



...Advancing the Science of Arthritis, Rehabilitation, Bone, Muscle, Skin and Oral Health

Greetings from the Scientific Director: Excellence is all Around Us



Dr. Cyril Frank
Scientific Director

“Improved health for all Canadians, more effective health services and products, and a strengthened Canadian health care system.” In a nutshell, this simple statement

is at the very heart of what CIHR is all about. And building a healthy, robust research environment is at the heart of how we intend to get there.

To achieve this lofty goal, we’ve created a plan that not only enables us to continue supporting innovative, independent research but also gives us the flexibility to fund strategic research initiatives – the Request for Applications (RFA) program. As it turns out, this program has become a very instrumental part of our plan demanding that we continue to build relationships and work closely with all our stakeholders to identify and address some of the most pressing health issues of the day.

Overall, we believe that our plan is a solid one. However, it would not be complete if it did not also include a mechanism

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IMHA’s Quality of Life Research Awards

recognizing the persistence and patience of investigator-initiated research

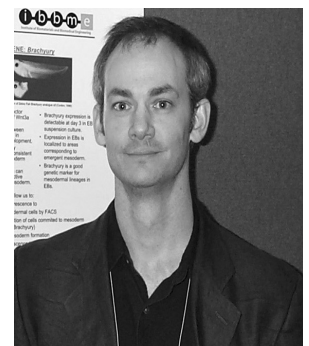
Outstanding research and excellent researchers are two of the five “Outcome Categories” that CIHR has identified as being critical to its success. And so, in 2003, IMHA established an awards program – the Quality of Life Research Awards - to recognize investigator-initiated research efforts that focus on diseases and conditions of the musculoskeletal system.

In March, IMHA was pleased to announce the winners of its 2004 awards competition - Dr. William Stanford (IMHA’s overall award winner), Dr. Harvey Goldberg, Dr. Pierre Borgeat, Dr. Klaus Wrogemann, Dr. Nicholas Mohtadi and Dr. Bing Siang Gan. Each of these award winning research initiatives (showcased below) provide an excellent example of how mature research can create a foundation of knowledge that is sure to lead to a better future for those suffering from a broad array of diseases and conditions of the skin, teeth and musculoskeletal system. A more lengthy series of interviews with each award winner will be featured over the course of the year under our “Spotlight on Research” feature on our website

Dr. William Stanford, University of Toronto

The Role of Stem Cell Antigen-1 (Sca-1) in Bone Development and Homeostasis

Reduced bone mass associated with arthritic conditions can lead to increased risk of fractures, deformation, collapse of joint surfaces,



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for recognizing the very excellence we encourage and support. And so, in this special “awards” issue of *IMHA On The Move*, we are very pleased to share with you some shining examples of the excellent research that is going on all around us.

At our stakeholders forum in March, we were pleased to announce the six winners of IMHA’s 2004 Quality of Life Research Awards – research initiatives that cover the gamut from a potential model for age-related osteoporosis to a potential diagnostic DNA test(s) for rare forms of muscular dystrophy.

For the second year running, IMHA was a proud sponsor of the Canada Wide Science Fair. This year, our Quality of Life “Student” Research Award was presented to a research “duo” - two exceptional students whose interest in science led them to explore the medicinal properties of green tea resulting in the creation of a cream that is both a sunscreen and a skin rejuvenator “Tea-riffic Skin”.

Also, for a second consecutive year, IMHA was pleased to collaborate with the Canadian Association of Dental Research (CADR) to sponsor the annual CADR-IMHA Student Research Awards. Selected by a panel of 12 leading oral health researchers from across the country, four trainees working in dental and oral health research received their award at the CADR’s business meeting in early March.

In keeping with our “Physical Activity, Mobility and Health” theme, IMHA welcomed the

opportunity to become a sponsor of the 2003 SIRC Research Awards. The Sports Information Resource Centre (SIRC) leads the world in providing sport, fitness and sports medicine information through its bibliographic database SPORTDiscus. This year, to celebrate its 30-year history, SIRC created an award to recognize innovative sports research that is changing the world of sport.

