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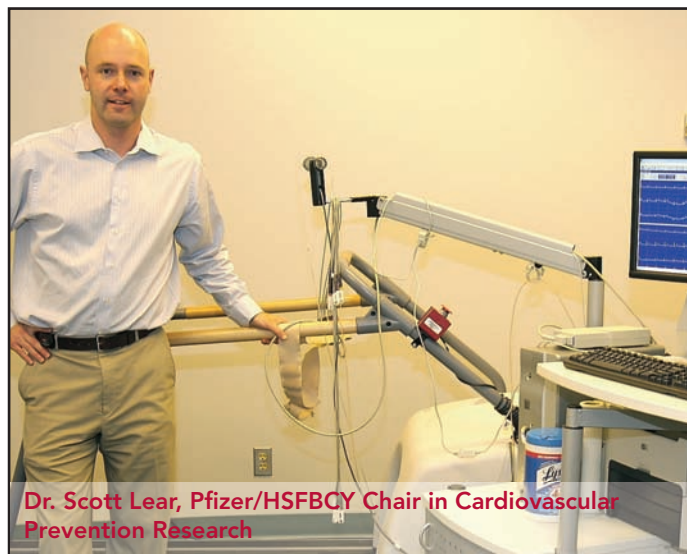
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Pfizer/HSFBCY Chair in Cardiovascular Prevention Research

In 2007, the Heart and Stroke Foundation of BC & Yukon partnered with Pfizer, St. Paul's Hospital, and Simon Fraser University's Faculty of Health Sciences to create a Chair in Cardiovascular Prevention Research. Based at St. Paul's Heart Centre, the purpose of the Chair is to help make BC a world leader in research, policy, and practice around CVD prevention. The job of the Chairholder is to develop an innovative research program into CVD epidemiology, population and global health, and health services.

For Dr. Scott Lear, who has just been appointed as the first holder of this new Chair, this means a focus on the influence of the social and physical environment on heart health and disease. Dr. Lear is one of BC's leading young cardiovascular investigators and his research into the social dimensions of heart health has already made waves. In 2008, his finding that the health of new immigrants declines significantly with the first five years of arriving in Canada was national news.¹ The same study, the Multi-Cultural Health Assessment Trial (M-CHAT), also made a major contribution to our understanding of differing levels of CVD risk among people of different ethnicities by showing that fat accumulates in the body differently depending on ethno cultural background.²



ROB MOSES PHOTOGRAPHY

Dr. Scott Lear, Pfizer/HSFBCY Chair in Cardiovascular Prevention Research

Currently, Dr. Lear is involved in three inter-related research programs, two of which are supported by the Heart and Stroke Foundation.

1. The BC Alliance for Telehealth Policy and Research is a consortium of researchers, practitioners, and Health Authorities that looks at using the Internet and other electronic means of communication to manage chronic disease.

Currently, HSFBCY funds the project in which Dr. Lear and his team provide internet-based rehab for cardiac patients in rural and remote areas of BC. The tools and processes they have developed for heart patients are now serving as a template for the design of a more comprehensive internet-based chronic disease management program.

2. The Multi-Cultural Health Assessment Trial (M-CHAT) is an ongoing study of the psychological, social, and cultural factors that influence cardiovascular risk.

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Pfizer/HSFBCY Chair in Cardiovascular Prevention Research - cont'd

As noted above, some of its major findings have related to the heart health of immigrants and differences in the relationships between risk factors and biology among ethno cultural groups.

3. The Prospective Urban and Rural Epidemiological (PURE) Study, led by Dr. Salim Yusef at McMaster University, is a 120,000 person, 17 country study, including Canada, that looks at the relationships between changes in urbanization and heart health, connecting social change to biological change. Although CVD mortality has declined significantly in developed countries, it is rising rapidly in developing countries, a fact many people attribute to the lifestyle changes that accompany economic development.

As part of PURE, the Heart and Stroke Foundation of Canada, in partnership with CIHR, is funding Dr. Lear and an associate to look at the connection between the social and physical environment and CVD risk in 440 communities around the world. In particular, they will be examine whether aspects of the built environment, physical activity levels, nutrition, and tobacco use are related to cholesterol and triglyceride levels. As well, they will look at whether this relationship is influenced by the national income per capita.

