



John Antoniou is a hip surgeon

WHEN YOU SAY “HIP”, MANY people think “fashionable”, “stylish” or “aware”. Others think of a painful hip joint damaged by arthritis that limits their mobility and enjoyment of life. The solution to the arthritic hip, pioneered in the 1920s, is to remove the damaged areas of the joint and replace them with artificial hip socket components. The first artificial hip was made of glass and did not last long. Plastic and metal components were tried with greater success.

Sir John Charnley, a British orthopaedic surgeon, revolutionized hip replacement surgery in 1962 by using a plastic hip socket and a metal prosthesis, which became the standard for this type of surgery. The replacement parts give patients pain-free mobility but eventually wear out and may need replacement after 15-20 years. This limits hip replacement surgery to older people or people who lead a less active life.

An innovation in hip replacement surgery has been introduced to North America by orthopaedic surgeon Dr. John Antoniou that removes only the diseased portion of the hip and



Left to right, John Antoniou and Peter Bienkowski

replaces it with metal components. The new technique called Articular Surface Replacement (ASR) is a less invasive form of surgery that allows for a quicker recovery period.

Dr. Antoniou, a Network member, is an Assistant Professor in the Division of Orthopaedic Surgery at McGill University and a Project Director in the Orthopaedic Research Lab at the Jewish General Hospital in Montreal, where he recently performed the first ten ASRs. The patients were able to walk the day after surgery and spent only four or five days in the hospital prior to going home. The Canadian Institute for Health Information (CIHI) reports that the average length of stay in hospital in Canada after a hip replacement operation

was 9.7 days in 2001-2002.

The great benefits of ASR, in addition to a quicker recovery time, are that patients can maintain an active lifestyle after the surgery and the components should last up to 35 years. This makes surgery more attractive to younger people, particularly the baby boom generation. CIHI reported that the number of hip replacements performed on people under age 55 in Canada increased by 30 per cent between 1994-95 and 2000-2001. Dr. Antoniou's first ASR patients are all enjoying an active life now and one played tennis seven weeks after surgery. Dr. Antoniou is now training surgeons from across Canada in the new technique.

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Dr. Antoniou has both a degree in medicine and a PhD in experimental surgery from McGill University. He was recently awarded the Gold Medal in Surgery for 2004 by the Royal College of Physicians and Surgeons of Canada for discovering a synthetic peptide of link protein that stimulates the biosynthesis of Collagens II, IX and proteoglycan by cells of the intervertebral disc. The award is a national recognition for original work by young clinical investigators.

With a father who was an orthopaedic surgeon and a mother who was a physician, Dr. Antoniou was exposed at an early age to science and medicine. His father was one of the first surgeons to perform hip replacement surgery in Canada, having had experience with this type of surgery in Europe in the 1950s. Dr. Antoniou decided to become an orthopaedic surgeon because his father was a role model and because of the instant gratification he gets in fixing a broken bone or in helping someone walk.

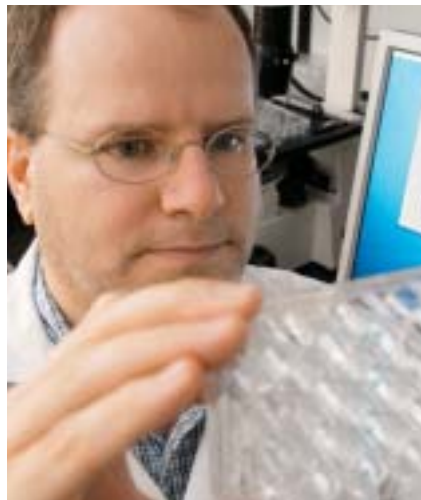
The research project for his master's degree turned into a research project for a PhD. After completing his residency in orthopaedics he started his research on the effects of ageing and degeneration on the intervertebral disc, spine and lower back pain. His research led to an interest in matrix turnover, tissue engineering and quantitative MRI imaging of the intervertebral disc.

An introduction by Dr. Max Aebi to Dr. Robin Poole, CAN's Scientific Co-Director, recruited Dr. Antoniou into arthritis research. He says, "Dr. Poole's enthusiasm about arthritis research and his interest in the molecular changes associated with the disease inspired me to explore this area further. My work with Dr. Poole brought me into the Network and I learned early on the value of a network for someone involved in scientific research. The importance of exchanging ideas and developing close collaborations is crucial to performing original and clinically relevant research."

