Winter 2010

JointVentures

The Canadian Arthritis Network's Industry Newsletter

Scientific consensus sought under the Mediterranean sun

Members of Canada's paediatric research community are actively leading the formation of an international research consortium to study the complex group of diseases collectively referred to as Juvenile Idiopathic Arthritis (JIA).

RECOGNIZING THE NEED for international collaboration, two dozen paediatric rheumatologists, from six countries, met in Genoa, Italy, (September 27-29, 2009) to address the research needed to understand the "biologic basis for clinical heterogeneity in childhood arthritis."

The representatives from Canada, Italy, the United Kingdom, Germany, the Netherlands and the United States met to seek consensus on four questions (see A-D in Table) and to develop a research question that the group would collaborate on (see E in Table). The top consensus answers for A-D are also included.

The meeting took place at the Gerolamo Gaslini Foundation's head office, Villa Canali Gaslini. The Foundation has as its mission: health care, aid and assistance for children, and support for the Giannina Gaslini Institute.

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Paediatric rheumatologists meet in Italy

Despite the warm fall temperatures and the stunning scenery, the doctors came to work and work they did.

Drs. Rae Yeung and **Brian Feldman**, from Toronto's Hospital for Sick Children, took on the leadership and facilitative roles with the UK's Dr. Lucy Wedderburn and the Netherlands' Dr. Berent Prakken rounding out the steering committee. During the meeting itself, Dr. Feldman facilitated the nominal groups process – a means for reaching consensus from a group – that took place. Drs. Yeung and Feldman, along with three of the four other Canadian participants, are members of the Canadian Arthritis Network (CAN).

Due to the limited patient numbers and the wide ranging clinical presentations in JIA (in Canada, one in 1,000 children under age 16 has JIA), only a collaborative international research consortium can fully investigate and develop predictors and patterns of disease that transcend national and ethnic groups. Another advantage of working together is the ability to pool resources.

Half of the funding for the meeting was provided through CAN's International Partnership Initiative (IPI) in order to solidify the formation of the consortium. CAN's IPI partners covered the remaining expenses for their representatives to

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Scientific consensus

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attend, and the Gaslini Foundation was also a generous sponsor of the meeting.

Despite the challenging goal of seeking consensus from the paediatric leaders of six countries on the topic of which symptoms and characteristics define childhood arthritis, the meeting was successful and ended on a positive note. Representatives from all the countries were transparent about their resources and current levels of funding, and were very enthusiastic about working together on a shared project that would have a lasting legacy for children with JIA in their countries and around the world.

After Italy

With Phase 1 of the research plan completed – namely forming a research consortium – the brand new Understanding Childhood Arthritis Network (UCAN) planned to tackle Phase 2 next: developing a pilot project and conducting feasibility testing.

UCAN's first undertaking was to submit proposals to various national and international funding agencies. This would provide UCAN with funds for the small feasibility project. If successful, it will submit follow-up applications in two years to seek support for a much larger project. UCAN also agreed to submit a meeting report to a peer-reviewed journal on the outcome of its efforts in Italy.

Canadian paediatric rheumatologists, funded by CAN, are already doing ground-breaking work and offering a model of how to conduct multi-disciplinary, transdisciplinary research. Now they appear to be successfully exporting this model internationally. According to Dr. Yeung: "It's very exciting for Canadian doctors to be leading an international initiative to define a new

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Message from the Co-Scientific Directors

A NEW YEAR CAN BRING about a sense of rejuvenation in an organization as employees return from vacation rested and motivated to tackle new projects. For the Canadian Arthritis Network (CAN), 2010 will see the launch of two brand new funding programs that fit nicely with our updated strategic plan (2009-2012).

CAN's new **Knowledge Translation and Exchange (KTE) Program** was developed in partnership with the Canadian Institutes of Health Research's (CIHR) Knowledge Synthesis and Exchange Branch (KSE) and Institute of Musculoskeletal Health and Arthritis (IMHA).

This program endeavors to consolidate knowledge and expertise on CAN/arthritis-related research topics and maximize translation to the knowledge user/receptor community to benefit Canadians. There are two types of funding opportunities in the program: KT Supplement Grants and KT Synthesis Grants.

While KT Supplement Grants are intended for those who have already completed a CIHR or CAN grant/award and now want to share the results, both types of grants are designed to assist researchers in getting their important findings to end users. A distinction of the KT Synthesis Grant is that it supports collaborating with government and industry and other knowledge-users to determine whether existing information is sufficient or other reviews need to take place.

