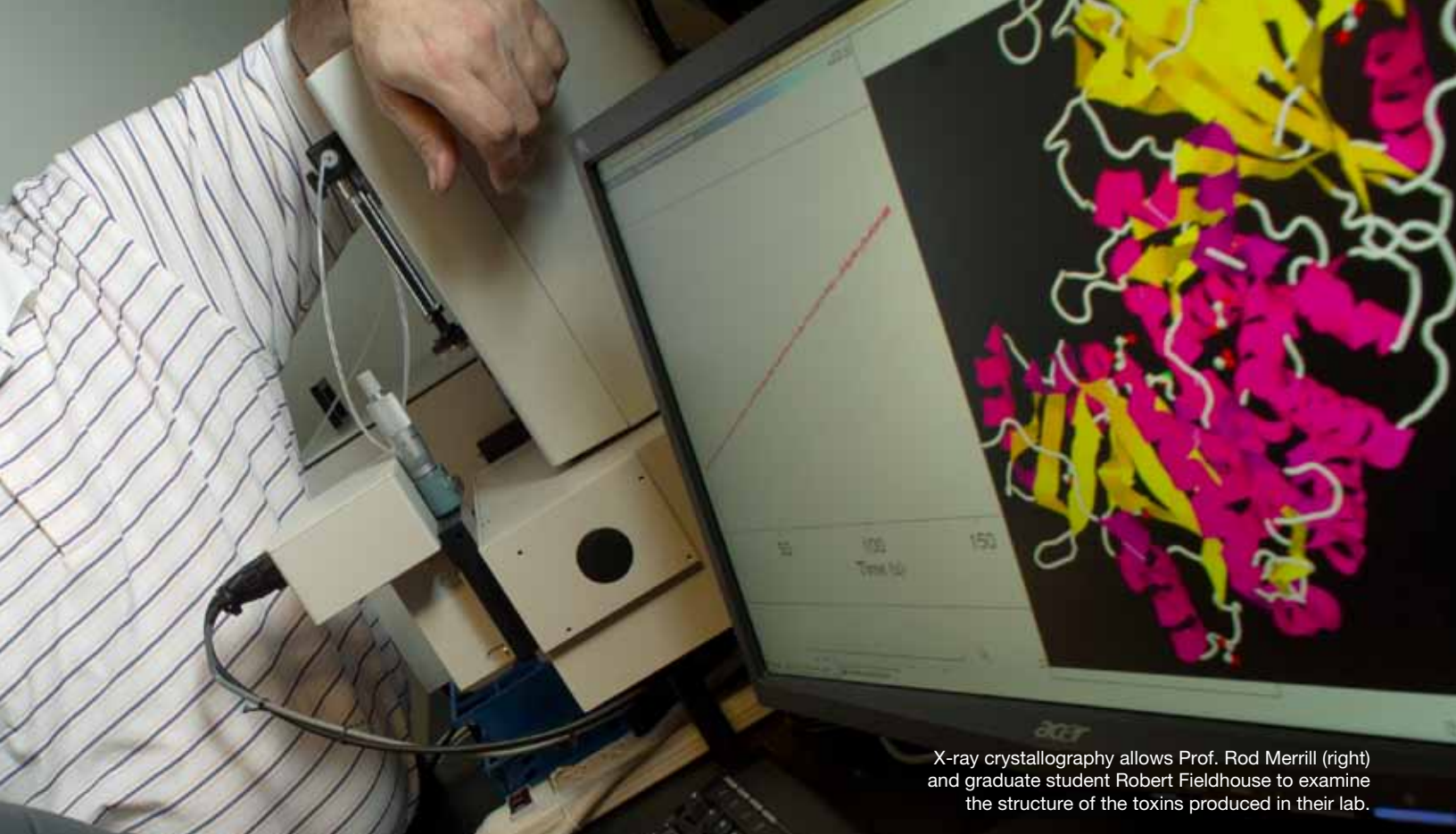
Prof. Amanda Wright

Cue the inhibitor

Biochemists fight antibiotic resistance through new approaches to understanding toxins

BY ROBERT FIELDHOUSE

Photo by Nicole Yada |



X-ray crystallography allows Prof. Rod Merrill (right) and graduate student Robert Fieldhouse to examine the structure of the toxins produced in their lab.

