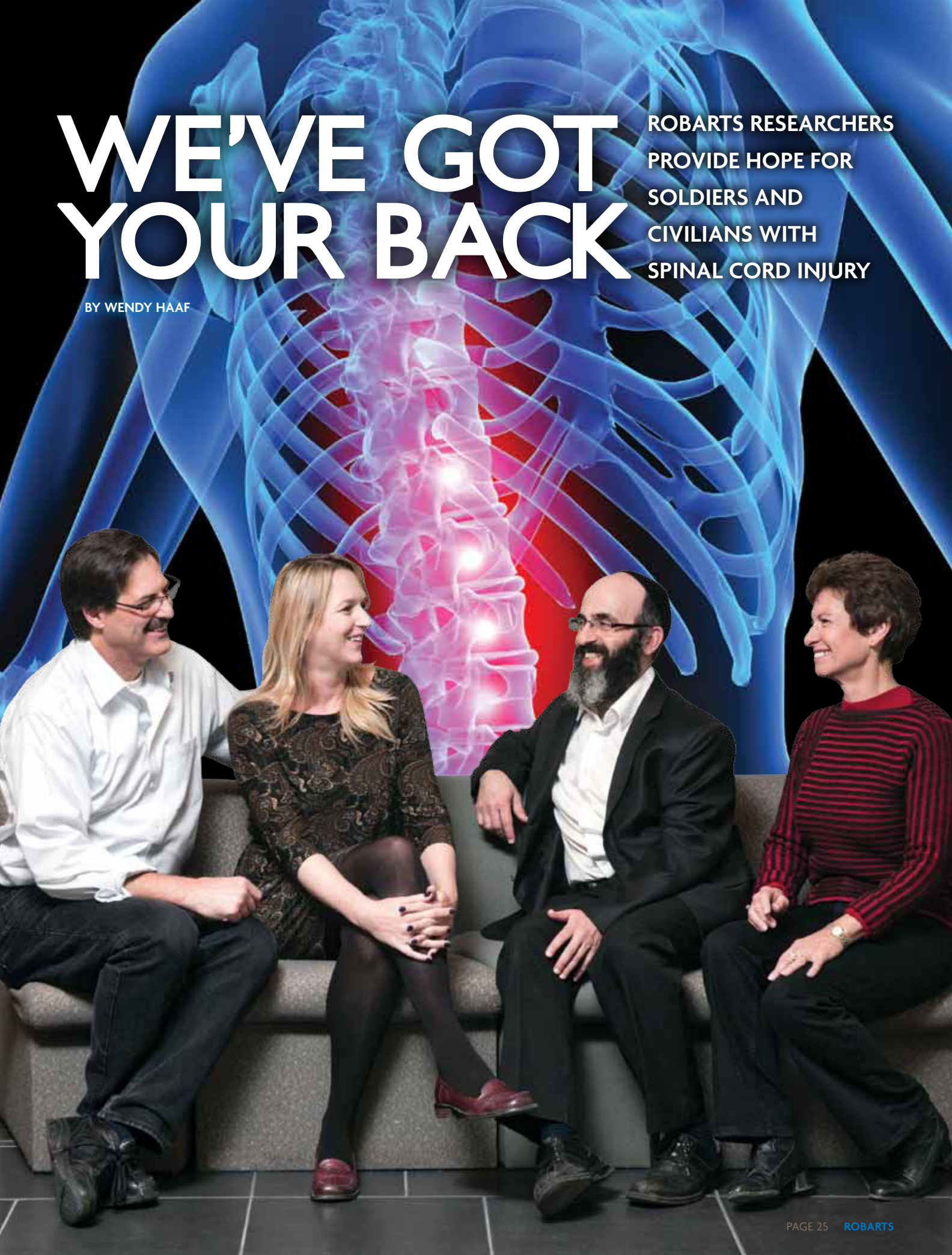
WE'VE GOT YOUR BACK

ROBARTS RESEARCHERS PROVIDE HOPE FOR SOLDIERS AND CIVILIANS WITH SPINAL CORD INJURY

BY WENDY HAAF



PICTURED ABOVE: Greg Dekaban (top) and Lynne Weaver with colleague Dr. Feng Bao (bottom)

After being blown onto his back in an IED explosion, a soldier is still able to wiggle his toes in the ambulance, but three days later, his legs are paralyzed. Thanks to the tireless efforts of four Robarts scientists, most recently supported by grants totalling more than $1.9 million from the United States (US) Department of Defense (Congressionally Directed Medical Research Program) and the US Naval Medical Research Centre, someday, such stories could end a good deal more happily.

Soldiers and sailors will not be the sole beneficiaries; if the research continues to live up to its promise, the findings could also change the lives of the tens of thousands of civilians per year who sustain similar injuries in Canada and the US.

In the first 72 hours following a spinal cord injury, immune cells, principally monocytes and neutrophils, flood the site killing many neurons that were not affected by the original insult. "As the damage spreads up the cord, you can go from a small injury to something that has wide-ranging effects," explains Greg Dekaban, PhD, a Robarts scientist in the Molecular Brain Research Group and professor in the Department of Microbiology and Immunology at Schulich.