These grants may be used for the following: to disseminate research results through specialized publications; to develop/maintain/update websites; to produce and distribute written materials in various formats; to cover travel costs for meetings; to provide salary for new hires; to develop educational CD-ROMs, etc.

CAN's financial contribution to the KTE Program totals $560,000 over the next fiscal year (April 1, 2010 – March 31, 2011). Including contributions from the KSE and IMHA, up to $850,000 is available to be awarded for successful KT applications.

The **Platform Program** focuses on creating platforms that will ultimately improve research efficiency by eliminating duplication and repetition between labs and individual researchers. CAN will fund the creation of shared resources or infrastructure that will facilitate research, the utilization of research results and training.

Phase I takes the form of the Rapid Impact Platform Program. This program will support initiatives that can be up and running quickly. This may take the form of funding activities that involve bringing experts together to establish practice guidelines, workshops, functional groups or compendiums of knowledge. Key selection criteria will emphasize initiatives that will produce a concrete product (e.g. guidelines, standards of practice, or standard operating procedures) with legacy potential and that offers value to a significant number of CAN members.

CAN will fund up to six platforms of up to $60,000 each, over two years. A Phase II program will be announced later this year.

Auf Wiedersehen, Aurevoir, Adios, さようなら

This year bids farewell to the popular and much subscribed **International Partnership Initiative** (IPI). You have read in these pages about the many and diverse meetings and workshops run jointly with our international arthritis partners. As well, hundreds of CAN investigators, trainees and consumers have benefited from attending and presenting at conferences around the world. This issue of *Joint Ventures* features three more significant activities funded through the IPI.

Happy New Year!

Sincerely,

Claire Bombardier   Monique Gignac

Scientific consensus

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paradigm in disease classification and management of JIA, but it's especially exciting because of the potential long-term benefits for children around the world."

Table

A. How shall we define the study population? In what group(s) of children should we study the biologic basis for heterogeneity in childhood arthritis?

Answers

- All inflammatory arthritis greater than two weeks, less than three months, in treatment naïve children
- Children of all ethnicities

B. What are the dependent variables (clinical outcome) in our study population?

Answers

- Treatment response
- Long-term outcomes
- Traditional and novel markers of inflammation

C. What are the most important determinants/independent variables (modifying factors, risk factors) in our study population?

Answers

- Integrated immune response over time
- Genotype

D. What are the core facilities/ infrastructures needed to answer our study question?

Answers

- Centralized data management
- Network of biobanks
- Standardized SOPs
- Biostatistical core

Research Question: E. In children with inflammatory arthritis – greater than two weeks and less than three months, who are treatment naïve – does an integrated immune response over time and genetic predisposition affect treatment response, long-term outcome and markers of inflammation? ■

New effort to increase arthritis research capacity in aboriginal communities

Approximately 300,000 Canadians, roughly one percent, suffer from Rheumatoid Arthritis (RA), but within aboriginal communities RA occurs at twice the national rate.

Left to right: Dr. Hani El-Gabalawy and Dr. David Robinson

THIS REALITY WAS THE IMPETUS for a conference entitled "International Symposium on Rheumatic Diseases in Indigenous North American Populations: from Molecules to Communities," held in Winnipeg (September 2009). The University of Manitoba hosted the symposium, organized by **Drs. Hani El-Gabalawy** and **Brenda Elias**, Canadian Arthritis Network (CAN) members, Dr. David Robinson, and a steering committee that included Indigenous consumer input.

"Virtually anyone who has anything to do with arthritis research in aboriginal populations in North America was at the symposium," says El-Gabalawy. The 150 participants included scientists and policy makers from Canada, the United States and Mexico. "We also had true representation from indigenous communities — the Chiefs of two aboriginal communities and their Health Directors, aboriginal health advocates, members of these communities with arthritis, and indigenous investigators from our university's Centre for Aboriginal Health Research."

The Winnipeg symposium – funded through CAN's International Partnership Initiative, the Canadian Institutes for Health Research (CIHR), other academic partners and industry members – set a large, two-pronged agenda. The corresponding white paper has been submitted to CAN and CIHR to address two major goals: to identify research priorities out of the clear gaps in aboriginal arthritis research knowledge, health care services and access to care; and, to determine ways to study the health questions that will arise out of the research priorities.