Antibiotic resistance is on the rise, making harmful bacteria armed with protein toxins increasingly worrisome, says a University of Guelph professor who's trying to find new ways to identify these toxins, figure out how they work and disarm them.

Prof. Rod Merrill, Molecular and Cellular Biology, and his team want to unlock the structural and functional mysteries of several toxins that enter target cells, alter key proteins and cause cell death – leading to disastrous outcomes for the infected individual.

They know that many bacteria use the same attack strategy, including *Vibrio cholerae,* which causes cholera; *Bordetella pertussis*, which causes whooping cough; and *Corynebacterium diphtheria*, which causes diphtheria. Understanding toxin structure and function makes it possible to find small molecules that can bind to – and inactivate – them.

"Bacteria wreak havoc using an arsenal of virulence factors, including protein toxins," says Merrill. "We're trying to figure out toxin structures so we can find inhibitors that will make people less dependent on antibiotics, which are becoming less and less effective."

To do so, they produce a protein toxin in the lab, using safe bacterial strains, and then purify it. The pure toxin is then mixed with chemicals under specific conditions that allow the toxin to form crystals – similar to making rock candy from sugar crystals. But finding the right conditions for the mix is the challenge.

Enter Dr. Hee-Won Park, a collaborator at the University of Toronto's Structural Genomics Consortium. He's an expert at finding crystal conditions; he uses many toxin variants and various chemical environments to test for crystals in a high-throughput fashion.

Then the researchers shoot the crystals with X-rays. The crystals scatter the X-rays in a specific pattern that allows Merrill and Park to calculate a toxin's three-dimensional structure with the help of computers. These structures allow them to find complementary small molecules that bind the toxin and physically block it from binding specific cell components. These small molecule inhibitors may one day prevent the toxin from causing harm.

Merrill and his team test the toxins (and the inhibitors that block their activity) with yeast cells. The yeast normally die from the toxin. If they don't, the researchers know the inhibitor is working.

Already, Merrill has found several excellent inhibitors against *Pseudomonas aeruginosa* exotoxin A and cholix, a new toxin he and collaborators found in *Vibrio cholerae*.

Next, Merrill and his team hope to track the toxin's motions as it reacts with its target, using advanced X-ray technology that produces many images.

"We'd like to make a movie of the toxin in action," says Merrill. "Fully understanding the mechanism will lead to the best possible inhibitors and, ultimately, the best treatments."

The University of Guelph research team includes graduate students Danielle Visschedyk, Zachari Turgeon, Adin Shniffer and Rob Fieldhouse; post-doctoral fellows Amanda Rochon and Ravi Ravulapalli; technicians Dawn White, Caroline McGregor, Patrick Edwards and Gerry Prentice; and undergraduate students Rob Gale, Sarah Legree and Alissa Cait.

Collaborators include Drs. René Jørgensen of Carlsberg Laboratory in Denmark and Roland Pfoh of the University of Toronto; Profs. Dev Mangroo of the University of Guelph, and Emil Pai and Matthieu Schapira of the University of Toronto; Norman Oppenheimer of the University of California at San Francisco; and Carmay Lim of Academia Sinica in Taiwan.

This research is sponsored by the Canadian Institutes of Health Research, the Canadian Cystic Fibrosis Foundation, the Human Frontier Science Program and the Natural Sciences and Engineering Research Council.

| Photo by Martin Schwalbe

Turning the page on toxins

A *Research* magazine story helped turn this writer into a toxin hunter

BY ROBERT FIELDHOUSE

Newly identified cholera- and anthrax-like toxins threaten human health, but they could also hold the key to new vaccines, drugs and cancer treatments. I became interested in protein toxins as a SPARK student, reading in the pages of *Research* about Prof. Rod Merrill, Department of Molecular and Cellular Biology.

Merrill's work on a protein toxin that punches holes through target cells to kill them caught my attention. Now, as a PhD candidate in the Merrill lab, I've worked on a new computational approach to identify and characterize novel toxins. Our team has uncovered several new toxins including Chelt, a cholera-like toxin from *Vibrio cholerae*, and Certhrax, an anthrax-like toxin from *Bacillus cereus*.

Chelt is cholera toxin with a twist – the usual cell-entry portion is swapped with a different structure.

And Certhrax is anthrax lethal factor with a twist – it has similar cell-entry machinery but kills target cells a different way.