¹ Heart and Stroke Foundation of Canada, 2008. *Life in Canada more deadly for immigrants?* Accessed March 1, 2010. <http://www.heartandstroke.com/site/apps/nlnet/content2.aspx?c=iklQLcMWJtE&b=4696993&ct=6241383>

² Scott A Lear, et al, 2007. *Visceral adipose tissue accumulation differs according to ethnic background: results of the Multicultural Community Health Assessment Trial (M-CHAT)*. *American Journal of Clinical Nutrition*, 86: 353-359.

HSF Research on Obesity, the Built Environment, and Health

In 2007, HSFC funded nine research projects through its Built Environment, Obesity, and Health Initiatives. A key part of the Request for Applications involved knowledge translation and required the research teams to work with local community or government organizations – what they call knowledge users – so that the results of the research might directly inform planning and development.

Since then, some of those projects have garnered a lot of attention. Locally, two of the three BC projects funded under this initiative focused on issues involving bicycle use. Both were part of a much larger program called Cycling in Cities (www.cher.ubc.ca/cyclingincities). UBC's Michael Brauer led a project called Understanding the Impact of the **Built Environment on Decisions to Cycle as a Mode of Urban Transport** that looked at when, why, and where people decide to use their bicycles. This project yielded an interactive map of the Lower Mainland (www.cyclevancouver.ubc.ca) that can be used to identify the best cycling route depending on your personal preferences. You can plan routes to minimize traffic, pollution, elevation, and distance.

The other bicycling study, headed by Kay Teschke, also of UBC, was called **Bicyclists' Injuries and the Cycling Environment** (www.cher.ubc.ca/cyclingincities/injury.html). This project played an important role in the debate leading up to the 2009 decision to install dedicated cycling lanes on the Burrard Bridge.

Two other studies from this initiative have also announced important findings about the linkages between the environment and obesity.

The Quebec Adipose and Lifestyle Investigation in Youth, known as the QUALITY study, is led by Tracie Barnett, a researcher in Social and Preventive Medicine at Montreal's Sainte-Justine Hospital Research

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Research on Obesity, the Built Environment, and Health - cont'd

Centre. The research team recruited 632 children (and their families) who live in the Montreal area. The researchers followed each family for two years, looking at physical health, including fatty tissue, BMI, and fitness, and behaviours like physical activity and diet. At the same time, they mapped the characteristics of the neighbourhoods where the families lived so that the study could address the relationship between health, behaviour, and the urban environment.



Study participants lived in a variety of different neighbourhoods. Family incomes ranged from \$31,000 to \$141,000 per year. Forty two percent of the children were overweight and 22% were obese.

One of the first findings from the QUALITY study seems like common sense to most of us – especially if we work at the Heart and Stroke Foundation. The study provides scientific evidence for the claim that proximity to parks is strongly correlated with higher levels of physical activity in children.¹ In a paper delivered at the March 2009 American Heart Association conference on Nutrition, Physical Activity, and Metabolism, QUALITY announced results showing that for every additional park located within a half mile of the family residence, girls are more than twice as likely to walk to school and boys are 60% more likely to walk for leisure.

The different uses of walking between boys and girls is also an interesting point.

The QUALITY study has also found that access to convenience stores is directly related to obesity², a conclusion that echoes another HSFC- funded study in this program led by John Spence at the University of Alberta: **The Shapes of Things to Come: A Longitudinal Study of Environmental Determinants of Overweight Among Children.**³ Using 2002 health survey data from Alberta's Capital Health Region, this research team compared respondents' self-reported BMI with the Retail Food Environment Index or RFEI. This measures the relative proportions of convenience stores, fast food restaurants, grocery stores, and produce vendors.

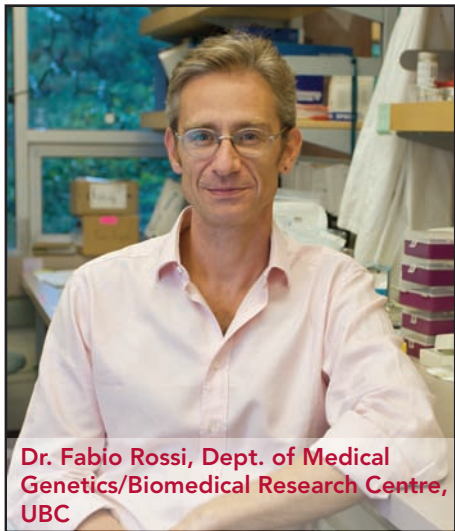
The researchers calculated the RFEI for a radius of 800 metres and 1600 metres from each person's residence. Not surprisingly they found that there were higher rates of obesity when the ratio of fast food and convenience stores was higher than grocery or produce outlets. On average people were exposed to four times more fast food and convenience outlets than grocery and produce outlets within 800 metres of their homes.