Although it was not our award to give, we are extremely proud that CIHR saw fit to present its inaugural Partnership Award to one of our major stakeholders – The Arthritis Society (TAS). Under the outstanding leadership of TAS President Denis Morrice, also a member of IMHA’s Board, TAS has become a true model of what partnerships can achieve and should be recognized for its tremendous contribution to health research and to the betterment of all Canadians.

Whether we created the awards program or simply collaborated with others, what’s really important is that we’re making an effort to recognize our researchers. Unfortunately, it’s only the tip of the iceberg, for research excellence is truly all around us. Still, it’s a start. And it’s my most sincere wish that these programs will serve as a signal that we appreciate the efforts of all IMHA researchers who are laboring to improve the quality of life of Canadians. Please read on and be amazed! ■

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and the inability to affix implants to bone surfaces. The further weakening of bone brought on by osteoporosis only complicates these risks and can even increase morbidity. Genetic analysis of bone development in the mouse, however, has not only begun to shed light on normal skeletal development, but pathologies like osteoarthritis and osteoporosis as well.

Dr. William L. Stanford and his colleagues have determined that mice lacking a protein known as Sca-1 exhibit age-related osteoporosis. “We think the stem cells in these mutant mice are taking the pathway of differentiation more often than the path of self-replication,” says Stanford. “The pool of stem cells diminishes as the mice age, not because of an aging phenomenon, but really due to a loss of stem cells as they divide”.

Stanford’s goal is to study the role of Sca-1 in bone development, to determine how age-related skeletal defects are affected by the loss of this protein. The cellular basis of osteoporosis in a mouse deficient of this stem cell protein will also be examined to determine the functional role of the protein in human cells. Currently, there are few good aging models for any disease. Hopefully, Dr. Stanford’s research will uncover at least one pathway leading to osteoporosis and osteopenic disorders, resulting in new diagnostic, prognostic and/or therapeutic strategies.

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The Arthritis Society receives CIHR Partnership Award

advancing arthritis knowledge and treatment

In large part, the very foundation of CIHR’s success rests heavily upon its ability to form solid partnerships with a broad range of stakeholders – stakeholders who bring tremendous value to the work of CIHR because they too are in the process of shaping the future of health care. The Arthritis Society (TAS) is an excellent example of such an organization, and the deserving recipient of CIHR’s 2003 inaugural “Partnership Award”, created to recognize the outstanding contribution partners are making in helping CIHR achieve its goals.

In accepting the award at the “Celebration of Excellence in Health Research” dinner on March 16, Denis Morrice, president of The Arthritis Society, noted that, “building relationships with the medical and scientific communities, industry and patient groups is a fundamental part of the Society’s strategy to meet the needs of people and move the arthritis agenda forward.”

Working closely with the Institute of Musculoskeletal Health and Arthritis (IMHA), The Arthritis Society has worked to create a network of those involved in arthritis research including funders, researchers and patients. In 2002, TAS jointly sponsored the first international Osteoarthritis Consensus Conference. This Conference not only resulted in a



TAS President Denis Morrice proudly accepts CIHR’s inaugural Partnership Award at the “Celebration of Excellence in Health Research” dinner. (from left to right: Monique Begin, Denis Morrice and Dr. Cy Frank)

\$5.5 million investment in osteoarthritis research, but the creation of the Alliance for the Canadian Arthritis Program (ACAP) - a program that now provides a forum for stakeholders to address issues of research, education and access to care.

TAS also played an instrumental role in the creation of the Canadian Arthritis Network (CAN). The first disease-specific national centre of excellence, CAN unites arthritis researchers from across the country.

TAS’ contribution to CIHR, however, goes far beyond being a partner. They have also been a valuable role model for many other things including their comprehensive web site, CIHR’s Common CV module and recently released Blueprint.

“TAS should be recognized as a role model for its overall contribution to the advancement of health

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Inquiring Minds

student award winners up for a creative challenge

If you're keen to compete, then the world is full of possibilities. That seems to be the philosophy the co-winners of IMHA's 2004 "Quality of Life Student Research Award", Ronan Macparland and Sarah Small, have embraced wholeheartedly. The grade-eleven students from St. John's who received the award at the Canada Wide Science Fair (CWSF) in May, are already seasoned performers in national music competitions. For instance, Ronan sang an operatic aria in his audition for TV's *Canadian Idol* talent contest and made it to the finals in Toronto.