Genome sequencing projects have ushered in a data-rich era, but making sense of the available information remains challenging. A new protein toxin is a needle in the haystack because such toxins often have little similarity to known examples.

We've developed a tactic called fold recognition to detect new toxins based on protein structure similarity. Combined with rules for filtering possible toxins, including, for example, conservation of key amino acids needed for enzyme function and a yeast-based screening step in the lab, we identified the new toxins.

Now, we're pinpointing details of each toxin such as 3-D structure, the strategy the toxin uses to leave one cell and enter another, and how the toxin interacts with molecules in the target cell. Eventually, I'd like to use supercomputers to simulate toxin function and find new inhibitor drugs that could prevent them from causing harm.

Protein toxins aren't all bad, however. For example, modified toxins that activate the immune response without causing harm are the basis for many vaccines. Also, toxins are used to kill cancer cells in some therapies.

M.Sc. graduate Zachari Turgeon and technician Dawn White made key contributions to this work, published in *PLoS Computational Biology*. Our team also includes PhD candidate Danielle Visschedyk and post-doctoral fellows Amanda Rochon and Ravi Ravulapalli, among others. This research was sponsored by the Natural Sciences and Engineering Research Council, and by the Canadian Institutes of Health Research.

Guelph Mercury tuesday

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The 'hole' story behind microscopic weapons

Guelph researchers have discovered how microscopic bacterial weapons breach our defences – which could be the first step towards finding a cure for certain infectious diseases.

Prof. Rod Merrill and research associate Abdi Musse, Department of Chemistry and Biochemistry, have found how numerous diseases – including cholera, diphtheria and even the yearly influenza epidemic – attack the human body.

"We've found a common mechanism that may be part of a 'villain' protein that invades our cells," says Merrill. "And that information could help us develop methods to fight these diseases."

Merrill and Musse were studying a bacterial protein called colicin E1, which is produced by *E. coli* bacteria and serves as a tool to kill other bacterial cells. It does so by forming a channel in the cell's membrane, effectively punching a hole in the cell and causing essential ions to leak out. Nearly all cells rely on these ions to carry out their everyday functions. Without them, they are unable to perform the essential processes of life, and quickly die.

These channel-forming colicins are so powerful that just one is enough to kill a normal cell. But exactly how colicin E1 performs its deadly duty remained a mystery – that is, until Merrill and Musse began probing the problem.

For colicin E1 to form a channel in the cell, the researchers reasoned, the protein must somehow change from hydrophilic – that is, something that will dissolve in water – to hydrophobic – something that resists mixing with water, such as oil. Using biochemical and biophysical techniques, they've shown that the protein turns itself inside out, so that a previously hidden hydrophobic core is exposed, allowing colicin E1 to plant itself inside the cell membrane of the target cell.

They've also found that the factor that initiates this change is a lowering of the pH, from a slightly alkaline or basic value to mildly acidic. A lower pH environment causes a cascade of specific events within the colicin structure, turning the protein inside out, readying it for insertion into the cell membrane – which disrupts the ion gradient and eventually kills the cell.

"At low pH, the protein essentially unfolds, but in a very specific manner," says Merrill. "With the colicin E1 core exposed, the protein can implant itself in a dagger-like fashion right into a cell membrane and form a hole into the cell, which dissipates the natural ion gradient within that cell."

Merrill and Musse have identified the common structural element within the colicin protein family that acts as the "trigger" for this activation mechanism. They've found that this trigger element is also present in a host of other "villain proteins" produced by numerous pathogenic bacteria that cause diseases such as diphtheria, cholera, influenza, and anthrax.

Armed with this new knowledge about how colicin E1 works, Merrill and Musse hope that their discovery will help other scientists learn more about similar pH-triggered diseases.

Paula Bialski

Abdi Musse has discovered how numerous deadly diseases – such as anthrax, cholera, diphtheria and even the flu – attack the human body and make millions of people ill every year.

"This pH-activated mechanism for pore-forming proteins is the method used in diphtheria toxin, cholera toxin, anthrax toxin and the influenza hemagglutin protein," says Merrill. "Now that we know some of the principles of how these diseases begin, we may be able to help find new ways to stop diseases that infect cells in this way."

This research was sponsored by the Natural Sciences and Engineering Research Council.

SPARK stories from the *Research* magazine are often published in the Guelph *Mercury*, through a long-standing partnerhship called SPARKplugs.

Photo by Martin Schwalbe |

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