THE UNIVERSITY OF BRITISH COLUMBIA

Morquio B Research

Your support is inspiring the pursuit of new knowledge for improved health.

Thank you.

COMMITMENT TO FINDING A CURE

In 2009, Dan and Tina Priest discovered that their son, Stephen, had a rare condition affecting the development of his bones and joints. While he is just like any other teenager – concerned with his school work, his friends, and the latest video games – his body is becoming less mobile and increasingly fragile. As Stephen continues to grow, there is the added risk that the disease could eventually affect his heart, lungs, and hearing.

The genetic illness is called mucopolysaccharidosis (MPS) IV B, or Morquio B Disease, and is currently known to affect fewer than 100 people worldwide. Since it is so rare, research into possible therapies and cures to Morquio B is equally rare, and people living with its devastating consequences currently have no access to treatment other than surgery. To help Stephen and people like him around the world, the Priests have dedicated themselves to creating a solution by raising funds and awareness for improved treatments and, one day, a cure.

Over the past seven years, their efforts have singlehandedly funded critical Morquio B research led by Dr. Sylvia Stockler, one of Stephen's physicians and Professor and Head of the Division of Biochemical Diseases in the UBC Department of Pediatrics. Dr. Stockler and her team are working with a growing international group of experts to expand knowledge and care options for people with Morquio B. Among these collaborators is Professor Dr. Eduard Paschke from the Medical University of Graz, Austria, who was involved in the discovery of Morquio B disease back in the 1970s.

As these researchers dedicate their expertise to understanding Morquio B, their findings are leading to a brighter future for people like Stephen.

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BUILDING A FOUNDATION OF KNOWLEDGE

The Morquio B MPS IVB Facebook Group has 96 members, and counting!

"We need to acknowledge Tina and Dan's hard work. On top of all they have achieved through their fundraising, Tina has also convened a highly motivated patient group on Facebook."

- Dr. Sylvia Stockler

MORQUIO B ONLINE PATIENT REGISTRY, A SUCCESS STORY

Following on the success of the international online patient registry, the UBC-based Morquio B study team is moving forward with coordinating a prospective cohort natural history study.

The patient registry, established in October 2012, has already helped enroll over one third of all known patients with the disease – an achievement only possible through the invaluable contributions of Tina and the wonderful online registry team: Maria Boldut and Maria Bleier.

The first of its kind in the world, the registry stores demographic and disease-specific data, which will be invaluable for future research and treatment development. Its success is due in large part to the patients, who were eager to enroll in the study and collaborate with the researchers. This kind of participatory research – increasingly favoured in rare disease research – demands strong relationships between academia, ethics review boards, and patient communities. The Morquio B team is proud to share that the results of this study have received international attention and have been accepted for publication in an international peer-reviewed journal.

With this critical groundwork in place, the UBC-based research group will begin using the data collected to define research priorities, develop best practices for patient care, as well as new drug therapies, and to prepare for clinical trials.

NEXT STEPS: THE PROSPECTIVE COHORT NATURAL HISTORY STUDY

The next goal of the research supported by the Priests' donation is to develop methodologies to be employed in clinical trials for new therapies.

Over the past year, Dr. Stockler together with her BCCH-based team have designed an international, multi-centre study of MBD that has a two-fold goal: 1) to investigate patient's bone health, analyze progression of orthopedic problems, and test patient's mobility and strength; and 2) to collect blood and urine samples to build a sample biobank for future research.

This study includes two clinical visits per year – one to establish baseline information, and a follow-up visit one year later to monitor any changes. Supported by physiotherapists and occupational therapists, researchers like Dr. Anthony Cooper and Dr. Heather MacDonald will measure the musculoskeletal function and endurance of their patients through a 6-minute walk test, a 3-minute stair climb test, a hand grip and a range of motion test. They will also establish measurable indicators of spine, hip, and lower limb development, employing bone X-ray studies and innovative technologies to assess bone strength and mineralization. Heart health, and inflammation as possible causes for pain and bone decay, will be tested as well. Finally, samples of blood, urine, and skin fibroblasts (i.e., cells found in the connective tissues that aid in wound healing) will be collected, all of which are important to standardize testing and to record measurable outcomes.

Because patients are scattered around the globe, the goal is to set up a number of study centres in North and South America, as well as in Europe, to make sure that every patient, irrespective of their geographic location, has the chance to participate.

ESTABLISHING ETHICAL STANDARDS

In any research study involving vulnerable groups of people, scientists must submit their proposed study to a Research Ethics Board for review. The UBC Research Ethics Board, spearheaded by Dr. Marc Levine, has been tremendously supportive in establishing the ethical framework for this international study.

The UBC team is also currently pursuing formal agreements with each of its international partners, to ensure that every centre understands and follows a similar protocol for data collection and data entry. Dr. Stockler's team recently formalized a contract with the Medical Genetics Centre in Porto Allegre, Brazil, and Dr. Roberto Giugliani will be the first scientist to start the study.