"When we do things like music, we get really involved and use our creative abilities," says Ronan. But when it came to science, they were searching for something more exciting. And then they found out about the Aventis Biotech Challenge, a school outreach program that introduces students to the real world of biotechnology by carrying out research projects of their own design. Entrants receive \$200 seed money and are assigned a scientific mentor to help frame the project. "We both said it was something we had to do," says Sarah, "because we're always looking for a challenge."

Their early thinking was to devise a use for some household-waste item that is normally tossed out. "We wanted to do something that was good for the environment, as well as good for society," says Ronan. "My mom's British, so we drink a lot of

tea in my house," which means a lot of used tea bags making their way to the trash. That observation led to a literature search about the medicinal properties of green tea. And with the help of their mentor — Dr. Christina Bottaro, a chemist at Memorial University — the two students decided to extract polyphenols from green tea that were deemed to have biological activity.

Using hot and cold ethanol extraction techniques on different brands of green tea, Ronan and Sarah blended the resulting compounds with a topical-cream base and then subjected the mixture to a number of tests. "We have a cream," says Sarah, "that's a hundred-percent UV absorbent. It's non-mutagenic, and it's a better anti-oxidant than vitamin C." Entering their combination sun screen and skin rejuvenator into the Challenge in May under the brandname, "Tea-riffic Skin," the two were thrilled to win an award for "greatest commercial potential."

Since then the awards have been piling up. In addition to IMHA's Quality of Life Student Research Award, Sarah and Ronan have won a silver medal in their division and category at the Canada Wide Science Fair, a Manning Innovation Achievement Award and a number of other honours. What's more, Memorial University's commercialization arm, the Genesis Group, is analyzing the cream's patent and market potential.



Ronan Macparland and Sarah Small show off a sample of their award-winning "Tea-riffic Skin" at the Canada Wide Science Fair.

"We never dreamed of winning the biotech challenge — let alone even going to the Science Fair nationals," says Ronan. "We just wanted to prove to ourselves that we could do this project well. The Institute's award, and all the others, have really encouraged us to continue in the future." ■

CIHR Partnership Award continued from page 3

research as well as improving the health of Canadians," said IMHA's scientific director, Dr. Cy Frank. "It has demonstrated results that could never be achieved by individuals acting alone. It has gained a reputation for its mutual trust, respect and commitment and has maximized the strengths and assets of each of its partners. TAS has proven itself to a true equal partner and a leader in advancing arthritis knowledge and treatment in Canada." ■

Dr. Harvey
Goldberg,
University of
Western Ontario
*Functional
Characterization of
Bone Sialoprotein*



Mineralized tissues like bone are comprised of type I collagen and a variety of non-collagenous proteins believed to have specific roles in the mineralization process. Bone sialoprotein (BSP) is associated with early mineral deposition in normal and pathological mineralization processes. It has also been shown to mediate bone-cell attachment, an activity that is important for both the formation and resorption (turnover) of mineralized tissues.

“Mineralization of soft connective tissues occurs in certain tumours, which cancer researchers believe is due to the presence of BSP,” says Dr. Harvey Goldberg. “It appears that many breast and prostate tumours produce BSP, which allows them to target to and colonize bone.” Over the past ten years, Dr. Harvey Goldberg and Dr. Graeme Hunter have focused on understanding how bone sialoprotein functions. The first to show that bone sialoprotein is a potent stimulator of bone mineral formation, Goldberg and Hunter have also characterized the general characteristics of the sites within the protein involved in this activity and those sites critical in binding to collagen.

Using a combination of site-directed mutagenesis, peptide synthesis and functional analysis in vitro and in vivo, Goldberg and Hunter intend to define the precise active sites involved

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NIH Launches Osteoarthritis Initiative

seeking new biological markers for osteoarthritis

In March 2004, the National Institutes of Health (NIH) announced that recruitment had begun for the Osteoarthritis Initiative (OAI), a public-private partnership between the National Institutes of Health and industry that will fund a multi-site contract to create a resource to hasten the discovery of biological markers for osteoarthritis.

