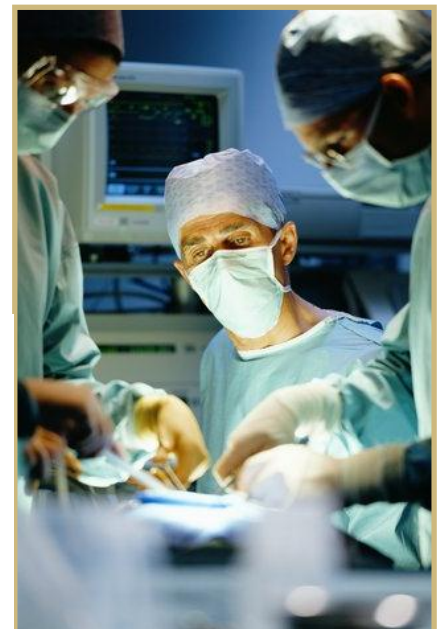


# Mesothelioma Research Program

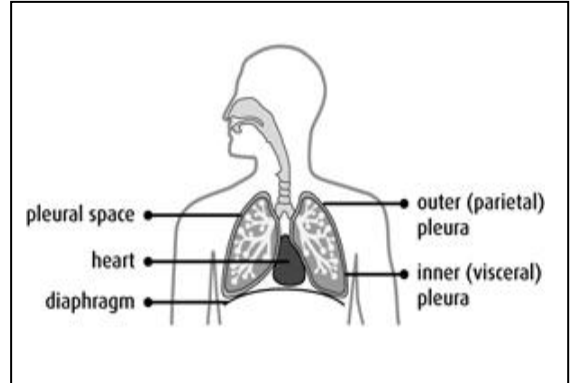


## Program Update 2012

*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.*

Home to the premier lung and mesothelioma cancer program in Canada, University Health Network (UHN) and The Princess Margaret are global leaders in the treatment of advanced lung diseases. Through donor generosity, The Princess Margaret has become a global leader in mesothelioma research and treatment. Our researchers and surgeons have pioneered many world firsts, including the world's first single and double lung transplants and, most recently, the first Canadian use of robotic surgery for early stage lung cancer.

Mesothelioma is an important focus of the Division of Thoracic Surgery at UHN with leading edge research facility and infrastructure for early detection, rapid assessment, diagnosis and treatment of mesothelioma. 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. Last year, The Princess Margaret saw almost 50 per cent of the entire Canadian incidence of this cancer.



Six months ago, the rapid assessment clinic would see one new patient a month; today that number has grown to 4-5 new patients per week. This growth indicates an increasing need for our work in communities all across Canada—work that has further reach beyond our borders.

Malignant Pleural Mesothelioma (MPM) is a rare form of cancer in the general population, but it is rather common among construction and industry workers who have been exposed to asbestos. MPM originates from the lining of the lungs (pleura), and is usually diagnosed quite late in advanced stages when treatment options are limited, and cure is no longer possible. However, if diagnosed early enough patients can benefit from treatment options and increased survival rates for this cancer.

What follows is an overview of the comprehensive approaches to diagnosing and treating Mesothelioma at The Princess Margaret:

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## Rapid Assessment and Management Program



*Dr. Marc de Perrot*

One of the primary goals of the Mesothelioma Research Team is to shorten the timeframe between diagnosis and treatment. Referral to a specialized centre can often be delayed by several months and the support is frequently not in place for the patients and their families.

At the University Health Network and The Princess Margaret, we have established a rapid assessment and diagnosis program where patients with pulmonary problems related to asbestos would be able to complete their assessment within one day in our centre. The goal is to provide 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 by direct referral from family doctors or occupational health clinics.

## Early Detection Program



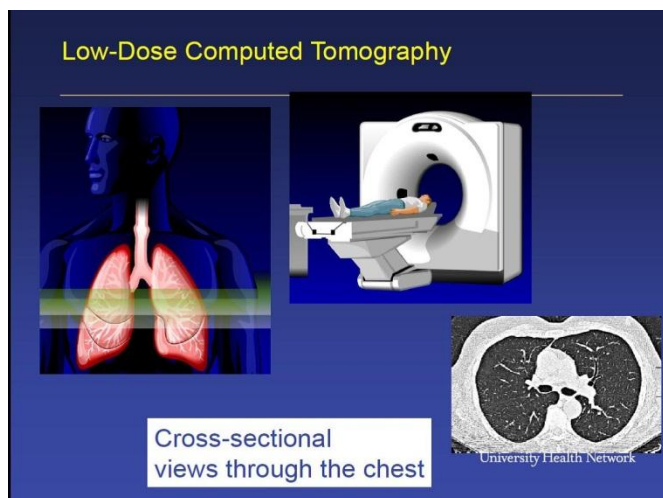
*Dr. Demetris Patsios*

The Princess Margaret is proud to be the only facility in North America conducting the Early Diagnosis of Mesothelioma and Lung Cancer in Prior Asbestos Workers using Low-Dose Computed Tomography (LDCT).