A similar process, involving neutrophils, also appears to occur when the spinal cord is damaged by decompression sickness (the bends) – hence the interest of the US Navy. Being able to halt this process, thereby preventing so-called secondary injury, could make the difference either retaining bowel and bladder control, or being able to continue to enjoy sexual intimacy. After 15 years of work, the spinal cord injury research team at Robarts is closing in on that goal.

"THE SOONER TREATMENT OCCURS, THE GREATER AMOUNT OF FUNCTION THAT'S LIKELY TO BE PRESERVED." LYNNE WEAVER

"We started from just understanding some of the basic behaviour of these blood cells," notes Dr. Lynne Weaver, a Robarts scientist and professor emeritus, who is still actively involved in the project. Weaver and Dekaban were aided in their efforts by Robarts scientist Paula Foster, PhD, whose expertise in cellular MRI enabled them to sequentially track, in live animals, the movements of the white blood cells that turned out to be primarily responsible for secondary injury – neutrophils and monocytes.

With cellular MRI, iron nanoparticles are injected into the bloodstream, where they are engulfed by these cells. The iron causes a distortion in the main magnetic field, causing the cells – which show up as black areas – to appear 100 times larger than normal.

"We can take multiple images over time, and see where cells in the cord accumulated, and when," explains Foster. "We can also measure the 'blackness', and relate that to the number of cells." The hardware and software that make all this possible were developed by Foster and other collaborators.

The research team has also used this technology to test a particular mouse antibody in an animal model and is working with a company to 'humanize' the antibody, making it suitable for human trials. Administered intravenously, the antibody locks onto CD11d, a protein on the surface of cells. CD11d is a 'passkey' the cells require to enter the spinal cord and organs; blocking it prevents them from doing so.

"We've shown this treatment really improves outcomes in a variety of models of spinal cord injury," says Weaver. "Not only does it spare neurons, thus preserving function, when we block inflammation with our drug, the animal model develops much, much less neuropathic pain, which is a common consequence of spinal cord injury."

For his part, Arthur Brown, PhD, a principal investigator at Robarts, has unravelled the antibody's impact on genes that regulate various aspects of inflammation. "There's a bad part of inflammation that you want to mitigate, and there's a good part, that if you're specific enough in your therapy, you don't get in the way of," notes Brown. Put simply, the treatment does just that, down-regulating the 'bad guys' and up-regulating the 'good guys'.

This pinpoint precision also appears to render the therapy very safe, which, combined with the fact it's delivered intravenously, means it could potentially be administered on-scene by medics or emergency personnel.

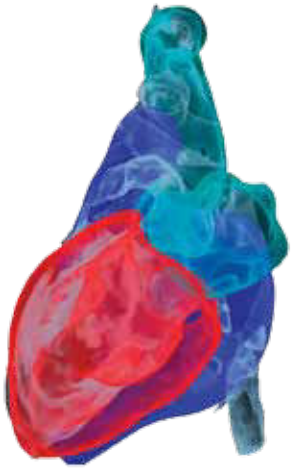
"WE CAN TAKE MULTIPLE IMAGES OVER TIME, AND SEE WHERE CELLS IN THE CORD ACCUMULATED, AND WHEN." PAULA FOSTER

"The antibody isn't something that, in our experience, is likely to cause harm, even if it were given as a false alarm now and again," says Weaver. "And the sooner treatment occurs, the greater the amount of function that's likely to be preserved."

Even sparing 10 per cent of the nerve fibres in a particular pathway involved in controlling leg muscles (the amount needed to support function) could make a world of difference to the futures of the 85,000 North Americans per year – most of them young, otherwise healthy men – who suffer spinal cord injuries. "A lot of people in wheelchairs don't care whether they walk again; they want to be able to feed themselves, or have some kind of continued marital relationship," says Weaver.

Although treatment for acute spinal cord injury remains an unmet medical need, thanks to continuing research being conducted at Robarts, and elsewhere in the world, there is indeed hope for improved neurological outcomes that will in turn lead to an enhanced quality of life for thousands of people currently living with the challenges imposed by these severe injuries.

PICTURED ABOVE: Paula Foster (top) and Arthur Brown (bottom)

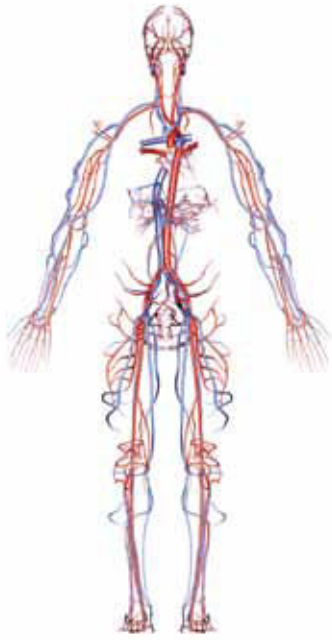


CARDIAC IMAGING BREAK-THROUGH FOR PATIENTS

September, 2010 – A new imaging technique providing a single, 3D high-resolution image of the heart could improve outcomes for patients requiring pacemakers, bypass surgery or angioplasties. For his study, **Dr. James White** used the 3-Tesla MRI to obtain the innovative imaging, revealing both its vasculature and the presence of scar tissues within the muscle. It works by using a 3D coronary image with continuous infusion of gadolinium, causing the blood-pool to light up brightly. As the contrast is infused, it provides a high-resolution, 3D image of the heart and coronary blood vessels. Twenty minutes later, a repeat image is taken in 3D to highlight the heart's scar. Because these two images are taken in an identical way, using the same MRI pulse sequence, they are perfectly suited for fusion together, creating a 3D image of the heart showing both the vessels and scar tissue.