Osteoarthritis is a degenerative condition whose hallmarks are joint pain and limited movement resulting from progressive loss of cartilage. It is the most common type of arthritis, especially among older people, and can occur in any joint, but most often affects the hands, knees, hips or spine. There are currently no treatments, other than surgical joint replacement, that significantly change the course of this disease, and clinical trials for new therapies are long, difficult and expensive.

Men and women age 45 and older at risk for developing OA, and those with early diseases, are eligible to participate in the OAI study. After initial screening, four centers around the United States plan to each enroll and follow 1,250 adults for five years (total enrollment of 5,000). Biological specimens (blood, urine, DNA), images (X-rays and magnetic resonance scans) and clinical data will be collected annually.

Biological markers – physical signs or biological substances that indicate changes in bone or cartilage- are critical in diagnosing and monitoring OA and developing new treatments. Ultimately, results from the OAI initiative may enable doctors to use biological markers to help identify people at risk for OA and people with OA at risk for disease progression. The markers could also help doctors assess the effectiveness of treatments.

The four clinical centers, selected in the summer of 2002, include the University of Maryland School of Medicine/Johns Hopkins University, the Ohio State University Medical Center, the University of Pittsburgh and the Memorial Hospital of Rhode Island/Brown University. A data coordinating centre at the University of California, San Francisco oversees the study conduct and will manage the resulting data. The Ohio State University and University of Pittsburgh centers enrolled their first participants the week of February 23, and centers in Maryland and Rhode Island began enrollment in late March and early April.

For further information on the OAI, please visit: *The OAI: A Knee Health Study* at <http://www.oai.ucsf.edu/clinics.asp>

in mediating the collagen-associated mineral nucleation and determine the mechanism of how bone sialoprotein elicits cellular events. Through their efforts, important information on the fundamental mechanisms of bone mineralization will be unveiled that could lead to the development of therapeutic agents and the integration of dental and orthopaedic implants.

Dr. Pierre Borgeat, Centre hospitalier de l'Université Laval

Leukotrienes, Lipoxins and Platelet-Activating factor: Assessment of Biological Significance in Neutrophil Trafficking



Inflammation is a complex process essential in helping the body defend itself against microbial invasion. In many inflammatory diseases such as arthritis, however, inflammation becomes chronic leading to progressive joint erosion. White blood cells (leukocytes) play an important role in the inflammation process. Neutrophils, the most abundant type of white blood cell, are usually the first to arrive in large number in inflamed tissue.

Whether they are involved in an inflammatory disease or simply defending the body from a foreign substance, white blood cells must cross through blood vessel

walls into tissues. This migration from blood to tissues is a crucial event in inflammation, and scientists believe that controlling their movement could represent a more efficient means of controlling inflammatory diseases.

Dr. Pierre Borgeat, from the Centre hospitalier de l'Université Laval and his colleague Dr. Sylvie Marleau at l'Université de Montréal, are working to define the role of molecules called inflammatory lipids that might play a critical role in the regulation of white blood cell migration into tissues. Dr. Borgeat's research promises to create a better understanding of inflammation, unravel the mechanisms involved in regulating leukocyte movement, and lead to the development of novel new approaches in treating inflammatory disease.

"The focus in treatment of rheumatoid arthritis recently," says Borgeat, "has been on these very expensive, high-tech biologics. These are very good drugs. But are they going to be used on a large scale in the future? Perhaps. I'm not so sure. It will depend on their cost and tolerability. I suspect that combination antagonists to mediators of inflammation would be cheaper."

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HIGH DEFINITION

population study brings osteoporosis into sharp focus

"The idea that you reach peak bone mass and maintain it for a variable but significant period of time is probably exaggerated," says McGill University endocrinologist Dr. Alan Tenenhouse, co-principal investigator for CaMos (Canadian Multicentre Osteoporosis Study). "I think you have to assume that bone loss, as measured by bone densitometry, begins very soon after peak bone mass is reached."