To date, we have screened over 1200 people and support is continuing to grow. Dr. Demetris Patsios, lead investigator, and Dr. George Dong are radiologists who are committed to detecting mesothelioma and lung cancer at an early stage. The aim is to screen people using LDCT of the chest, who have no symptoms, enjoy good health and who have either a strong history of exposure to asbestos or x-ray evidence of asbestos exposure in the form of damage to the chest lining.



*Dr. George Dong*



## Blood Test for Surveillance of Mesothelioma



*Katrina Rey-McIntyre, Clinical Research Assistant*

Blood biomarkers can be used to help diagnose and follow various cancers. As a tumour develops, it sheds certain proteins that can be detected in the blood. Some protein levels are much higher in patients with mesothelioma compared to healthy individuals with asbestos exposure. Increased levels of proteins in healthy subjects may be a predicting factor that a mesothelioma specific tumour is developing or recurring.

This work involves drawing a small blood sample at the time of CT screening, and looking for the proteins that could indicate cancer. Combining these tumour markers with CT scans may 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. Geoffrey Liu*

Drs. Ming Tsao and Geoffrey Liu, physicians and scientists at The Princess Margaret are currently investigating the proteins *soluble mesothelin related protein* and *osteopontin* in people who have a history of asbestos exposure. To date over 400 samples have been analyzed. This project also relies on Katrina Rey-McIntyre, the Clinical Research Assistant responsible for all blood samples collected from participants in the early screening program.

# Radiation Combined With Surgery – A World First



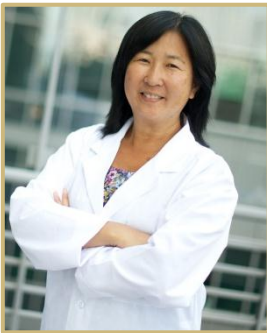
*Dr. John Cho*

The Princess Margaret and Toronto General Hospital at the University Health Network are committed to finding a cure and always strive to improve clinical outcomes for this serious disease. One such approach is to combine radiation and surgery.

Drs. John Cho, Marc de Perrot and Ron Feld are conducting an on-going phase I/II mesothelioma study starting with an accelerated 1 week course of radiation followed by surgery the next week. This study is **a world first** and pinpoints the right amount of radiation that is safe to use for the patient. In addition to being safer, this treatment is also much shorter (around one month) compared to previous therapies that took 4-6 months. Eighteen patients have undertaken this trial since 2008, and most are still alive. This is a significant result for mesothelioma treatment. A second phase of this trial will include 25 patients and is set to begin shortly. Preliminary results were presented in April at this year's Mesothelioma & Thymoma Working Group meeting in Toronto to discuss expansion into a multi-institutional national and international study.

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## Personalized Immune Therapy



*Dr. Pam Ohashi*

There is growing interest and success in a very exciting and innovative approach using the body's own immune system to combat cancer. Dr. Marc de Perrot and collaborators Drs. Linh Nguyen and Pam Ohashi have been developing a new program that focuses on using the immune system to fight Malignant Pleural Mesothelioma. Some cells of the immune system called white blood cells, have the ability to kill cancer cells. A population of white blood cells known as T cells, can be grown in the laboratory from the patients' tumours. In this way, a large number of T cells can be made and then implanted back into the patient to fight the disease.

Recent tests have shown that 50% of patients with melanoma have responded to this approach, and tests for mesothelioma patients will begin in January. This type of treatment is an especially effective treatment for older patients who may not be able to undergo invasive surgery, and is less toxic than standard treatment. It is a personalized therapy that provides patients with a better quality of life.