A CANADIAN FIRST USING STRONGEST MRI

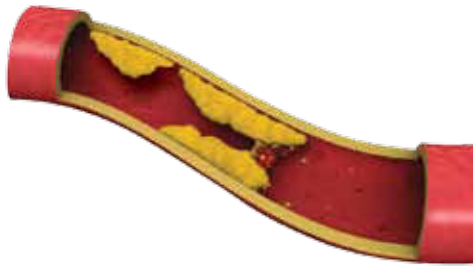
March, 2011 – When compared to common 1.5T MRIs, the 7-Tesla MRI (7T) provides images of the brain with much stronger resolution and contrast. Currently, there are two ongoing studies using Canada's only human 7T MRI. The work of Imaging Scientist **Robert Bartha, PhD**, studies the metabolic and structural changes in the brain in subjects with Alzheimer's disease. Neurologist **Dr. Jorge Burneo**, along with the assistance of Bartha, is scanning patients with temporal lobe epilepsy where a 1.5 MRI failed to locate the origin of the seizure. Working together, the team hopes the 7T scanner will reveal the originating region of the seizures for surgical intervention. This may decrease the need to use intracranial electrodes which carry potential risks for the patient.



SUCCESSFUL STRATEGY TO REGENERATE BLOOD VESSELS

April, 2011 – A developing type of treatment for heart attack and stroke patients is called Therapeutic Angiogenesis. Developed by **Dr. Geoffrey Pickering** and his team, the strategy includes a biological factor, fibroblast growth factor 9 (FGF9), being delivered at the same time the body is making its own effort to form new blood vessels in vulnerable or damaged tissue. The result allows for the formation of highly functional new blood vessels in tissues that are starved for oxygen. FGF9 stimulates the supporting cells of the vessel wall to envelop the newly formed and fragile blood vessel wall, allowing for the regenerating blood vessels to perform strongly, constricting and relaxing to ensure the right amount of blood and oxygen flow to the tissues. The findings were published online in Nature Biotechnology.

RESEARCH RESULTS



JUVENILE DIABETES RESEARCH COORDINATED AT ROBARTS

June, 2011 – Robarts has been named the Clinical Operations Centre (COC) for the Juvenile Diabetes Research Foundation (JDRF) Canadian Clinical Trial Network. This network brings together the country's top physicians, scientists, researchers and innovators to accelerate the development of treatments and a cure for Type 1 diabetes and its complications. Serving as the COC, Robarts will have primary responsibility for activities pertaining to clinical trials conducted by the Canadian Clinical Trial Network (CCTN). Robarts will work with all clinical sites that participate in the Canadian T1D Clinical Trial Network, providing critical services for the design, implementation, oversight and analysis of CCTN-supported clinical trials and associated mechanistic studies. The Clinical Operations Centre will also establish collaborations with existing T1D clinical trial networks.

STUDYING PRION PROTEIN IN PROGRESSION OF ALZHEIMER'S

July, 2011 – Scientist **Marco Prado, PhD**, along with his team of researchers at Robarts, is studying the role prion protein plays in the progression of Alzheimer's disease. The research questions the interaction of the prion protein with amyloid beta, one of the toxins in Alzheimer's. This interaction could be affecting the way neurons function, or even causing their death. Prado's recent work has provided novel evidence for a role of prion protein, however, how signaling by the prion protein influences neurological disorders is still unknown. In support of the project, Prado has been awarded a $600,000 grant from PrioNet Canada to continue research, which could lead to novel therapeutics for neurodegenerative diseases like Prion diseases, Alzheimer's, Parkinson's and ALS.

BETTER DIAGNOSTICS COULD REDUCE RISKY SURGERY

August, 2011 – Using 3D ultrasounds to identify ulcers in the carotid arteries has been discovered to be an effective way to pinpoint the small number of high-risk patients with asymptomatic carotid stenosis (ACS) who would benefit from surgery to prevent stroke. The discovery, made by **Dr. David Spence**, was published online in *Neurology*, the medical journal of the American Academy of Neurology. Spence's 3-year study found that if three or more ulcers were found in the carotid arteries using 3D ultrasound, the patient was at a high risk of stroke and could benefit from medical intervention. This finding is important as it could drastically reduce the number of unwarranted medical interventions on patients with ACS, when most of the patients would be better off with medical therapy treatment, as opposed to surgery.