Charlies Foundation for Research
GETTING BETTER TOGETHER.

MAY 2014

Charlies Foundation *for Research*

Newsletter

Things have definitely been busy for us here at the Foundation and without further ado, I'll jump straight in!

We've got a new look! I mentioned some months ago that we were in the midst of some considerable changes – well we've almost made it!

As of the 1st of April 2014, the Sir Charles Gairdner Research Foundation officially became **Charlies Foundation *for Research*.**

We're incredibly excited about this evolution and I have no doubt we will continue to grow onto bigger and brighter things.

Broadly speaking, it's still business as usual for the Foundation and that is, funding and supporting critically important patient-centred research at Sir Charles Gairdner Hospital.

The organisational restructure was a way to modernise our approach to our business and to ensure we're well positioned for the future.

A new office! Please stay tuned to this one. Again, this is very exciting for all of us here at the Foundation and we will be sure to keep updates rolling on our website.

A new website! In line with our organisational restructure we have also been busily constructing a new website for the Foundation. We're very close to launching the new site so again please stay tuned.

Bianca Wheeler
Executive Director

Professor Anna Nowak is a Medical Oncologist and member of the Perth Mesothelioma Centre and National Research Centre for Asbestos Related Disease (NCARD). She has participated actively in mesothelioma research over the past 10 years, and has received international recognition in this area, working closely with other researchers in this field at Sir Charles Gairdner Hospital and UWA.

Professor Anna Nowak with the painting she was awarded by the Asbestos Diseases Society of Australia Inc. as the Eric G Saint Memorial Award recipient for 2014. The painting – Bush Medicine Leaves – is by Gloria Petyarre.

Professor Nowak has been active in pre-clinical research in this disease – a terminal cancer caused by the mineral substance which was widely used in construction and other industries in Australia until the late 1980s.

Her laboratory work in mesothelioma includes a PhD thesis on combination chemo-immunotherapy in a murine model; this work was awarded at local, national and international level, winning the International Mesothelioma Interest Group New Investigator Award in 2002. She returned to UWA in 2005 to pursue laboratory work and clinical translational work in mesothelioma after a postdoctoral fellowship working in clinical trials research. She has given numerous oral presentations and published abstracts of her work at national and international meetings.

More recently Professor Nowak was presented a prestigious award by the Asbestos Diseases Society of Australia (ADSA) for her work with sufferers of asbestos-related diseases.

The Emeritus Professor Eric G Saint Memorial Award 2014 was presented on Sunday 16 March in Perth by the Hon. Kate Doust MLC in recognition of Professor Nowak's visionary and innovative approach to oncology treatment, and for the compassion, understanding and excellence in care she tirelessly provides to asbestos disease sufferers.

"It is a great honour to have been recognised amongst a team of committed scientific and clinical researchers centred here in Western Australia where we have the highest incidence of mesothelioma of anywhere in the world," Professor Nowak said.

"I am grateful to ADSA and the National Centre for Asbestos Related Disease (NCARD) for the joint commitment to awareness raising, fundraising, research into a cure and, importantly, providing the very best in care and support to mesothelioma sufferers and their families."

Rose Marie Vojakovic AM of ADSA said Professor Anna Nowak was an inspiration to the society. "It gives our members great pleasure to acknowledge Professor Nowak's invaluable contribution to the treatment of mesothelioma with the awarding of the Eric G Saint Memorial Award to her at our AGM on Sunday," Rose Marie said.

Much of Professor Nowak's study and work since 1997 has focused on mesothelioma, with many areas of her research having progressed to clinical trials which have gained international attention and showed some promise.

"We are definitely making progress on treatment with drugs that target particular molecules of the cancer and also in chemo-immunotherapy, which seeks to bring about an immune response to the cancer by combining immunotherapy with chemotherapy," Professor Nowak said.

"What is especially lovely about the work we do with the ADSA is that we have a very close link back to those who are suffering with the disease. Patients come to us from the ADSA for ongoing care and therefore we never lose sight of the end goal in our research."