Dr. Antoniou is an active member of CAN and hopes to instil his passion for arthritis and spine research in his current and future residents and fellows. ■

Michael Underhill

A childhood interest in taking things apart and putting them back together again turned into a career in arthritis research for CAN member Michael Underhill. Now he takes cells apart to figure out how they function and which signals regulate development of cartilage and bone.



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A GENETICS COURSE IN HIS third year at university exposed Dr. Underhill to scientific research, which led to a PhD from the University of Western Ontario in membrane transport with research on the mechanisms underlying drug resistance to methotrexate. He followed this with postdoctoral work at Duke University in North Carolina on developmental biology and signal transduction.

Serendipity brought Dr. Underhill into the area of arthritis research. At Duke University he worked on retinoic acid, a signalling molecule. Some of the transgenic animals he worked with had receptors for retinoic acid that were over-expressed and those animals developed skeletal defects. This triggered Dr. Underhill's interest in the skeleton and the mechanisms that regulate skeletal formation.

Dr. Underhill continued his work on retinoic acid and its role in cartilage and bone formation at the University of Western Ontario as an Assistant Professor. He filed patents for his discoveries that if you antagonize the retinoic

acid pathway, you can stimulate cartilage and bone formation. He then licensed these technologies to a pharmaceutical company in the U.S. His next step was to create a company, Coregen Inc., to develop the use of retinoic acid receptor (RAR) antagonists to enhance bone and cartilage regeneration. Dr. Underhill credits CAN "with making people like myself more aware of the need to patent technologies to protect them so they can be turned into therapeutics. Supportive people in the Network like Drs. Jane Aubin and Robin Poole, the Scientific Co-Directors, helped enormously."

A former colleague at the University of Western Ontario, now at the University of British Columbia, offered him a position there. He is in the process of re-locating his laboratory to Vancouver where he will be an Associate Professor in the Department of Anatomy and Cell Biology. His research will use bioinformatics coupled with high-throughput functional assays to define the regulatory networks that operate to control chondrogenesis and osteogenesis.

The research in Dr. Underhill's laboratory focuses on a number of signalling pathways identified to be important in skeletogenesis, these include the retinoids, WNTs, fibroblast growth factors and bone morphogenetic proteins. He will investigate how these signalling pathways work together to coordinate formation of skeletal tissues. Coregen will focus on RAR antagonists and bone formation. One application they will be looking at is enhancing spinal fusion. Other applications in the short term will be directed at enhancing fracture repair. Ultimately, he would like to examine the utility of these potential therapeutics in slowing and/or reversing the progression of osteoarthritis. ■

Karl Rudolphi: An industry scientist's perspective

Partnerships are a hallmark of the Canadian Arthritis Network and Dr. Karl Rudolphi of Aventis is enthusiastic about the mutual benefits.



AVENTIS SPENDS almost €3 billion a year on R&D but like other large pharmaceutical companies, it has emphasized new technologies and

target identification, simultaneously losing expertise in systemic pathophysiology. As a result it has benefited from the expertise within CAN.

Dr. Rudolphi is a veterinary surgeon with a PhD in pharmacology and pathophysiology. He joined Hoechst (a predecessor of Aventis) in 1978 and now leads the *in vivo* pharmacology section for osteoarthritis. He is particularly interested in novel quantitative imaging techniques to assess osteoarthritic joint damage. He was introduced to the Network by Dr. Robin Poole, CAN's Scientific Co-Director and has established collaborations with CAN members.

Aventis sponsored a characterization of the rabbit OA model in Dr. Sheila Laverty's laboratory at the Université de Montréal. This was followed by a pharmacodynamic study with Drs. Sheila Laverty, Robin Poole and Ken Pritzker to test a new compound using intra-articular administration in the rabbit model.

The project involved an exchange of scientists and technicians for the transfer of knowledge from the Aventis laboratories to those of the CAN members. The Aventis personnel gained technical expertise in surgical techniques, immunohistology and chondrocyte culturing in Canada. Further collaborations are planned on rabbit studies as well as

an involvement in the Network's new pain theme.