This information will help to inform the direction of CAN's second National Aboriginal Arthritis Research Initiative (NAARI II), launched during the Winnipeg symposium. This initiative follows NAARI I (2007-2009), which worked to develop community-based, collaborative and participatory arthritis research strategies between Canadian scientists and First Nations, Inuit and Métis communities.

While other aspects of aboriginal health, such as diabetes, have been studied in more depth, relatively little ground has been broken in studying arthritis in indigenous communities. Twenty-five percent of Aboriginal Peoples report having rheumatic or arthritic disease, according to University of Manitoba data.

"CAN is eager to help build more capacity and training in aboriginal arthritis research to make advances in

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Three views of SNOW

For the third time, members of the Canadian Arthritis Network (CAN) were among the 160 attendees at the Segal North American Osteoarthritis Workshop (SNOW III) in Chicago, Illinois, (October 1-3, 2009).

THIS YEAR'S THEME WAS "**Post Traumatic Arthritis of the Knee as a Model for the Study of Osteoarthritis**". (Read the Winter and Autumn 2008 issues of *Joint Ventures*, online, for some history and background of SNOW. The articles below were edited due to space constraints.)

CAN attendees at SNOW

By JOHN CODERRE, London (Ontario), Consumer Perspective

AS A CONSUMER, I noted that the greatest advances in the early detection of osteoarthritis (OA) appear to be coming from Imaging Technology. I also have hope that the great amount of work being done in the biomarker field may soon produce results that will give the clinicians a means of detecting early OA before pain and radiographic evidence is available.

Unfortunately, once detected, there are still few therapies available to inhibit or stop the progression of OA. No disease-modifying osteoarthritis drugs (DMOADs) as yet. However, this is the first conference that I have attended that has even suggested that there are DMOADs in the clinical trial phase. There was no indication as to the extent these new medications might modify the progress of the disease, but this is encouraging news to those of us with OA.

During SNOW, I was bemused and somewhat taken aback by the frequent statement that Patient Reported Outcomes (PROs) are the "gold standard" for clinical trials. It may be somewhat heretical to say so, and I have great respect for the scientists who have developed such scales of PRO as WOMAC, KOOS, Oxford and others, but I had hoped there might be something better as the "gold standard". I strongly suspect, without any scientific evidence, that we patients have less confidence in PROs than do the scientists.

That is partly because, as I tell the medical students to whom I demonstrate MSK assessment procedures as a Patient Partner, we have all learned to lie and cheat during the course of our chronic illness. We "lie" about our pain and loss of function because we don't want to be thought of as wimps or to cause less stress to our family and friends. We "cheat" to cope. We compensate for loss of range of motion by finding other ways of accomplishing what others do "normally". As patients, we have all been asked about our pain and our abilities to perform physical activities. We answer as best we can, although sometimes we find the questions ambiguous. But it is always difficult for us to overcome our natural propensity to downplay the effects of our illness on our bodies.

I suspect that patient compliance has a high correlation with patient confidence in the outcome measure being used. As science moves closer and closer to being able to diagnose and treat OA in its early, pre-radiologic and, hopefully, pre-symptomatic phases, PROs may become less and less needed as the "gold standard" and will be replaced by reliable biomarkers and measurements obtained by increasingly sophisticated imaging techniques such as MRI and Optical Coherence Tomography (OCT). As patients, we are ready for such a change.

By DR. ROBIN POOLE, Professor Emeritus McGill University, Researcher Perspective

THIS YEAR'S TOPIC was selected by the organizing committee as one of great importance since this type of OA affects a much younger and more physically active population. It also provides a human model of OA where we know the starting point (joint injury). Moreover, we know that it involves

changes in biomechanical loading of joint tissues – such as cartilage and bone – as well as inflammation.

By studying a human model we have the chance to follow OA development over time, detect early changes and see how they progress, leading ultimately to a loss of joint function with a final requirement for joint replacement. This appealed to both academic and industry colleagues who are all trying to better understand the natural history of OA and it appealed to the organizers since the topic offers considerable scope for collaborative, multidisciplinary studies.

SNOW has become one of the finest meetings of its kind offering a smaller, very manageable workshop format with attendance from leading international researchers and North American trainees in a wide variety of disciplines. It is also unique in the United States in that consumers, especially from CAN and the Arthritis Foundation (AF), play an active role questioning research directions, outcomes and acting as conduits for knowledge dissemination.

