Mesothelioma Research Program at The Princess Margaret

2013 Update

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The Princess Margaret Cancer Centre has achieved an international reputation as a global leader in the fight against cancer and delivering personalized cancer medicine. The Princess Margaret, one of the top 5 international cancer research centres, is a member of the University Health Network, which also includes Toronto General Hospital, Toronto Western Hospital and Toronto Rehabilitation Institute. All are research hospitals affiliated with the University of Toronto. www.theprincessmargaret.ca

Introduction

Over the years, your commitment to mesothelioma research and treatment has resulted in patients living longer and healthier lives. By training thoracic surgeons, radiologists, clinicians and researchers, and by enhancing and expanding the Mesothelioma Research Program at The Princess Margaret, we are developing early diagnosis and novel therapeutics to combat a form of cancer that has few treatment options.

With an emphasis on providing customized health expertise, we are creating the new gold standard in cancer care: Personalized Cancer Medicine.

At The Princess Margaret, Personalized Cancer Medicine encompasses four main themes:

1) **Detect** – finding cancers earlier
2) **Diagnose** – analyzing cancers more precisely
3) **Target** – targeting treatment more specifically
4) **Support** – providing comprehensive physical and emotional support

In the following report, we will highlight some of the recent activities of our Mesothelioma Research Program.

Thank you again for your assistance, which is allowing us to move one step closer in our goal of conquering cancer in our lifetime.

"On behalf of my colleagues and collaborators in the Mesothelioma Program at UHN and around the world, I would like to convey our profound gratitude. Your generous support continues to provide vital research opportunities which enrich our program, help us forge new international partnerships, and inspire discoveries that transform the standard of care for patients everywhere. Thank you."

- Dr. Marc de Perrot

Detect

Diagnose

Target

Support

Mesothelioma Research Program Update

Overview

Malignant Pleural Mesothelioma (MPM) is a rare form of cancer in the general population, but is rather common among construction and industry workers who have been exposed to asbestos. MPM originates from the lining of the lungs, and is usually diagnosed quite late in advanced stages when treatment options are limited, and a cure is no longer possible.

However, if diagnosed early enough, patients can benefit from various treatment options and increased survival rates.

Mesothelioma is an important focus of the Division of Thoracic Surgery at University Health Network (UHN), with a leading edge research facility and infrastructure for early detection, rapid assessment, diagnosis and treatment options. **The Mesothelioma Research Program, led by Dr. Marc de Perrot, is the only program of its kind in North America.** We see more patients with this disease than any other centre in Canada and The Princess Margaret is uniquely poised to bring about the eradication of mesothelioma on a global scale.

Rapid Assessment and Management Program

At UHN and The Princess Margaret, we have established a rapid assessment and diagnosis program where patients from all across Canada with pulmonary problems related to asbestos would be able to complete their assessment within one day in our centre. This is a multidisciplinary team approach with physicians, surgeons, nurses, respiratory therapists, social workers, and researchers to improve efficiency in the prevention, diagnosis, support and management of asbestos related diseases. This program is accessible to all patients with lung problems and previous asbestos exposure through direct referral from family doctors or occupational health clinics. *(Please see page 10 for referral information, etc.)*

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Early Detection Program

The Princess Margaret is proud to be the only facility in the world conducting the Early Diagnosis of Mesothelioma and Lung Cancer in Prior Asbestos Workers using a Low-Dose Computed Tomography (LD CT) study in conjunction with our Mesothelioma Research Program.

Our aim is to screen people using LD CT, who have no symptoms, enjoy good health, and who have either a strong history of exposure to asbestos or have findings on a chest x-ray that show evidence of asbestos exposure in the form of pleural plaques.

Lead investigator, **Dr. Demetris Patsios**, and **Dr. Zhi (George) Dong** are radiologists who are committed to detecting mesothelioma and lung cancer at an early stage.