Aventis and CAN are also collaborating on training. Aventis is offering training to young scientists to familiarize them with the pharmaceutical industry environment and the modern aspects of drug development along the value chain.

Dr. Rudolphi recognizes the importance of the input of consumers in CAN and greatly appreciates the opportunities he has had to meet consumers at the CAN annual scientific meetings. His encounters with people with arthritis in Canada have changed his views on the future direction of arthritis research. He now realizes how important it is to obtain feedback from patients being treated with new therapies to improve the profile of drugs developed in the future.

What is the future of drug development for arthritis? Dr. Rudolphi says "Osteoarthritis presents challenges unlike other diseases. It becomes symptomatic only when it is very advanced. This highlights the need to find methods for early diagnosis." The other great challenge is to deal with the pain of arthritis, which is disabling. He says, "Too much emphasis has been placed on discovery of pure disease-modifying agents. We have to find novel targets and novel drugs for the treatment of osteoarthritis-specific pain. We need compounds that target both the symptoms and joint destruction."

Dr. Rudolphi's vision of future drug development involves more collaboration. In his view "This is the way of the future. We can't do it alone because medical science is too complex and we want results quickly. The CAN model of collaboration is the model of the future." ■

Canadian Arthritis Network 2004 Annual Scientific Conference



Tourism Vancouver

Plan to attend the Canadian Arthritis Network's 2004 Annual Scientific Conference in Vancouver, November 11-14. You will hear about the latest developments and meet the scientists who are at the leading edge of arthritis research. Register early and save up to \$250.

POSTER AND PLENARY SESSION TOPICS INCLUDE:

- Bioengineering for the Restoration of Joint Function
- Disability in the Workplace
- Inflammatory Joint Disease
- Informatics for Research in Arthritis
- Knowledge Translation and Exchange
- Osteoarthritis
- Pre-clinical Models of Arthritis
- Training Opportunities in Arthritis Research

KEY DATES

Program
July 15

Deadline for advance registration
August 27

Deadline to submit abstracts/posters
September 30

Deadline for trainees to submit
application for travel awards
September 30

Please visit our website at
www.arthritisnetwork.ca for more
information and to register.

Travel awards are available to
graduate students and postdoctoral
fellows involved in CAN research.
Please visit the website for further
information.

Diane Lacaille

What happens to people when they are diagnosed with rheumatoid arthritis? How does arthritis affect the ability of people to find and maintain employment? These questions intrigue Network member Dr. Diane Lacaille and form the basis of her career in arthritis research.

DR. LACAILLE IS A RHEUMATOLOGIST who became a CAN scholar. Born and educated in Montreal, she received an MD degree from McGill University and specialized in internal medicine. She received her training in rheumatology and epidemiology in Vancouver, which is now home for Dr. Lacaille, her husband and three young children. She is an Assistant Professor in the Rheumatology Division of the University of British Columbia and a research scientist at the Arthritis Research Centre of Canada.

Rheumatology appealed to Dr. Lacaille because it allows her to develop a long-term relationship with patients, unlike other specialties. She says, "Arthritis is a chronic illness. We can't cure it but the treatment can have a big impact on people's lives and if I can reduce the level of disability, I can make a significant difference."

She credits both CAN for supporting her in the initial phase of her career and her research mentor, Dr. John Esdaile, for her success as a young researcher. Dr. Lacaille's research projects are unique. She is looking at employment issues that

arise for people with arthritis and developed a program to help people with inflammatory forms of arthritis remain in the workforce. Self-employment is a promising alternative for people with arthritis but very little research has been done in this area.

In a CAN-funded project Dr. Lacaille was able to identify 27,000 people with rheumatoid arthritis (RA) in British Columbia and the health services they used. She looked at the level of care provided at the population health level, whether there are gaps, why, and what could be done about it. She found that RA is under-treated in British Columbia. Approximately half of the RA population are followed by their family physicians, are not referred to a rheumatologist and do not receive disease modifying anti-rheumatic drugs, considered essential in the treatment of RA.

The success of her CAN-funded project led Dr. Lacaille to collaborate with the British Columbia Ministry of Health on its chronic disease management strategy for arthritis. This initiative looks at the way chronic diseases, such as arthritis, are managed in an attempt to



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identify and address gaps in health care. The outcome was a chronic disease management strategy. The next phase of the research will survey people with RA to identify other gaps in care, why they exist and whether the gaps make a difference in outcomes.

