The Princess Margaret Hospital Foundation
University Health Network

mesothelioma
research program

program update 2008

We are pleased to provide you with an update of progress made over the past year in the Mesothelioma Research Program at The Princess Margaret/University Health Network. Here are a number of distinct but inter-related projects encompassed within the Program. Progress in each of these areas will be summarized individually.

the early detection project

This research study is designed to detect mesothelioma and lung cancer at an early stage using low-dose computed tomography. The aim is to screen people who have either a strong history or chest x-ray evidence of asbestos exposure.

Dr. Demetris Patsios

Each person enrolled in the study undergoes a comprehensive interview questionnaire focusing on asbestos exposure history and other possible contributing factors. A small sample of blood is then obtained for use in associated studies aimed at the early detection of mesothelioma (see below for a description of some of these studies). Each participant then undergoes a Low Dose Computer Tomography (CT) scan of the chest. Our chest radiologist reads the scan and a report is generated which is sent to the participant's family physician.

Depending on what is found on the scan, the participant is asked to return for further scans at regular intervals. If there is concern of an abnormal finding, further diagnostic studies are arranged.

To date, three cases of malignant pleural mesothelioma, three cases of malignant peritoneal mesothelioma and eight cases of lung cancers have been discovered since the study was launched in March 2005 under the leadership of Dr. Heidi Roberts. We have screened over 700 participants and this study continues to grow under the guidance of Dr. Demetris Patsios and our project coordinator Brenda O'Sullivan.

We continue to actively recruit individuals to this study from high-risk occupations. In order to qualify for the early detection study, individuals must have been exposed to asbestos at least 20 years ago, and/or have pleural plaques, be 30 years of age or older, in general good health with no prior cancers.

identifying risk factors in mesothelioma patients

Dr. Geoffrey Liu

Many people are exposed to asbestos. Yet, only a small proportion develops mesothelioma. Drs. Geoffrey Liu and Ming Tsao, two physicians and scientists at the Ontario Cancer Institute and The Princess Margaret, are studying the interaction between asbestos exposure (such as the amount of exposure and the type of asbestos) and genetic (inherited) factors that determine how the body responds to asbestos.

Studies are underway to determine the genetic factors associated with a patient's response to drug therapy, while other studies are focused on developing animal models of human mesothelioma to better understand the basic mechanisms of this cancer.

Dr. Ming Tsao

This year we have collected over 350 blood samples for analysis, and have begun looking at biomarkers (proteins in the blood) that can predict for either the presence of mesothelioma, or for predicting how well someone does after diagnosis. These samples represent the largest set of samples in Canada and one of the largest set of samples around the world related to mesothelioma from all causes, and will contribute greatly to our understanding of this disease, how to diagnose it, and how to treat it over time.

To participate in the Mesothelioma Research Program, please call: 416.340.5686

blood tests for the early detection of mesothelioma

Dr. Marc de Perrot, a surgeon scientist at The Princess Margaret and the University Health Network, is investigating *mesothelin* and *osteopontin*, two mesothelioma markers, to detect early disease in populations exposed to asbestos. Blood tumour markers, which are proteins associated with tumours, are frequently used to help diagnose various cancers, to follow response to treatment and to help diagnosis cancer early. Working in collaboration with Drs. Liu and Tsao, our hope is that by understanding these factors, we can identify new treatments for this deadly disease. Combining these tumour markers with screening CT scans may provide an even earlier detection of mesothelioma than CT scans alone. Our screening program should therefore lead to more patients being diagnosed at an earlier stage of the disease, which gives them greater hope for a cure. Furthermore, these markers can be used to detect recurrence of the disease as well as measure the effectiveness of treatment.

Dr. Marc de Perrot

development of immunomodulation therapy

Dr. Masaki Anraku

Dr. de Perrot and fellow researcher, Dr. Masaki Anraku, previously reported that *cytotoxic* CD8 T-lymphocytes play a critical role in tumor-cell killing in human malignant pleural mesothelioma (*J Thorac Cardiovasc Surg*, 2008). In our research lab, we developed an animal model of mesothelioma to further explore the role of lymphocytes and their therapeutic potential. By using this model, it was found that mesothelioma-bearing mice can survive longer if we block *regulatory* T- lymphocytes (cytotoxic T-lymphocyte suppressor). Moreover, our study suggests that *regulatory* T cell blockade combined with Pemetrexed (a chemotherapy drug used for human mesothelioma) can effectively suppress mesothelioma growth and prolong animal survival by inducing greater anti-mesothelioma immune reaction. We are currently working on developing a vaccine to treat patients with mesothelioma in the future.

ongoing treatment studies for patients with mesothelioma

Drs. John Cho, Marc de Perrot and Ron Feld are clinical oncologists specializing in the aggressive treatment of early stage mesothelioma. The best survival has been found in patients who complete chemotherapy, surgery and radiation. However, previous work at the University Health Network has shown that lymph node involvement in the middle of the chest was associated with significantly poorer outcomes. They are developing new ways of treating early stage mesothelioma by using a short course of radiation followed by surgery and reserving chemotherapy for patients at greatest risk of tumour recurrence. By changing the order of chemotherapy, surgery and radiation around, it may be possible to improve treatment outcomes and reduce over treatment time and side effects.

Dr. John Cho

Dr. Ron Feld

announcement from dr. michael johnston

Due to increasing commitments in my new position in Halifax, I have stepped down as Head of the Mesothelioma Research Program in February. I am very pleased to report that Dr. Heidi Roberts has taken the position. Dr. Roberts has been a key member of the Program since its inception. As a highly respected chest radiologist she instituted the Mesothelioma Early Detection Study – a landmark study that continues to expand its scope. I am sure that Dr. Roberts will bring strong leadership and further advancement to the Mesothelioma Research Program.

Dr. Michael Johnston

dr. heidi roberts

In 2002, Dr. Roberts joined the Department of Medical Imaging at the University Health Network/Mount Sinai Hospital, where she has a co-appointment as Associate Professor of Radiology at the University of Toronto. Currently, Dr. Roberts is a staff radiologist in the Cardiopulmonary Section of the Department of Medical Imaging. She has published more than 20 peer-reviewed papers on subjects related to body imaging, predominantly pulmonary embolism as well as 30 peer-reviewed papers on the utilization of contrast agents for magnetic resonance imaging and neuroimaging of stroke and brain tumors. Her research emphasis switched to the early diagnosis of mesothelioma and lung cancer. As of January 2007, Dr. Roberts has been appointed as the site director for Medical Imaging at Women's College Hospital.

Dr. Heidi Roberts

"I feel very honored to take over the leadership of the Mesothelioma Research Program from Dr. Michael Johnston. In 2005, we started the mesothelioma early detection program, and it has been very successful. I am looking forward to my increasing involvement in all other aspects of the Mesothelioma Research Program. "

support for the mesothelioma research program provided by:

- Asbestos Workers Local 110
- Building and Construction Trades Council of Ontario
- International Association of Heat and Frost Insulators and Asbestos Workers Local 95 of Ontario
- International Association of Heat and Frost Insulators and Asbestos Workers (U.S.)
- International Brotherhood of Boilermakers Local 128
- I.U.O.E. local 793
- Master Insulators Association of Ontario
- Mechanical Contractors Association Toronto
- Mechanical Industry Advisory Committee (MIAC)
- Motley Rice LLC
- Ontario Pipe Trades Council
- Sarnia Occupational Health Clinic for Ontario Workers
- United Association of Journeymen & Apprentices Local 67
- United Association of Plumbing and Pipe Fitting Local 46
- and many others

For further information or details on how to support this program, please contact:

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