How it works: At the time of CT screening, a small blood sample is drawn and used as a biomarker. Blood biomarkers help to diagnose various cancers, earlier. Increased levels of proteins in healthy subjects may be a predicting factor that a mesothelioma specific tumour is developing because protein levels are much higher in patients with mesothelioma. Combining tumour markers with screening CT scans could provide an even earlier detection of Mesothelioma than CT scans alone. Early diagnosis means more effective treatment, giving those affected with mesothelioma a greater chance for a cure.

Dr. Ming Tsao, a physician and scientist at Princess Margaret, is currently investigating the proteins soluble mesothelin related protein and osteopontin in people who have a history of asbestos exposure.

From top:
Dr. Demetris Patsios
Dr. George Dong
Dr. Ming Tsao

Mesothelioma Research Program Update

SMART Treatment

The Princess Margaret and Toronto General Hospital at UHN, are committed to finding a cure while also striving to improve clinical outcomes for this serious disease.

Drs. John Cho, Marc de Perrot and **Ron Feld** have completed the phase I/II Surgery for Mesothelioma After Radiation Therapy (SMART) study, where 25 suitable patients received an accelerated one week course of radiation followed by surgery the next week. This study was a world first, developed and funded completely with support of The Princess Margaret Cancer Foundation Mesothelioma Research Fund. Epithelioid mesothelioma patients treated with SMART appeared to do better than others who had encouraging survival outcomes. The study is currently being readied for publication and has been submitted for presentation at the **15th World Conference on Lung Cancer** in Sydney, Australia in October, 2013.

From top:
Dr. John Cho
Dr. Ron Feld
Dr. Licun Wu

Research: Chemo-immunotherapy

The function of the immune system relies on balance of immune suppression and enhancement. Overwhelming immunosuppresion would result in tumours or infections and strong immune enhancement would cause autoimmune diseases. Suppression of the immune system is quite common in cancer development. Researcher **Dr. Licun Wu** is attempting to improve the results of chemotherapy by enhancing the immune system to fight cancer cells.

Our studies have demonstrated that removing the immune brakes (regulatory T cells and CTLA-4 receptor) during intervals of chemotherapy resulted in tumour growth delay and longer survival rates of tumour-bearing mice.

Another strategy we are testing is activating NKT cells to promote anti-tumor immunity. We expect that these approaches could be translated into clinical trials for mesothelioma in the near future.

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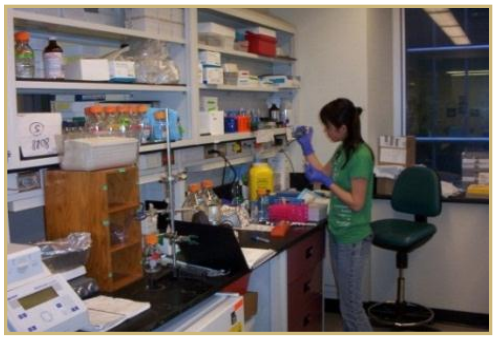
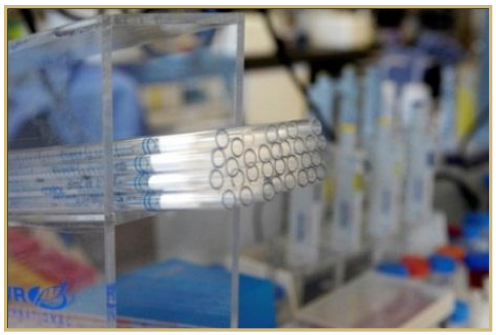
We are also studying the "abscopal effect" induced by local radiotherapy and how this can be enhanced by immunotherapy in the mouse model. The abscopal effect is a phenomenon in the treatment of metastatic cancer where localized irradiation of a tumor causes, not only a shrinking of the irradiated tumor, but also a shrinking of tumors far from the irradiated area. While this phenomenon is extremely rare, its effect on the cancer can lead to the disappearance of malignant growths throughout the entire body. Our results suggest that this effect may depend on activation of the immune system.