The cohort identified in the CAN-funded project forms an observational database that will be a source of valuable information for many years. It could provide data about care received, impacts, work disability and outcomes of joint surgery. Information from this database supplements information gathered in clinical trials because it provides data obtained in real-life settings, in large samples and over long periods of time.

The cohort will be unique because it will provide self-reported information as well as accurate information on health care services and medications used, obtained from administrative databases. Dr. Lacaille says, "I would not have been able to do this without CAN. The CAN funding was seed money that allowed me to develop the cohort and now I can obtain peer-reviewed funding from granting agencies to answer specific questions." ■

Carlo Marra

Pharmacist, assistant professor, head of a health economics program, arthritis researcher and CAN scholar.

THOSE ARE CARLO MARRA'S credentials. He is one of the next generation of arthritis researchers, funded by CAN through its training program. "If not for CAN I would not be working in arthritis; I would have done something different," says Dr. Marra. "CAN was interested in funding my training and instrumental in guiding my career."

Dr. Marra wanted to extend his education after he obtained a B.Sc. in pharmacy so he completed a hospital residency in pharmacy, trained as a clinical pharmacist and obtained a doctorate, Pharm.D. After five years of research, he realized he needed more training for his research in health economics, where he was investigating the cost-effectiveness

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Carlo Marra

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of new drug therapies for various conditions. Pharmaceutical companies are interested in his work because they have to show that new drugs are not only effective but that they are cost effective before they can be listed on many Canadian provincial formularies.

His search for more training brought Dr. Marra into contact with Network members Drs. John Esdaile and Aslam Anis, who recruited him into arthritis research and became his thesis supervisors. Dr. Marra obtained his PhD this spring and he has been appointed Assistant Professor in the Faculty of Pharmaceutical Sciences at the University of British Columbia and the

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Head of the Health Economics Program at the Vancouver Coastal Health Authority’s Research Institute.

Dr. Marra evaluates the incremental cost-effectiveness of new health care strategies or new drug therapies. Not only does he examine their acquisition costs, he looks at what they do to global costs. He also assesses health-related quality of life in cohort settings and randomized trials. In addition, he is particularly interested in the use of community-based pharmacists to improve health care. He is investigating whether multidisciplinary interventions initiated by community pharmacists can affect health status, have an impact on health care and the cost-effectiveness of delivering that care. As such, he believes that pharmacists can make a significant contribution. ■

The CRRC is up and running

The Canadian Rheumatology Research Consortium (CRRC) is up and running and is a runaway success!



Left to right, John Riley, Lina Gazizova, Deborah Weber, Ed Keystone and Chris Nelson

NEGOTIATIONS CURRENTLY underway with 14 pharmaceutical companies will shortly result in clinical trials in Canada for a number of new therapies for rheumatoid arthritis.

The CRRC has generated a great deal of excitement in the Canadian pharmaceutical industry and among rheumatologists, leading to the possibility of the development of new sites and the expansion of the Consortium.

CAN member Dr. Ed Keystone, chairman of the CRRC, says, “We have been very successful in attracting clinical trials in a short period of time and we are looking at developing more sites for specialized trials. The response from industry has been very positive – people appreciate what we are doing – our big picture approach.”

The CRRC is conducting study reviews, budget negotiations, start-up and calls for sites. The database on all site information is complete with details of resources available, the number of trials completed and their trial experience. The patient database is populated and the CRRC is selecting a vendor.

The establishment of the CRRC was supported by the Network and the CAN-CRRC partnership creates a research environment that offers a highly desirable bench to bedside to community range of arthritis-related expertise and services.

The CRRC, created in 2003, is an unparalleled alliance of high quality academic and community rheumatology trialists. It is a not-for-profit, federally

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CRRC

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incorporated body, with 52 members in eight provinces. All CRRC members have expertise in the conduct of all phases of pharmaceutical and biotechnology industry-sponsored clinical trials and provide consulting services specific to arthritis research. They are members of the Canadian Rheumatology Association and are certified either by the Royal College of Physicians and Surgeons of Canada or the College of Physicians of the Province of Quebec.