¹ American Heart Association, 2009. Children Living Near Green Spaces Are More Active. Retrieved Feb. 10, 2010 from: <http://www.sciencedaily.com/releases/2009/03/090312114757.htm>.

² University of Montreal, 2009. Proximity to Convenience Stores Fosters Child Obesity, Study Finds. Science Daily, Dec. 18. Retrieved Feb. 10, 2009 from <http://www.sciencedaily.com/releases/2009/12/091217102300.htm>.

³ John C. Spence, et al, 2009. Relation between local food environments and obesity among adults. BMC Public Health 9: 192. Doi:10.1186/1471-2458-9-192.

HSFBCY Funds New Discoveries



Dr. Fabio Rossi, Dept. of Medical Genetics/Biomedical Research Centre, UBC

Two HSFBCY-funded geneticists at UBC's Biomedical Research Centre – Kelly McNagny and Fabio Rossi – published papers last year on important developments in their labs.

How Blood Vessels Develop

The system of blood vessels in our bodies is highly complex – each of us is partly made up of about 96,000 kilometres of arteries, veins, and capillaries, enough to circle the earth two and half times.¹ Dr. Kelly McNagny's paper focuses on the mechanisms by which cells form into the tubes that are blood vessels. This

has important implications for our understanding of both congenital vascular defects and the formation of tumors, which need new blood vessels to feed their growth.

The process by which new vessels are formed out of existing ones – called angiogenesis – has long been known. But how cells organize themselves around the hollow tube through which blood flows, called the lumen, has been more of a mystery. Now however, as part of an international research team of scientists from Germany, the Czech Republic, Italy, Japan, and the US, Kelly McNagny and his post-doctoral fellow, Michael Hughes (who is supported by an HSF Research Fellowship) have helped identify how the lumen forms in the new vessels of the developing body.²

Until now, evidence pointed in two directions. The dominant model has been that the tubular formation develops first within individual cells. The idea is that small, hollow formations within each cell, called vacuoles, join together to create a tube-like space. This tube then expands as it connects with similar tubes formed in neighbouring cells. A second model is that the cells that form the blood vessels pack together tightly in a cylinder. This is then hollowed out as the cells retreat from the centre, allowing a tube-like space to form inside the cylinder formation. Although both models have been observed in experiments, it is unclear how either process takes place.

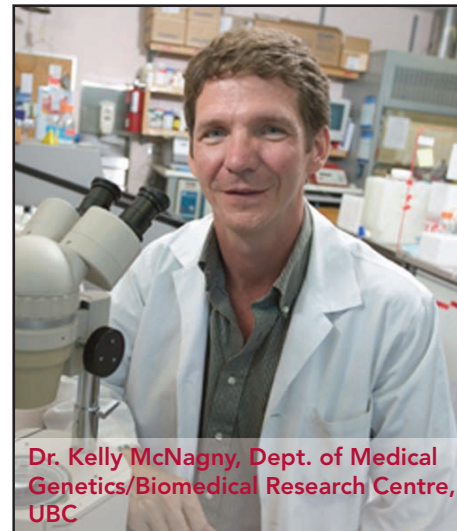
However, not only has this research team been able to show that the formation of the aorta follows the second model, it has also identified how this happens. Initially, the cells that make up the inner lining of the blood vessels are packed tightly together. As the cylinder develops, a group of molecules known as CD34 and podocalyxin move from the interior of the cells to the outer walls, where the cells come into contact with each other.

These molecules play two roles. First, they are negatively charged on the outside and thus repel the adjoining cells, helping to push the tightly packed cells apart. Second, they organize other molecules, known as actin filaments that help give the cell its shape and structure. As the lumen forms, the cells must, of necessity, change their shape to allow the tube to form.

This discovery is a major step forward in our understanding of how the circulatory system develops.