If Tenenhouse can speak with any degree of certainty, it's because of the enormous wealth of data he and epidemiologist Dr. Nancy Krieger (now co-PI), as well as colleagues at nine clinical centres across Canada, have collected over the years. "We have a data base that contains seven years of follow-up," says Tenenhouse. "It started with just over 9400 men and women aged 25 or older, selected at random. We have five-year cohort retention of better than 85 per cent, which is quite astounding."

Up to 1500 variables can be attributed to each study participant, including bone-density measures of spine and hips, as well as spine X-rays in people aged 50 or more. Serum, urine and DNA samples have also been collected from a subset of the cohort for study of factors related to bone health, osteoporosis and fracture. What's more, quality-of-life measures have been routinely taken throughout the study. Some preliminary observations from the CaMos data bank suggest that peak bone mass occurs at an earlier age than thought, that the prevalence of

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Annual CADR-IMHA Student Research Awards

student investigators take oral health research in new directions

On March 11, 2004, The Canadian Association for Dental Research and the Institute of Musculoskeletal Health and Arthritis (IMHA) came together to recognize excellence in oral health research presenting the CADR-IMHA Student Research Award to four deserving students at the CADR business meeting in Honolulu. The two first place winners also represented Canada in the international Hatton Awards Competition at the annual meeting of the International, American and Canadian Associations for Dental Research held in Honolulu, Hawaii in March 2004.

Trainees working in dental and oral health research in Canada were eligible to apply for a CADR-IMHA Student Research Award by submitting a manuscript describing their studies. Winners were selected by a panel of 12 leading oral health researchers from across Canada.

The Canadian Association for Dental Research and the Institute of Musculoskeletal Health and Arthritis would like to take this opportunity to recognize the following award winners:

Junior Award Winners

Mr. Houman Nourkeyhani, a York University science student, was awarded first place in the Junior category. His research project entitled "Molecular cloning and characterization of the human osterix (SP7) gene" was conducted at the University of

Toronto under the supervision of Dr. Bernhard Ganss. Mr. Nourkeyhani's research is related to the genetic regulation of bone formation in humans. He is presently pursuing graduate studies in the Faculty of Dentistry at the University of Toronto,

Mr. Craig C. Humber, a student in the University of Saskatchewan's DDS program, received second place in the Junior category and conducted his research under the supervision of Dr. Richard Ellen at the University of Toronto. Mr. Humber's study entitled "Chymotrypsin-like peptidase and prtP gene expression in *Treponema denticola* biofilms" focused on the role of this pathogenic bacterium in periodontal disease. Craig's research at the University of Toronto was made possible by a summer studentship from "NORTH", a CIHR strategic training program.

Senior Award Winners

Ms. Dilani Senadheera, a PhD student at the University of Toronto, Faculty of Dentistry received first place in the Senior category. She conducted her research under the supervision of Dr. Dennis Cvitkovitch. Her paper entitled "Streptococcus mutans covR/S genes control adhesion, biofilm formation and competence" focused on the role of the bacterium *S. mutans* in the development of dental caries. Dilani is supported by a fellowship



This year's 2004 CADR-IMHA Student Research Award Winners were selected from a panel of 12 judges. (from left to right: Craig Humber, Dilani Senadheera and Houman Nourkeyhani)

from the "Cell Signals" CIHR strategic training program.

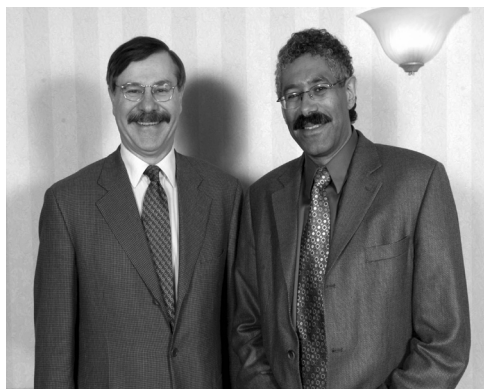
Dr. Vinay Bhide from the MSc (Periodontology) program at the University of Toronto was awarded second place in the Senior category. Dr. Bhide conducted his research under the supervision of Dr. Christopher McCulloch at the University of Toronto. Dr. Bhide's research, "Decorin regulates collagen binding and internalization by fibroblasts" investigated the control of connective tissue turnover by collagen synthesis and degradation. ■

Frontiers in Inflammatory Joints Diseases Conference

stakeholders collaborate to reduce the impact of inflammatory joint diseases

Leading medical researchers, clinicians, policy makers, consumers (patients) and industry representatives gathered in Toronto from May 7 – 9, to identify research priorities for inflammatory joint diseases. Today, more than four million Canadians suffer from arthritis, and approximately 300,000 of these people have their quality of life impacted by the most devastating types of arthritis—inflammatory joint diseases.