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The CRRC offers:

- a single point of contact for access to a national network representing the majority of Canadian community and academic rheumatology clinical trialists;
- access to expertise for trial design or data review;
- faster study start-up;
- rapid recruitment and generation of high-quality clinical trial data;
- enhanced efficiency and quality of existing clinical trial sites and development of new clinical trial sites;
- an opportunity for industry to contribute to the development and implementation of investigator site standard operating procedures;
- an efficient and effective business approach based on fairness, transparency and credibility;
- a separation of scientific and business relationships;
- an infrastructure to enable collaborative opportunities: tissue bank, pharmacoconomics, databases, and working with other consortia. ■

For further information, contact Linda Bennett at 416-586-5912 or visit the website www.rheumtrials.ca

Find a cure

“Find a cure” was the message from Logan Graham, age 9, at the Frontiers in Inflammatory Joint Diseases Conference held in Toronto May 8-9.



Left to right, Rob Inman and Hani El-Gabalawy

“IF YOU CAN’T FIND A CURE fast enough, please find something to stabilize it long enough,” he added. Logan has juvenile arthritis and is one of the founders of the Children’s Arthritis Foundation. He joined other people with arthritis, scientists, policy makers, and representatives of pharmaceutical companies to provide input into the development of a national research agenda for inflammatory joint disease.

Chaired by Network members Drs. Hani El-Gabalawy and Rob Inman, the Conference was hosted by the Canadian Arthritis Network (CAN), The Arthritis Society (TAS), the Institute of Musculoskeletal Health and Arthritis (IMHA), the Canadian Institutes of

Health Research. The conference was generously sponsored by: Abbott Immunology, Amgen, AstraZeneca, Aventis, Merck Frosst, Pfizer, Schering Canada Inc. and Wyeth. The first day of the program was dedicated to consumers and included presentations on ethics in clinical trials and informed patient advocacy. On the second day, Canadian and international scientists reported on the latest developments in research on inflammatory joint disease with presentations on biomedical perspectives, clinical trials, gene therapy, population health studies and health services research.

The Conference was the first step in the development of the strategic research themes that will guide future R&D in this area. Strategic research themes are based on pressing issues, address population health and offer Canadians the greatest possible health benefit. They build on existing Canadian research strengths. A working group involving representatives from CAN, TAS and IMHA is refining and consolidating the themes. ■



The organizing committee, left to right

Back row: Susan Kapilik, Henri Ménard, Lisa Cirella, Chris Nelson, Ciaran Duffy

Middle row: Denis Morrice, Claire Bombardier, Dafna Gladman, Mary Kim, Arthur Bookman, Tineke Meijers

Front row: Rob Inman, Sharon McConnell, Hani El-Gabalawy, Robin Poole

New co-chairs for CAN's Consumer Advisory Council

Jay Fiddler and Jean Légaré are the new co-chairs of the Network's Consumer Advisory Council. They were recently elected by the Council when the terms of office of Cheryl Koehn and George McKiel came to an end.

JAY FIDDLER HAS BEEN THE British Columbia representative on the Council. She was diagnosed with Still's Disease three years ago at the age of thirty and brings the newly diagnosed perspective to her work. Along with her work in CAC, she is also a member of the Consumer Research Advisory Council of the Arthritis Research Centre of Canada.

Currently, Ms. Fiddler is working on her PhD at the University of British Columbia in the Department of Sociology. Her doctoral research focuses on the institutional policies that underline the development of donor recruitment strategies, with a particular emphasis on the social factors that influence the effectiveness of such strategies in attracting new donors. This research is supported through a Canadian Blood Services research fellowship award. She is also a co-investigator on a two-year study funded through the CIHR/Bayer partnership program and entitled, *"The Social Determinants of Blood Donation: Examining the Role of Social Capital, Ethnicity, Identity and Trust."*

Jean Légaré has been the Quebec representative on the Council. He was diagnosed with rheumatoid arthritis at the age of 38 and became a very active arthritis advocate, involved in a number of organizations. He served on the board of directors of Association des arthritiques de Québec, is vice-president of the Canadian Arthritis Patients Alliance, was a member of the steering committee of the Best Medicines Coalition, is a Master Trainer with the Arthritis Self-Management Program, and is a member



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of Patient Partners® in Arthritis as well as the Quebec City Site Coordinator for that program. He was the consumer delegate of the Quebec branch of the Arthritis Society at Arthritis 2000 which led to the application for creation of the Canadian Arthritis Network (CAN) and serves as the co-chair of CAN's Consumer Advisory Council. He recently chaired the Consumer Day at the Frontiers in Inflammatory Joint Diseases

Conference, which was held to establish the Canadian research agenda for inflammatory joint diseases.