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## Chemo-Immunotherapy



*Dr. Licun Wu*  
*Research Associate*

The overall aim of this study is to improve the outcome of mesothelioma by combining chemotherapy with immunotherapy. Although first line chemotherapy using the drugs Cisplatin and Alimta could prolong survival compared with Cisplatin alone, the effect is limited. Cancer cells tend to repopulate during the breaks between chemotherapy treatments. Evidence has shown that the rate of repopulation of surviving cancer cells accelerates over time, so better approaches to stop this process need to be developed.

The function of immune system relies on balance of immune suppression and enhancement. Overwhelming immunosuppression would result in tumour or infection; on the contrary, strong immune enhancement would cause autoimmune diseases. Suppression of the immune system is quite common in areas where cancer develops. Researcher Dr. Licun Wu is attempting to improve the results of chemotherapy by enhancing the immune system to fight cancer cells. Our previous studies have demonstrated that depleting regulatory T cells can impact cancer microenvironment when combined with chemotherapy. This depletion between cycles of chemotherapy could improve the outcome of chemotherapy in our models. More strikingly, blocking a protein receptor called CTLA-4 during the intervals of chemotherapy has resulted in tumour growth delay and longer survival of tumour-bearing mice. We expect that this CTLA-4 blockade could be translated into clinical trials for mesothelioma in the near future.

## Ongoing Treatment Studies



*Dr. Ron Feld*

Every person diagnosed with mesothelioma should undergo a thorough investigation and be offered appropriate treatment. Depending on the extent of disease and the general health of the patient, this treatment can vary from an aggressive attempt to cure to a means of 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 Princess Margaret Hospital.

### Success Story

In the year 2000, this patient was a 21 year old university student who was unfortunately diagnosed with Mesothelioma of the left chest. He was treated using a Trimodality approach: induction chemotherapy followed by a surgical procedure to remove part of the lung lining (the pleura), part of the pericardium (the lining of the heart), part of the diaphragm (the muscle that separates the chest and abdomen), and the diseased lung. The third part of this approach is radiation therapy. This approach worked. He recovered well from this extensive surgery and it is now 12 years since his treatment. He is a University of Toronto graduate and is doing extremely well. His CT scan shows no evidence of recurrence in the chest or abdomen.



## Peritoneal Mesothelioma

While mesothelioma often affects the lining of the chest cavity (pleural mesothelioma), it can also affect the lining of the abdominal cavity, a condition known as malignant peritoneal mesothelioma. Dr. Andrea McCart, a surgeon-scientist, has opened a new surgical program to provide surgery in combination with intraperitoneal (injected into the body cavity) chemotherapy for eligible patients. This is an important improvement as patients with malignant peritoneal mesothelioma previously had to receive this treatment in the USA.

In her laboratory, Dr. McCart is developing oncolytic viruses (viruses which specifically infect and kill cancer cells) as a treatment for peritoneal cancers, including peritoneal mesothelioma. Because peritoneal mesothelioma is often caught too late, it is impossible to safely remove all of it by surgery alone. Dr. McCart hopes that after performing surgery to remove the majority of the cancer, the virus will target the remaining cancer cells and prevent recurrences of this devastating problem.



*Dr. Andrea McCart*

## Interventional Thoracic Surgery Suite



*Dr. Kazu Yasufuku*

A new Interventional Thoracic Surgery Program was established under Dr. Kazuhiro Yasufuku, highlighted by the opening of a state-of-the-art Interventional Thoracic Surgery Suite at the Toronto General Hospital in July 2010. This Suite, **the first of its kind in North America**, is a hybrid endoscopy/surgical suite capable of general anesthetic equipped with high-end technology to look inside the body. The Suite provides leading-edge procedures such as diagnostic bronchoscopy (the visual examination of the lungs and air passages) airway stenting (tube-shaped devices that are inserted into an airway), photodynamic therapy (a treatment that uses light to kill cancer), VATS pleuroscopy (examining the space between the 2 layers of tissue that line the lungs), and management of pleural effusion (a buildup of fluid between the layers of tissue that line the lungs and chest cavity).

The Suite is integrated with our existing intervention programs: minimally and ultra-minimally invasive surgery, image guided therapeutics and basic research. It also helps fast track patients referred to the Mesothelioma program by performing diagnostic and therapeutic procedures in a minimally invasive way as a day procedure.