Hosted by The Arthritis Society (TAS), The Canadian Arthritis Network (CAN) and the Canadian Institute of Health Research's (CIHR's) Institute of Musculoskeletal Health and Arthritis (IMHA), the conference proved to be an effective means of identifying patient-centred research priorities, strengthening existing partnerships and building new networks.



The FIIJD Conference was co-chaired by Dr. Robert Inman and Dr. Hani El-Gabalawy.

Participants included 38 consumers and parents of children who have been diagnosed with this debilitating group of diseases. These individuals from across Canada had an equal voice at the table and contributed their ideas to the development of the research agenda. According to nine-year old Logan Graham, who lives with the challenges of juvenile arthritis, researchers need to, “find a cure for arthritis. If you can't find a cure fast enough, please find something to stabilize it long enough.” Logan attended the conference with his parents, Pam Sherwin and John Graham.

Heather Howe, an active volunteer of The Arthritis Society, cautioned attendees to not, be misled by the lack of applause for the speakers. “The room is filled with people who have had inflammatory joint diseases for years, if not decades.” The fact that many found it too painful to clap their hands was only one example of how their lives have been impacted by these diseases. Some also found it difficult to pull doors open and even cut their food.

According to Dr. Elizabeth Badley of the Ontario University Health Network: “The limitations these people face affect their quality of life. They also impact on their ability to remain

HIGH DEFINITION continued from page 6

osteoporosis in women aged fifty or more is 18 per cent, and that oral contraceptive use by women aged 25 to 45 is associated with lower bone mineral density.

As might be expected, Tenenhouse sees the study's huge potential and considers this storehouse of information “invaluable, not only for bone disease but also for a variety of other things. We're going to have an enormous amount of information on a very random population, and it's our policy to make it available to anybody with a serious research question they wish to test. Maintaining the data base is, in my opinion, critical.”

In the short term, the future is pretty well assured. CaMos was recently awarded a \$4.2-million operating grant from the Institute of Population and Public Health which, along with the support of generous industry partners, will extend the life of the program until March, 2010. According to Tenenhouse, the new funding will permit detailed analysis of the huge library of biological samples taken during Phase I and, above all, will allow further follow-up of the study population: “The longer we follow, the more precise and accurate our data become. With the fine detail coming into focus after lengthy follow-up, we're much more likely to achieve our long-term goals of fracture prevention.”

For any such intervention to be effective, though, it will almost certainly need to be initiated at a very early age. One of the many questions Phase II will try to resolve

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Sports Information Resource Centre Picks a Winner

study keeps coach, athlete and sports scientist's interests in mind

On March 29, 2004 Dr. Gordon Bell, professor of exercise physiology in the Faculty of Physical Education and Recreation at the University of Alberta, became the first winner of the 2003 SIRC Research Award presented at the Annual Canadian Sport Awards dinner held in Toronto.

The Sports Information Resource Centre (SIRC) leads the world in providing sport, fitness and sports medicine information through its bibliographic database SPORTDiscus. In 2003, SIRC commemorated its three decades of history by creating the SIRC Research Award as a means of recognizing innovative sports research that has changed the world of sport.

Dr. Bell has researched acute and chronic exercise responses of rowers since 1986. His research project, *"The Physiological and Performance Characteristics of Rowing: Issues and Concerns of Training and Competition for Canadian Rowers,"* is especially designed to provide information that can be used by coach, athlete and sport scientist.