I was impressed with the participation of CAN consumers at the meeting and the leadership role CAN investigators took as organizers, but what most impressed me was the very strong presence of CAN trainees. They presented many excellent posters and left an impressive image of the very high standards of CAN research.

The meeting resulted in the disclosure of new, unpublished scientific information and, as a result, there were excellent protracted discussions following the talks – a very important feature of the meeting. As well, there were plenty of opportunities for attendees to mingle, make new contacts and form new collaborations.

Overall the meeting was, in my opinion, the best SNOW conference to date, and others who have attended all three meetings agreed.

Personally, I came away from this meeting very stimulated and much better educated about post-traumatic OA and how it can be studied. I would like to see a follow up meeting looking at how closer multidisciplinary research collaborations can be established between Canadian and U.S. researchers. Already AF has launched a call for research proposals on this topic. I came away from SNOW III scientifically invigorated and proud to be a CAN member.

By CATHERINE FERLAND,
Université de Montréal,
Trainee Perspective

THIS THREE-DAY WORKSHOP was a very enriching experience to me as a Ph.D. student. In my opinion, it was a great reunion of world renowned scientists in the field of knee OA research. I witnessed honest camaraderie, laughter and fulfilling exchanges between leading researchers.

The workshop was set up in a way that the emphasis was on shared knowledge in order to unify all research involved in the anterior cruciate ligament injury and its consequences. The meeting seemed to focus on the "what is done" and the "how you would manage it" based on various specific fields of research. There were experts on gait analysis discussing the repercussions of the injury and how to evaluate the mechanic factors, experts on the reconstruction of the joint post injury, experts on molecular consequences of the injury, and also people living with post traumatic injury. All together, they tried to evaluate the consequences, but also the many ways to minimize the effects of diminished quality of life. Discussions emerging from each presentation were rich in arguments and ideas between attendees providing new avenues of potential strategies to minimize the impact of this injury.

As a CAN trainee, I had the chance to meet other Canadian trainees. To gather outside Canada was an experience that made me feel part of a team. I also felt a kinship with some CAN investigators. And I felt like an ambassador of CAN. Speaking for all trainees present at the SNOW conference, I do believe we are all thankful for this opportunity and we are eager to attend other international conferences in the future to give us the opportunity to meet with established investigators.

This was a very motivating conference and it gave me new ideas for future post-doctoral opportunities. ■

CAN's new Director of Research and Development

On September 21, 2009, **Brian Bobechko** joined CAN as the Director of Research and Development.

Although CAN has always had an officer dedicated to its R&D activities, never before has the role been associated with such high expectations. With its renewal mandate, the Networks of Centres of Excellence has challenged CAN to create as much impact as possible in the time remaining. Accordingly, a key Network priority going forward is to emphasize the dissemination of research findings and promote their application and implementation.

Prior to joining CAN, Mr. Bobechko was a Senior Consultant with SHI Consulting Inc. and involved in CAN's 2007 Strategic Planning Workshop in Toronto and the 2008 meeting in Vancouver.

In addition to his previous CAN experience, Mr. Bobechko also offers a deep understanding of the life sciences environment in Canada. He has experience working across all sectors, including with other chronic disease research organizations and government health organizations. He brings valuable skills in facilitating the commercialization of research, structuring partnerships, and providing strategic business planning support to biotech and pharmaceutical companies of all sizes.
Mr. Bobechko also has extensive knowledge of project management and planning. He served as the Managing Director for the Blueprint Initiative Asia Pte. Ltd., a bioinformatics company focused on archiving and querying biomolecular interaction data.
Mr. Bobechko holds a M.Sc. from the University of Toronto's department of Laboratory Medicine and Pathobiology.

Mr. Bobechko can be reached at **bbobechko@arthritisnetwork.ca** or by calling 416-586-4800 ext. 4117.