## National Recognition for Dr. Ming-Sound Tsao



*Dr. Ming-Sound Tsao speaking at the Canadian Cancer Society Awards for Excellence.*

On June 18<sup>th</sup>, Dr. Ming-Sound Tsao was honoured with the prestigious O. Harold Warwick Award from the Canadian Cancer Society for Excellence in Cancer Research at The Princess Margaret Hospital.

The O. Harold Warwick Award is named after one of Canada's early cancer researchers and is awarded to a scientist whose research has had a major impact on controlling cancer in Canada.

Dr. Tsao is recognized globally as a leading lung cancer molecular pathologist. He has published close to 300 scientific papers in highly ranked peer-reviewed journals, including *The New England Journal of Medicine* and *Nature*. Dr. Tsao has been a generous contributor to the peer-review system in Canada, and is an outstanding teacher and mentor, dedicated to training the next generation of pathologists and clinicians in molecular and translational research.

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## Media Attention for Mesothelioma Patients at PMH



Recently there has been a lot of media attention about asbestos. Why? Mesothelioma, lung cancer, interstitial lung disease and asbestosis remain major health problems in Canada. These diseases are known to potentially be related to previous asbestos exposure and the number of people affected is rapidly increasing. The damaging effects of asbestos in the workplace will be with us for decades.

Every week members of building trades, prior asbestos workers, and their family members with known secondhand exposure, from all over Ontario come to The Princess Margaret to participate in the Early Detection Program. Mesothelioma can take 20 - 50 years to develop. Symptoms are subtle and non-specific. Every year we are seeing an increase of people being diagnosed. If detected early, patients can

benefit from treatment options and increased survival rates for this cancer.

The Mesothelioma Program and the Early Detection Program at The Princess Margaret have been recently showcased on CBC's *The National*, and Dr. Marc de Perrot is interviewed.

**To watch the 'Asbestos Screening Fears' video please visit:**

[http://www.cbc.ca/video/#/Shows/The\\_National/Health/1274854987/ID=2213512052](http://www.cbc.ca/video/#/Shows/The_National/Health/1274854987/ID=2213512052)

# To Participate in the Mesothelioma Research Program



*Brenda O'Sullivan,  
Clinical Research  
Manager*

**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](mailto:brenda.osullivan@uhn.on.ca).

**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, radiologist, clinicians and researchers for future generations.

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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## Support for the Mesothelioma Research Program Provided by:

- Asbestos Workers Local 110
- Building and Construction Trades Council of Ontario
- Canadian Mesothelioma Foundation
- 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
- I.U.O.E. 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
- Many others

# Personalized Cancer Medicine at The Princess Margaret

Every mesothelioma patient is unique. Every mesothelioma patient's cancer is different. So it follows that individualized treatment will get the best results.

We're embarking on a Billion Dollar Challenge to create Personalized Cancer Medicine for patients at The Princess Margaret, across Canada and around the world. This exciting initiative will raise one billion in the next five years to fund the most cutting edge research that will have greatest impact on patients, including mesothelioma patients, and take us closer to our vision: To Conquer Cancer in Our Lifetime.

The Princess Margaret has an international reputation as a global leader in the fight against cancer and is considered one of the top five comprehensive cancer treatment and research centres in the world. None of this would be possible without the generous support, commitment and dedication of our donors and our community.

The Princess Margaret definition of Personalized Cancer Medicine encompasses four main themes:



**Detect - Find cancer earlier.** Detecting cancers early leads to better outcomes. We are working on new molecular imaging technology that can see cancers when they are microscopic as well as monitoring the efficacy of treatment. We'll also discover new biomarkers – indicators of cancer that can be detected through blood and other tests.



**Diagnose – Analyze cancer more precisely.** Analyzing cancers more precisely will lead to a better understanding of each patient's disease and more customized and effective treatment. Defining the genetics of every patient and his/her tumor will be a large part of tailored treatments.



**Target – Pinpoint cancer without damaging healthy tissue.** Targeted surgery, radiation and drug treatments will focus on the cancer and leave healthy tissue intact. We'll develop new “targeted” therapies” including immune therapy and treatments directed at cancer stem cells and epigenetics, and accelerate advances in surgical and radiation therapy like imaged-guided and minimally invasive treatments.



**Support - Transforming patient care.** By providing programs and strategies to help patients and their families live with cancer and the physical and emotional side effects of cancer treatment, we will reduce stress and improve the patient experience through psychosocial support, new nursing models, Survivorship, and patient education.

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## For more Information or to Support the Mesothelioma Program at The Princess Margaret, please contact:



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