How Fat Expands

The second paper is published by Fabio Rossi and his team, who specialize in stem and progenitor cells. In this case, they are looking at the progenitors of fat cells - adipocytes - and their influence on the relationship between diet and the formation types of different types of fatty tissue. A progenitor cell is like a stem cell but much less versatile. While a stem cell can differentiate into almost any kind of cell in



Dr. Kelly McNagny, Dept. of Medical Genetics/Biomedical Research Centre, UBC

ROB MOSES PHOTOGRAPHY

ZOOMPHOTOGRAPHICS

HSFBCY Funds New Discoveries - cont'd

the body, progenitor cells are themselves more developed and thus more limited in their possibilities, able to develop into only one or a limited number of cell types. Also, stem cells are able to differentiate an unlimited number of times. Progenitor cells, however, have a limited life span.

It is now well known that different types of fatty tissue have different effects on the body. Subcutaneous adipose tissue (SAT) is much less harmful than visceral adipose tissue (VAT). While SAT builds up under the skin, usually around the hips and thighs, VAT develops around the vital organs in the belly. The Rossi study shows that they also build up quite differently under the impact of a high fat diet.

The researchers found that while SAT contained significant concentrations of adipocyte progenitors – that is cells that differentiate into new fat cells – VAT contained virtually none. If that's the case, how and why does VAT get bigger?

It turns out that fatty tissue can expand in one of two ways. *Hyperplasia* involves the multiplication of cells. *Hypertrophy* is the expansion in the size of the existing cells. In the case of VAT, cells get bigger by storing more and more lipids from a high fat diet. In other words, they expand by hypertrophy. This is not the case for SAT. The high concentration of adipocyte progenitors indicates that this type of fat expands by hyperplasia – the production of new cells.

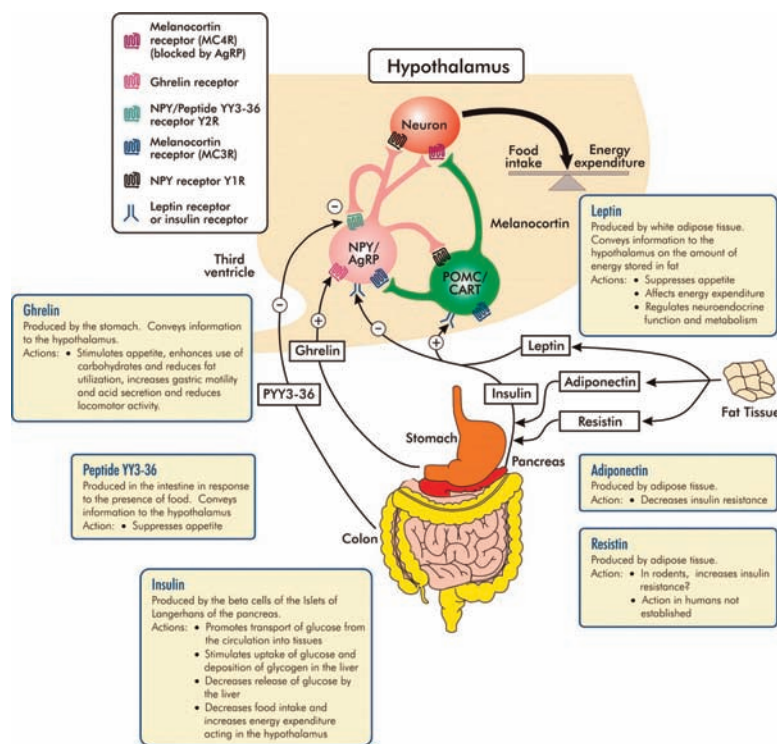
What does this difference mean for health? Adipocytes enable us to store energy for later use. However, they also play a key role in the metabolism by contributing to insulin regulation, and therefore blood sugar balance. One of the reasons that the build-up of VAT is so bad for health is because the expansion of fat cells by hypertrophy, as each cell takes on more and more lipids, impairs their function, throwing the metabolism out of balance. By contrast, adipocytes in SAT remain smaller and retain their metabolic function.

Although the reasons for this difference in the mechanism of expansion between the two types of fat is, as yet, unexplained, Rossi's group has made an important breakthrough in our understanding of how fat helps regulate metabolism and how obesity contributes to metabolic disorders.