INTRODUCING THE MORQUIO B TEAM

The UBC-led Vancouver project team continues to expand, growing the vision and expertise available to complete the natural history study.

Dr. Sylvia Stockler-Ipsiroglu, MD, PhD, MBA, FRCPC, is Professor and Head of the Division of Biochemical Diseases in the UBC Department of Pediatrics and Program Director of Biomedical Diseases at BC Children's Hospital. She is a leading authority on rare diseases with a focus on treatable inborn errors of metabolism. She also serves as the project leader of TIDE BC, a collaborative care and research initiative whose goal is to provide timely diagnosis and treatments for children with treatable forms of intellectual disability.

Dr. Judith G. Hall, MD, OC, is Professor Emerita within the UBC Department of Pediatrics and Medical Genetics and a member of the Canadian Medical Hall of Fame (2015). An internationally-recognized expert in rare genetic conditions affecting children's growth, Dr. Hall has over four decades of experience in genetics and pediatrics. She has not only developed new ways to classify genetic abnormalities, Dr. Hall has worked with physicians to create guidelines for the care of common genetic disorders, and with parent groups to help clarify the best care options available for genetic diseases affecting their children. Dr. Hall advised on the design of the Morquio B study protocol.

Dr. Nataliya Yuskiv, MD, MPH, PhD, Research Manager in the UBC Division of Biochemical Diseases, has been instrumental in developing the study protocol and producing all of the documents needed to manage patient histories, including the informed consent forms, information letters, and questionnaires. She is also overseeing the recruitment and assessment of international study sites for their capacity to administer the natural history study and subsequent studies.

Dr. Anthony Cooper, MBChB, FRCS, is a Clinical Assistant Professor with the UBC Department of Orthopaedics and a pediatric orthopaedic surgeon at BC Children's Hospital. Dr. Cooper's research interests include improving bone health and mobility to enhance quality of life for his young patients. As Co-Investigator on the Morquio B project, he is currently leading development of the bone health protocol. His research team, under the leadership of Ms. Harpreed Chhina, will also develop an online database to collect patient data from all of the participating international study centres. Dr. Cooper will also be responsible for reviewing all patient x-rays and skeletal images collected from the international centers, to ensure accuracy and monitor any changes.

Dr. Heather MacDonald, PhD, is an Assistant Professor in the UBC Department of Orthopaedics, a scientist at the Child & Family Research Institute, and a member of the Centre for Hip Health & Mobility. Her research interests include the relationship of exercise to bone health, as well as the use of imaging techniques to monitor the effects of chronic diseases on the growing skeleton. Dr. MacDonald will offer her expertise in imaging techniques to evaluate the hip bone strength of Morquio B patients.

Mrs. Lauren Hershfield, an Occupational Therapist, and **Mrs. Lorelyn Meisner**, a Physiotherapist, will lead the musculoskeletal function and endurance assessments of study participants at BC Children's Hospital. They have also provided useful guidance on the most appropriate assessment methods for Morquio B patients.

Dr. Kathrin Stoll, PhD, a Research Associate within the UBC Department of Pediatrics, is exploring funding opportunities that would help expand the natural history study into other countries, and make available the biobanked samples for future research.

Dr. Iman Abumansour, MBBS, worked on a systematic literature review on genotype and phenotype correlations in Morquio B disease, and **Dr. Mojgan Yazdanpanah, MD, MSc, DSc, PhD,** and **Dr. Nahid Yazdanpanah, PhD,** provided their expertise in database analysis, all of which have been invaluable in informing the ongoing studies.

EXPANDING THE NETWORK OF INTERNATIONAL COLLABORATORS

As you might imagine, with only 100 known individuals with Morquio B disease around the world, organizing a prospective natural history study requires a massive coordinated effort. Dr. Stockler and her team have made great progress in growing a community of international patient advocates, physicians, researchers, and industry partners – all of whom have interest in developing a better understanding of the disease and how to intervene in its progressive effects.

In addition to a strong UBC team based at BC Children's Hospital, physicians and researchers from medical genetics, research genetics, and biochemical laboratories in Austria, Belgium, Brazil, Germany, Switzerland, Poland, and the USA have joined the Morquio B study team. To round out this expert cohort, the UBC-based study team is approaching academic and industry collaborators in Switzerland and the USA, as well.

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Thank You

Thanks to the Priest family and their incredible community of supporters and donors, Dr. Stockler and her team have established a vibrant and growing network of scientists and health care professionals who are united in their determination to solve the genetic mystery underlying Morquio B disease. With the critical infrastructure now in place, Dr. Stockler and her collaborators will be able to capture important patient data on the natural course of the disease, which will in turn provide them with a useful starting point for future research projects and clinical trials.

Every year we shed a little more light on this rare genetic disease, and every year we strengthen our ability to intervene. We remain grateful for the passion and perseverance of patient advocates like Dan and Tina Priest, who share Dr. Stockler's conviction that through patient-centered research we can create healthy futures for children like Stephen.