A sponsor of this year's awards, IMHA's Scientific Director, Dr. Cy Frank noted that "studies like these make an important contribution towards improving the performance of our competitive athletes. But, more importantly, they shed light on conditions of the musculoskeletal system that can help us improve the quality of life of all Canadians." ■

Quality of Life Research Awards continued from page 6



Dr. Klaus Wrogemann, University of Manitoba

TRIM32, the Gene for Limb-Girdle Muscular Dystrophy Type

2H is a Putative E-3 Ubiquitin Ligase

Muscular dystrophies are diseases of muscle weakness and wasting. The cardinal problem is that individual muscle cells die too early. Dr. Klaus Wrogemann and his colleagues at the University of Manitoba are studying a form of limb girdle muscular dystrophy (LGMDs) frequently found in Hutterites.

While LGMDs are relatively rare, in the Hutterite population of the North American plains they are very common – at least a hundred times more so among members of these close-knit, religious communities than in the general population. To date, of the 10 recessively inherited forms of LGMD so far identified in the general population, type LGMDH2 has been seen exclusively among the Hutterites. "For recessive diseases to occur, both members of a couple have to be carriers of the same gene mutation," says Wrogemann. "If you have two parents who are carriers of the altered gene for LGMD2H, then they have a one in four chance in each pregnancy that a child will have the disease."

Most recently, Wrogemann and his group have identified TRIM32 as the causative gene for this condition and are studying how mutation in this gene could lead to muscular dystrophy. One possible explanation is that this gene may be involved in controlling the quantity of one or several specific muscle proteins. When the causative gene is mutated, these muscle proteins (which still have to be identified) become overabundant resulting in muscular dystrophy. If this idea proves correct, it will not only enhance our general understanding of how mutations can result in muscular dystrophy, but also contribute to the development of more effective treatment strategies.

Dr. Nicholas Mohtadi, University of Calgary

Arthroscopic Electrothermal Capsulorrhaphy Versus Open Capsular Shift for Patients with Shoulder Instability: A Multi-centre Randomized Clinical Trial



People with unstable shoulders develop pain and inflammation and often get arthritis. Dr. Nicholas Mohtadi and his team at the University of Calgary are working to develop a new less invasive surgical technique to treat shoulder instability. This new technique involves inserting a heat-generating probe into the shoulder using a small operating telescope called an arthroscope. The heat probe shrinks the ligaments thereby tightening the joint making

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it more stable and less likely that the shoulder will dislocate or pop out.

“Typically,” says Mohtadi, “thermal energy is used to cauterize tissue to stop bleeding. It’s also used to ablate tissue. This procedure is a less aggressive variation on that theme. The temperatures we use are much lower than those one would use to cauterize.” But does heat work as well as the traditional open method? And how do the risks of complications compare? To answer these and other questions requires access to a relatively uncommon type of patient — usually a young female who has loose shoulder ligaments, has failed supervised rehabilitation and who has no other medical conditions.

After receiving a potential candidate’s consent, Mohtadi and the other surgeons involved in the trial closely examine the shoulder while the patient is under general anesthesia, putting the joint through its range of motion and comparing it with the opposite shoulder. Then comes a diagnostic arthroscopy that allows the surgeon to “carefully evaluate the structures on the inside of the shoulder to determine the exact pathology,” says Mohtadi. “The main reason is to make sure there isn’t additional pathology. That’s the final criterion for admission to the study.”

When Mohtadi and his colleagues have conclusive evidence, they plan to present them at national and international meetings, and publish the results in a peer-reviewed journal. This clinical trial is also the first study undertaken by JOINTS

Canada (Joint Orthopaedic Initiative for National Trials in the Shoulder in Canada). Mohtadi credits the project with “allowing us to bring together from across Canada a number of shoulder surgeons, research assistants and other people interested in shoulder research. It’s very significant from that standpoint.”

Dr. Bing Siang Gan, Lawson Health Research Institute

*Molecular Mechanisms of Dupuytren’s
Contracture*



Dupuytren’s contracture (DD) is a disease of the hand that results in an inability to straighten the fingers.

Unfortunately, the only accepted treatment to date is surgical resection of the affected tissues followed by prolonged post-operative rehabilitation. Because the cause of Dupuytren’s contracture is unknown, the development of alternative therapies has been hampered. Epidemiologic data suggests, however, that these changes may be the result of an inheritable genetic defect, although no marker for this disease has been identified to date.