¹ American Heart Association. *Heart, How It Works*. Accessed online on 26 Feb. 2010: <http://www.heartsources.org/presenter.jhtml?identifier=4642>.

² Boris Strlic, et al, 2009. *The molecular basis of vascular lumen formation in the developing mouse aorta*. *Developmental Cell* 17: 505-515.

³ Aaron WB Joe, et al, 2009. *Depot-specific differences in adipogenic progenitor abundance and proliferative response to high-fat diet*. *Stem Cells*, 27: 2563-2570.



Tea to Protect Against Stroke?

There's been much talk in the past few years about the healthful effects of drinking green tea. Apparently, it's more than just talk. A group of UCLA researchers found a clear association between tea consumption reduced risk of stroke using a meta-analysis. A meta-analysis is a study in which the researchers reassess the data gathered in other studies and then compare the differences and similarities. In this case, they used rigorous statistical methods to identify the variation between the different studies.



The researchers looked at 10 studies from six different countries – Japan, Finland, the Netherlands, the US, Australia, and China – all of which have different tea-drinking habits, not to mention different ranges of lifestyles and socio-cultural conditions. Despite these differences, drinking three or more cups of tea per day was linked in all the studies to a lower risk of stroke. This reduced risk applied regardless of the kind of tea consumed. Black tea was just as effective as green tea. The link held across the different countries as well, so it's not an effect of society or culture, diet or level of physical activity or different rates of income inequality, in any particular country.

At this point, we don't know the mechanisms by which tea affects stroke risk. The authors cite three possibilities. Animal studies have shown an inverse relationship between blood pressure and tea drinking. However, clinical studies in humans have not supported this conclusion.

A second possible link is through the active ingredient in tea, molecules known as catechins. Animal models have shown that catechins block increases in nitrous oxide in the blood. Too much nitrous oxide damages the arteries.



Tea Fields

Yet another possibility is the presence of an amino acid, theanine, in tea. Theanine is able to cross the blood-brain barrier and contains glutamate, a key neurotransmitter. During stroke, the over-production of glutamate is a key factor in the cascade that leads to brain damage. However, evidence points to theanine having a protective effect during stroke, limiting the extent of damage caused by an arterial blockage.

A key shortcoming of the research they examined is that none of the studies involved a randomized controlled trial (RCT), comparing a randomly selected group of people who drank tea with another, and similar group of people who drank no tea. Instead, most of the studies involved comparisons of tea-drinkers with the general population. RCTs provide the best evidence of causal relationships, rather than simply an association between two things, like tea drinking and level of stroke risk.

More on Fructose



Choose your sugar wisely

In the last Research News Review, we looked at a clinical study that shows an association between fructose consumption – especially high fructose corn syrup – and hypertension. Now another clinical study points to a link between fructose and metabolic disorders.¹

The study compared two groups of people who were already overweight or obese. One group consumed fructose-sweetened drinks while the other group consumed glucose-sweetened drinks. Fructose and glucose are the two major simple sugars in the

North American diet. Beverage consumption was adjusted for each person in the study to provide 25% of energy requirements over a period of 10 weeks.

The results were very interesting. Individuals in both groups experienced weight gain. However, only the people consuming fructose-sweetened beverages had significant increase in visceral adipose tissue (VAT). This is the 'bad' fat that forms around vital organs in the belly and is linked to metabolic syndrome. Adipose, or fatty tissue is now understood to be a key element in the hormonal system. It is the source of adiponectin, a protein that is vital for a number of things including the regulation of blood sugar. But the more adipose tissue you have, the less adiponectin your body makes, throwing your metabolism out of kilter.

The fructose group also saw increased production of lipids – LDL cholesterol – and triglycerides, both of which are key elements in atherosclerosis. As well, the people who drank fructose beverages saw a decline in their insulin sensitivity, a key feature in the development of type 2 diabetes.

About 250 million kilograms of fructose are produced annually, much of which is derived from corn syrup. As noted in the last article on fructose, corn syrup and its derivatives are central elements of the food system.

This was a very small study – 32 people – and needs to be replicated with a much larger group of participants. However, it raises some important questions that will be followed-up with more studies.

¹ Kimber L. Stanhope, et al, 2009. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. *The Journal of Clinical Investigation*, 119: 1322-1334.