Ongoing Treatment Studies

Every person diagnosed with mesothelioma should undergo a thorough investigation and be offered appropriate treatment. Depending on the extent of the disease, and the general health of the patient, this treatment may vary from being an aggressive attempt to cure, to controlling symptoms and making the person comfortable. The Tri-modality Study, a combination of chemotherapy, surgery and radiation for patients with early stage mesothelioma, continues at The Princess Margaret.



Upcoming Research Trial

A Phase 2, Randomized, Double-blind Study Comparing Tremelimumab to Placebo in Second- or Third-line Treatment of Subjects with Unresectable Pleural or Peritoneal Malignant Mesothelioma

Tremelimumab is a fully human monoclonal antibody or a "manufactured antibody", similar to ones that are made by the human body to fight off infection. This monoclonal antibody blocks cytotoxic T lymphocyte antigen 4 (CTLA4), which is found on cells of the immune system. CTLA4 seems to slow down the immune response, so blocking it with an anti-CTLA4 antibody may make the immune response more active. The idea behind developing this experimental drug is that stimulating the immune system could be a different way of killing cancer cells.

Currently, there are no approved second line treatments for mesothelioma after the first line of treatment with Cisplatin based regimens. This trial may lead to disease stability and improved quality of life for participants.

Mesothelioma Research Program Update

Support for the Mesothelioma Research Program is generously provided by:

- Asbestos Workers Local 110
- Building and Construction Trades Council of Ontario
- Geo A. Kelson Company Limited
- Imperial Oil Foundation
- 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
- International Brotherhood of Electrical Workers Local 353
- International Union of Operating Engineers Local 793
- Loretta's Legacy Foundation
- Master Insulators Association of Ontario
- Mechanical Contractors Association Toronto
- Mechanical Industry Advisory Committee (MIAC)
- Motley Rice LLC
- Ontario Pipe Trades Council
- Ontario Sheet Metal Workers and Roofers Conference Inc.
- Sarnia Occupational Health Clinic for Ontario Workers
- United Association of Journeymen & Apprentices Local 67
- United Association of Plumbing and Pipe Fitting Local 46

- A special thank you to all those donors honouring loved ones through their support.

Thank You

The work conducted through the Mesothelioma Research Program is helping Personalized Cancer Medicine develop at Princess Margaret Cancer Centre by providing our patients with the best targeted therapy with the least side effects. On behalf of all the patients who are benefitting from your generosity, thank you for your help with this important work.

To Participate in the Mesothelioma Research Program

The Early Detection Project continues to actively recruit individuals from high risk occupations. In order to qualify for the study, individuals must have been exposed to asbestos at least 20 years ago, and/or have pleural plaques on chest x-rays, be 30 years of age or older and in general good health with no history of prior cancers. For further information, or to schedule an appointment, contact: 416-340-5686 or brenda.osullivan@uhn.on.ca.

Brenda O'Sullivan,
Clinical Research Manager

The Rapid Assessment and Management Program continues to accept referrals. In the last year, the clinic has more than doubled in referred patients with asbestos related lung diseases. For further information on this program contact: 416-340-5686 or a referral can be faxed to 416-340-4964.

Hundreds of Canadians each year are diagnosed with Mesothelioma. This disease has few treatment options. We rely on partners like you to give our patients and their families hope.

Your donations are supporting further development of pioneering approaches to mesothelioma treatment, and will enhance and expand the Mesothelioma Research Program at The Princess Margaret. Your commitment will also help us invest in training thoracic surgeons, radiologists, clinicians and researchers for future generations.

Andrea Ebidia,
Clinical Research Assistant

Together, we can make a global impact on mesothelioma, increasing the quality of life through early diagnosis and novel therapeutics. You will be helping transform cancer care in Ontario, Canada and the world. The end result is more mesothelioma patients living longer and healthier lives.

Thank you for recognizing the crucial need for continued research and treatment in mesothelioma.

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