Mr. Légaré retired from Bell Canada after 31 years in network engineering. He is fluent in English, French and Spanish, and has worked as a telecommunications consultant in Haiti, Mexico and Spain. He now divides his time between his six grandchildren and his advocacy activities for people with arthritis. ■

Appointments to CAN's Board of Directors

Dr. Ann Clarke, Ms. Flora Dell and Dr. Stephen Lye were recently appointed to CAN's Board of Directors.



Dr. Ann Clarke

DR. CLARKE, a CAN member, is Associate Professor in the Divisions of Clinical Immunology/ Allergy and Clinical Epidemiology in the Department of Medicine at McGill

University. She is also an Associate Member of the Department of Epidemiology and Biostatistics and Co-Director of the McGill University Health Centre Lupus Clinic.

After receiving a medical degree from Memorial University, Dr. Clarke completed a residency in internal medicine and fellowship in clinical immunology and allergy at McGill University. She was awarded a postdoctoral fellowship at Stanford University and earned a master's degree in health services research. Dr. Clarke holds a Canadian Institutes of Health Research Investigator award, is a Fellow of the Royal College of Physicians of Canada and serves on the Medical Advisory Board of Lupus Canada.

Dr. Clarke's research has evaluated the cost of chronic paediatric and adult rheumatic conditions and cost-effectiveness of psycho-educational interventions. She has published studies on the economic consequences of rheumatic diseases. Her current research focuses on the risk of malignancy in Systemic Lupus Erythematosus and the potential factors mediating this susceptibility.



Ms. Flora Dell

Ms. Dell holds a master's degree in second language teaching from Laval University and is certified in Gerontology by the University of St. Thomas. She has extensive experience

in advocacy and has written publications relating to special populations.

Ms. Dell fostered the development of the Active Living Coalition of Older Adults (ALCOA) and served as vice-chair and on the executive. She is Chair of Stakeholder Relations and the Knowledge Exchange Task Force of the Institute of Musculoskeletal Health and Arthritis and on the executive of the Canadian Centre for Activity and Aging at the University of Western Ontario. Ms. Dell served on the executive of the Osteoporosis Society of Canada and was the founding member and past chair of the Osteoporosis Society of New Brunswick. She received the National Builder Award and the Queen's Golden Jubilee Medal.



Dr. Stephen Lye

Dr. Lye is Associate Director of the Samuel Lunenfeld Research Institute of Mount Sinai Hospital and Vice-President, Research of Mount Sinai Hospital. He is a professor of obstetrics

and gynecology and of physiology at the University of Toronto. His research is focused on defining the molecular mechanisms underlying the onset of term and pre-term labour and the mechanisms controlling early placental development. He is an advisor to The Genesis Foundation of Canada and Tommy's – The Baby Charity in the U.K., charitable agencies for research on women's health and problems associated with pregnancy. Dr. Lye holds a Canada Research Chair in Maternal, Fetal and Neonatal Health.

Dr. Lye's research has identified key genes that increase contractile activity of the uterine muscle during labour. With other members of the Institute and clinical colleagues in the High Risk Pregnancy Program at Mount Sinai Hospital, Dr. Lye is investigating the use of new therapeutic agents to prevent pre-term birth, the leading cause of neonatal death and disability. ■



CANADIAN ARTHRITIS NETWORK | LE RÉSEAU CANADIEN DE L'ARTHRITE

The Canadian Arthritis Network is the gateway to arthritis R&D in Canada, a single point of contact linking researchers, clinicians, academia, The Arthritis Society, the Institute of Musculoskeletal Health and Arthritis of the Canadian Institutes of Health Research, pharmaceutical and biotechnology companies, and government. In addition to funding research, the Network helps scientists bring their discoveries to market by facilitating technology transfer and commercialization of new arthritis products. The Network is a not-for-profit organization funded by the Government of Canada's Networks of Centres of Excellence.

Chris Nelson
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