Pumping out a new treatment for inflammatory arthritis and osteoporosis

By Brian Bobechko, CAN's Director of Research and Development

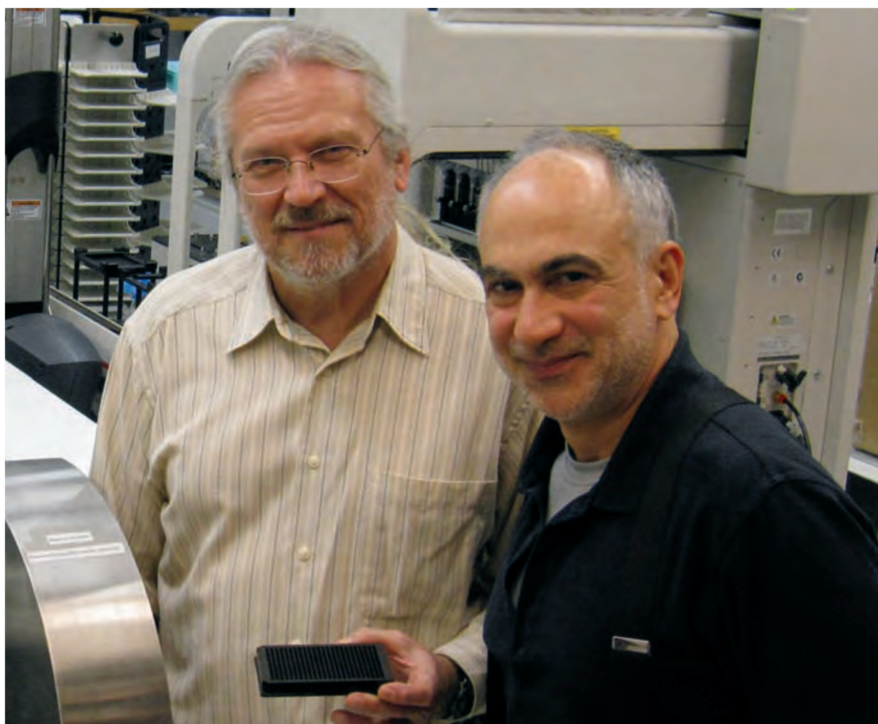
It seems like a relatively simple problem. Cells involved in bone remodeling (osteoclasts) have molecular pumps that pump acid onto bone causing its resorption and loss of bone density – a hallmark symptom of osteoporosis and inflammatory arthritis.

A LOT OF EFFORT has gone into exploring how to turn off the acid pumps with the goal of slowing down bone resorption and improving bone health. However, as is often the case in biology, the pumps of bone remodeling cells are very similar to the pumps in lots of other cells. The trick is to turn off just the right ones.

In a recent discovery, **Dr. Morrie Manolson**, an investigator with the Canadian Arthritis Network (CAN) and associate professor with the Department of Dentistry at the University of Toronto, and his colleague, Dr. Norbert Kartner, may have found just the right small molecule (drug) to do the trick.

The key to their recent discovery – and here comes some technical jargon – was their previous finding that the make-up of the multi-subunit osteoclast acid pump complex (vacuolar ATPase – a proton pump) involves an interaction between two parts that are highly enriched at the osteoclast cell surface (the a3 and B2 subunit isoforms). Together with genetic studies that suggested important roles for these parts in acid-pump function (bones get too dense when the a3 subunit is missing), Drs. Manolson and Kartner knew they had an interesting drug target.

By searching for small molecules that would specifically inhibit that unique molecular interaction, they hoped to block the acid pumping action without disrupting other important cell functions. However, even performing such a search was going to be a challenge, since bone surfaces suitable for controlled-laboratory testing in highly uniform and reliable formats are notoriously difficult to locate.



Left to right: Dr. Norbert Kartner and Dr. Morrie Manolson

They needed to find materials that would be suitable for assaying osteoclast function, and that could also be miniaturized for rapid, large-scale small-molecule screening.

Fortuitously, Corning Inc. was looking for someone to test its new synthetic bone assay plates (Corning® Osteo-Assay Surface), which provided an ideal collaboration to advance the small molecule screen. With these synthetic bone plates in hand, and funding from CAN and the Canadian Institutes of Health Research, Drs. Manolson and Kartner were able to secure the help of the Samuel Lunenfeld Research Institute's robotics facility in Toronto and screen 65,000 compounds to find just the right molecule.

Drs. Manolson and Kartner will be the first to tell you there is still a lot of work to be done before this discovery can offer a treatment for consumers. Optimizing their lead compound and looking at disruption of their target interaction in animal models will be a critical next step. But with the help of CAN's R&D support, they now have a provisional patent for the lead compound and are well positioned for second phase proof-of-principle funding. A number of potential industry partners have also shown interest. For Drs. Manolson and Kartner and their discovery pipeline, they've only just primed the pump. ■

2009 Annual Scientific Conference

Many ASC attendees said this was the 'best one yet'! The conference, held November 19-21, 2009, in Vancouver, drew over 300 people to hear a balanced program of basic and clinical science, along with the consumer perspective. Add to that, a boat cruise for trainees, an art gallery tour, a slew of awards, a public forum and the ever-popular gala dinner…check out some of the highlights below.