Putting a Toll on Atherosclerosis

Researchers from Imperial College London have identified a key role for an immune system protein in promoting atherosclerosis.¹ Toll Like Receptor 2, or TLR-2, sits on the surface of cells and recognizes certain types of harmful bacteria, viruses, and other substances that come into contact with the cell.

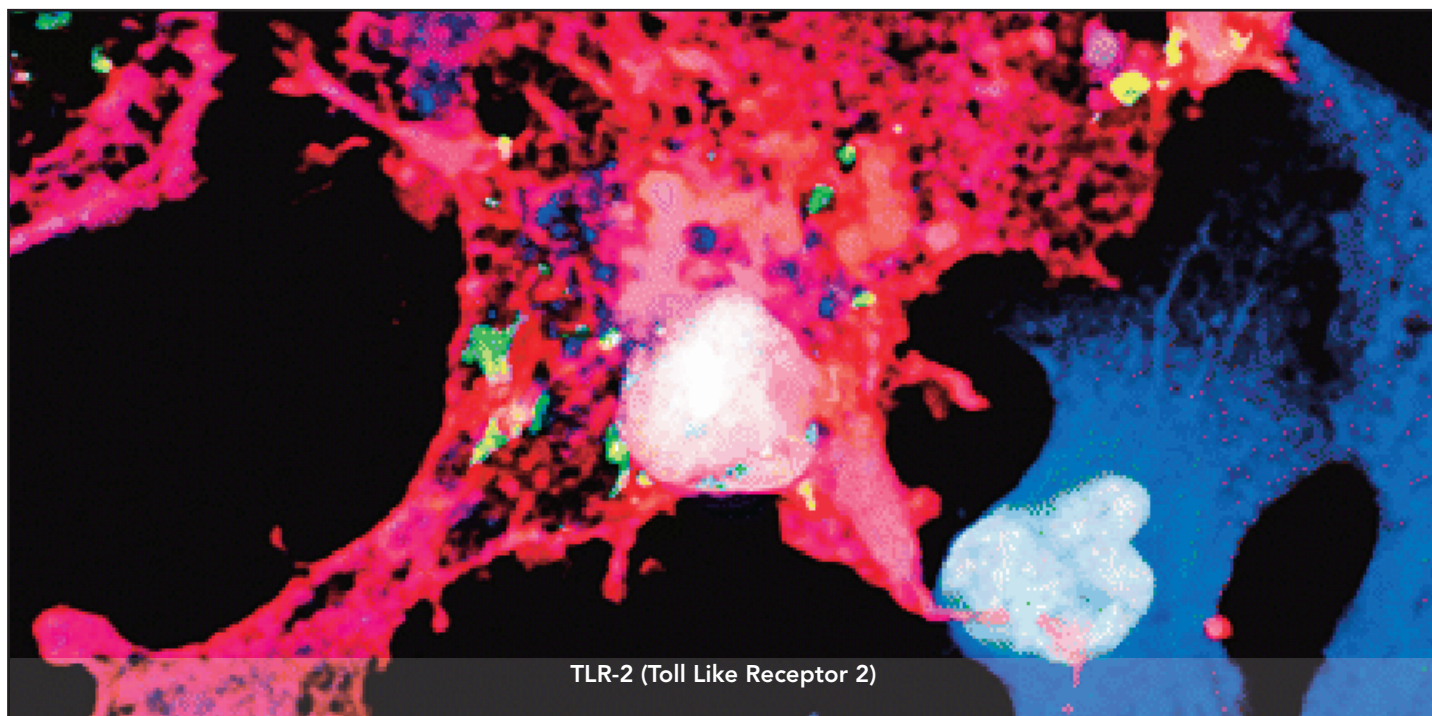
In normal conditions, TLR-2 then signals other immune proteins and cells – or antibodies – to come and deal with these pathogens. When these immune proteins are activated, they promote increased flow of blood to the affected area as blood vessel walls become permeable so the proteins can move into the tissue. As a result, the tissue becomes inflamed.

Inflammation is a sign that your immune system is responding to an injury or infection, as proteins eliminate pathogens and/or dead tissue and repair any damage. Without it, wounds would never heal. But if inflammation becomes chronic or long-term, the immune system is constantly activated in a particular area and the tissue there is never totally repaired. Instead, it's always irritated and swollen.