Dr. Bing Siang Gan and his colleagues (Dr. Jeff Howard at the University of Western Ontario and Dr. Benjamin Alman, at the University of Toronto) have observed that DD cells form significant amounts of stress fibres, which promote the cells’ ability to move about and latch onto one

another. “Stress fibres are complex anatomical structures that go from one side of the cell to the other. They push out the cell membrane at the front and pull it in at the back — somewhat like a water balloon rolling over a flat surface,” says Gan.

DD cells produce abnormally high levels of a cell-signaling molecule called beta-catenin, which initiates the multi-step process involved in stress-fibre formation. More beta-catenin, it would seem, leads to more stress fibres, and the more stress fibres there are the more the cells can expand and contract. Currently, Gan is in the midst of experiments that involve manipulating DD cells to lower their beta-catenin levels to see if they behave normally again. They are also looking at increasing beta-catenin levels to see if they will change into DD cells.

Ultimately, pharmacological intervention to reduce beta-catenin may become a new way for treating DD. Moreover, since beta-catenin is also implicated in wound-healing and certain cancers, mastering this particular cell-signaling pathway may have unseen dividends. “Although this disease is relatively easy to study,” says Dr. Gan, “it’s implications may be very, very broad.” ■

in the work force. Arthritis costs the Canadian economy more than \$4 billion per year.”

With regards to the identification of research priorities, “the message came through loud and clear,” said Dr. Robert Inman, Co-Chair of the conference and a Rheumatologist at the Toronto Western Hospital. “We must give more attention to the needs of children, and patients with rheumatoid arthritis (RA) and spondyloarthropathies.”

Following the conference, a working group of 20 stakeholders was given the task of synthesizing the suggestions and developing a clear set of research priorities. “What we have now is preliminary. Those of us who have been charged with identifying a final list of research priorities need to do more work,” said Inman.

Once these research priorities have been agreed to, the list will be incorporated into a request for applications (RFA) for researchers. It will also be used by government and industry funders to support these research priorities for the foreseeable future.

“If we are going to reduce the human suffering and economic costs associated with inflammatory joint diseases, we must work together,” stated Dr. Hani El-Gabalawy of the University of Manitoba. As Co-chair of the conference and a Rheumatologist, he also said, “we need to get the message out, people with inflammatory joint diseases benefit from early diagnoses and treatment. The longer it takes to go from the onset of symptoms to effective treatment, the more damage will be done.” This message was echoed

by many of the 100 or so clinicians and researchers who participated in the conference.

Mary Kim, an active volunteer and someone who was diagnosed with rheumatoid arthritis 11 years ago said, “the constant pain and stiffness makes it difficult for me to work. My hands are so weak I can hardly hold a fork. I have already had 8 surgeries on my joints and I am only 36. If this type of damage is preventable, we must do everything we can to educate people and increase access to approved medications.”

The Frontiers conference also had international implications. Robert Johnstone, the president of Arthritis and Rheumatism International (ARI) commented that he was, “impressed with the idea of starting a scientific conference with a Consumer Day. This is an idea that I will take away and share around the world.” ■

arises from the original study. “The youngest members of our cohort are 25 years old,” says Tenenhouse, “and there is now no doubt that peak bone mass is reached before then. We are proposing to look at people as young as sixteen to try to pinpoint that metabolic milestone. Most people believe that every individual has a peak bone mass that is partly determined by genetics and partly by environment. The question is, how do you ensure that everybody achieves their genetically determined peak bone mass by manipulating environment?” ■



**For further information
please contact:**

Doris Ward
Communications Manager
Institute of Musculoskeletal Health and
Arthritis
(403) 210-9899
doward@ucalgary.ca





410 Laurier Avenue W.
9th Floor, Address Locator 4209A
Ottawa ON K1A 0W9
www.cihr-irsc.gc.ca



Institute of Musculoskeletal Health
and Arthritis
Department of Surgery
Heritage Medical Research Building
University of Calgary
3330 Hospital Drive N.W.
Calgary, AB T2N 4N1

**For further information
please contact:**

Doris Ward
Communications Manager
(403) 210-9899
doward@ucalgary.ca