Dr. Mary Bell

Alex Chun

Dr. Paul Fortin and Cheryl Koehn

The Consumer Advisory Council, current and past members

Poster judging

Squamish Nation dancer

Travel Award winners

Dr. Robert McCormack

Vancouver Art Gallery tour

Speed "dating" session

New effort

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diagnosis and care, and NAARI is our attempt to make a difference," says Dr. Monique Gignac, Co-Scientific Director of the Canadian Arthritis Network and a participant at the Winnipeg symposium.

Critical to advancing knowledge and care in arthritis among aboriginal communities, El-Gabalawy emphasizes, is a commitment to relevant, community-based action research that is approved, planned, conducted and shared by and with aboriginal communities prior to publication or dissemination of results – and that aims to improve health services in conjunction with the research.

The guiding principles of Ownership, Control, Access and Possession (OCAP) underlined discussions during the Winnipeg symposium, as they do the guidelines under CIHR and the government's other funding agencies for conducting ethical research with aboriginal communities.

"The pockets of success that currently exist in participatory research were represented at the symposium," says El-Gabalawy. "Coming up with practical models for conducting such research successfully is very new and challenging. It also requires that indigenous participants be trained in basic research principles and learn what knowledge exists on the specific health question under study."

The highlights for future research arising out of the Winnipeg symposium include these keynotes:

- Inflammatory arthritis is not only highly prevalent in aboriginal populations, but the severity of this already aggressive disease is also greater in these communities. It is critical to understand the interplay between genetic, familial, and environmental factors (including health care services) in RA among indigenous people;
- Indigenous practices, such as traditional medicines and integrated models of health-services delivery, need to be further explored and applied;
- Consider delivery of care methods as remote communities, time of diagnosis, ongoing care and adherence all pose challenges (telehealth may be one option);
- The broad social determinants of health – education and income levels, cultural and family supports, social issues and health infrastructure – must factor into the study of arthritis in aboriginal communities, along with indigenous models of care that are holistic and include the family and community;
- Collective, rather than individual, informed consent to research involvement is an ethical consideration for discussion among scientists and indigenous communities, and a new approach for Canadian researchers.

For more information on NAARI II and to submit a research proposal by the March 30th deadline, please visit CAN's website at **www.arthritisnetwork.ca** and click on NAARI II.

The University of Manitoba is aiming to have the white paper approved for publication as a supplement to the *Journal of Rheumatology*. To receive a copy of the paper, please contact the CAN office. ■

CANADIAN ARTHRITIS NETWORK | LE RÉSEAU CANADIEN DE L'ARTHRITE

Today's arthritis research :: Tomorrow's cure

The Canadian Arthritis Network (CAN) is funded by the Networks of Centres of Excellence program (www.nce.gc.ca). CAN's vision is "**a world free of arthritis**" and it seeks to link Canada's leading researchers with partners who will help translate knowledge and innovations to improve the quality of life of people with arthritis, decrease the personal, societal and economic burden of the disease and promote the growth of the Canadian economy.

Claire Bombardier, MD, FRCPC
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Member of the Networks of Centres of Excellence

Honours and awards

CAN wishes to congratulate the following Network Investigators on the important awards they have received to recognize the excellence of their work. They are:

Dr. Catherine Backman (University of British Columbia), who received the Distinguished Scholar Award from the Association of Rheumatology Health Professionals, a division of the American College of Rheumatology;

Dr. Nizar Mahomed (Toronto Western Hospital), who was honoured with the first CIHR-CMAJ Top Canadian Achievements in Health Research Awards for leading a team, involving 35 hospitals, which introduced new procedures for hip and knee surgery;

Dr. Chris McCulloch (University of Toronto) who won the 2009 Distinguished Scientist Award for Research in Oral Biology from the International Association for Dental Research; and,

Dr. Carter Thorne (Southlake Regional Health Centre) who received the Dr. David Hill Memorial Award and the University of Toronto's Award of Merit, both to acknowledge Dr. Thorne's work as the architect behind The Arthritis Program (TAP) at Southlake. ■