Chronic inflammation of the interior walls of the arteries is a key feature of atherosclerosis. Inflammation occurs simultaneously with the accumulation of lipids (cholesterol) in the artery wall. The development of atherosclerotic lesions is marked by the ongoing presence of certain kinds of immune system proteins. Markers of inflammation are now also implicated in hypertension and other cardiovascular conditions.

The London researchers decided to look at the immune system side of atherosclerosis rather than the cholesterol side. They found that atherosclerotic lesions contained a high concentration of TLR-2 proteins. By blocking the production of this protein, they were able to stop the recruitment of antibodies. This research shows it may be possible to halt or delay the progression of atherosclerosis by blocking TLR-2 and preventing inflammation in affected arteries.

¹ Claudia Monaco, et al, 2009. Toll-like receptor-2 mediates inflammation and matrix degradation in human atherosclerosis. *Circulation*, 120: 2462 – 2469.



Sitting Down Can be Hazardous for Your Health

Many of us here at the Heart and Stroke Foundation spend a lot of time at our desks. In fact, a large proportion of the population spends much of its working days sitting down. So it's interesting to note that a study from a US-Canadian group of researchers on over 17,000 Canadians found that the greater the amount of time spent sitting down on a daily basis, the greater the risk for premature mortality, even for people who are otherwise physically active.¹ Since much of our workforce is office-based and largely spends its working time sitting down, this is a bit of a problem.

Extended periods of sedentary behaviour apparently cause the body to process lipids and sugars differently than it does when it is more active over longer periods of time. But even if you exercise on a regular basis, long periods spent sitting down are detrimental because of these differences in lipid and glucose metabolism.

That's why a group of researchers at the University of California, San Diego, has developed an 'active desk' to get people moving while they are working at their desks.² The desk

is composed of a treadmill with a desktop set for standing level work mounted over it. Turn on the treadmill at a slow walking pace and, viola, you can keep moving while you work at your computer. Ernesto Ramirez, the PhD candidate who invented the active desk says that:

"Being sedentary for long periods of time is a very new thing for humans from an evolutionary perspective. Our approach is to change people's environment so it's easy to get them moving. We spend eight to 10 hours per day sitting in front of computer, so why not spend some of that time walking?"

The active desk was put together with a US\$200 piece from IKEA and a US\$100 treadmill. Although brand new treadmill-desk combinations are available, they cost \$2,500-\$11,000 a piece.

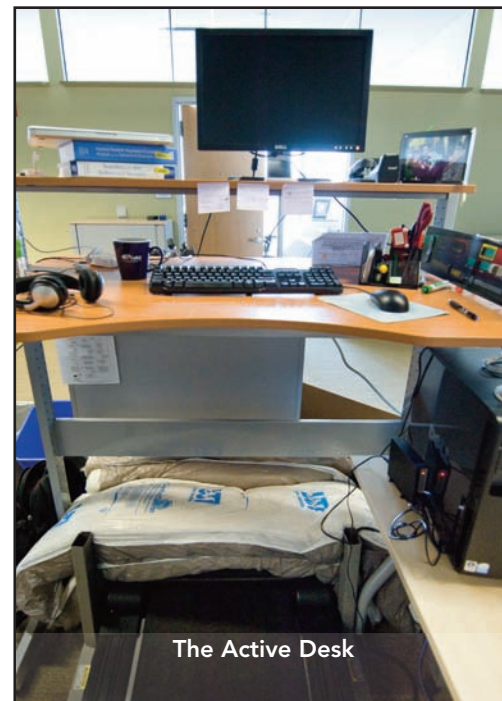
Ramirez's average speed on the treadmill is 1.5 mph, which is enough to burn 2.54 calories per minute. He's teaming up with a medical researcher to see if the active desk is a feasible alternative to the current sit-down office regime.

¹ Peter T. Katzmarzyk, et al, 2009. *Sitting time and mortality from all causes, cardiovascular disease, and cancer. Medicine and Science in Sports and Exercise*, 41: 998-1005.

² Tiffany Fox, 2009. *Active Desk Aims to Get Office Workers Up and Moving. UC San Diego News Centre, November 12. Accessed online Mar. 10, 2010 at <http://ucsdnews.ucsd.edu/newsrel/general/11-09ActiveDesk.asp>.*



Ernesto Ramirez works on the computer using his new invention, The Active Desk



The Active Desk

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