Professor Nowak's current research project *Analysis of regulatory T Cell function in advanced cancer patients following a combination therapy of low-dose cyclophosphamide and standard care chemotherapy* is part of the funding for Research in 2014 approved by the Research Advisory Committee with part funds donated by Charlies Foundation *for Research.*

Malignant pleural mesothelioma is a cancer of the lining of the lung that is caused by asbestos. Mining and milling of the most dangerous type of Asbestos, Blue Asbestos (crocidolite) took place in Wittenoom, in the north of WA in the 1950's and 60's. Many young men spent a few months working in Wittenoom, some taking their young wives and children with them. Asbestos products were widely used in WA and we are all likely to know someone who has been exposed to asbestos.

Unfortunately, WA is at the centre of the epidemic of mesothelioma, with the highest rate in the world of development of this deadly cancer. WA researchers have an obligation and an opportunity to be world leaders in researching treatments for mesothelioma, and a majority of people with mesothelioma have medical care at SCGH, home to a number of world experts in this disease.

Sir Charles Gairdner Hospital is home to a number of world experts in mesothelioma.

While chemotherapy remains standard care for mesothelioma, unfortunately it can only prolong survival and improve symptoms, it cannot lead to a cure. Recently, immunotherapies have shown very promising results in other cancers such as melanoma, even leading to very long term remissions in some people. Our laboratory work has also shown substantial benefits from combining chemotherapy with a new generation of immunotherapies in mesothelioma.

There is increasing recognition worldwide that chemotherapy and immunotherapy may work together to fight cancer cells. We have recently completed a clinical trial in people with mesothelioma, the aim of which was to kill tumour cells using chemotherapy in such a way that the immune system can recognise the tumour, and mount a response against it. However, previous studies have suggested that a particular type of immune cell, known as a 'regulatory T cell' may inhibit the ability of the immune system to effectively attack tumours. Therefore we have used an additional immunotherapy drug that has been reported to selectively reduce the numbers of regulatory T cells. It is hoped this may allow the immune system to effectively attack the tumour, as we have demonstrated using a similar treatment in a mouse cancer model. Preliminary data from this clinical trial strongly suggests that changes in the balance of subsets of immune cells will predict outcome for chemo-immunotherapy treated patients. The suppressive capacity of regulatory T cells appears to decrease as treatment progresses.

In order to confirm these preliminary observations, we are to perform a series of experiments to directly measure the number and potency of regulatory T cells in these people who have been treated with chemo-immunotherapy.

In other work by the same group and funded by the Foundation, we have performed the first funded study in the new Harry Perkins Institute for Medical Research Small Animal Imaging Facility, also trying to solve a clinical problem for people with mesothelioma. People with mesothelioma sometimes develop tumour masses in the chest wall which can be painful and unsightly, and can involve bones and nerves. These masses are often treated by radiotherapy. However, we know that radiotherapy works in only some people, and not in others.

A previous study in people with mesothelioma, using a PET scan, showed that these tumour masses were very 'hypoxic', that is, they had low levels of oxygen in the tumour masses, which may make them resistant to radiotherapy. We have mice, which develop mesothelioma tumours on their flank, and can use the Small Animal Imaging Facility to image the mice using a tiny PET scanner, showing that their tumours also have 'hypoxia'. We are now testing different drugs to see which ones lower hypoxia, and may be able to boost the benefits of radiotherapy in people with mesothelioma.

Our overall goal is to reduce pain and improve the quality of life of people with tumour masses from mesothelioma by improved radiotherapy treatment, and this project is making important steps towards that goal.

Other projects which were included in the 2014 Approved Funding by the Research Advisory Committee include:

Imaging and modulating hypoxia in malignant mesothelioma

Researcher: Roslyn Frances

Mesothelioma is a highly fatal thoracic cancer, which is caused by asbestos exposure. People with mesothelioma often develop large tumour masses in their chest which are painful, and may require treatment with radiotherapy. Large tumour masses may have central areas of low oxygen supply or 'hypoxia'. We have previously performed an imaging study in people with malignant pleural mesothelioma using a scan which detects hypoxia, F-Misonidazole (FMISO) PET.

This study showed that these large painful chest masses in people with mesothelioma are often hypoxic. Hypoxia is related to poor response to radiotherapy in many cancer types.

In order to further understand hypoxia in mesothelioma masses, we are now conducting a study in a preclinical mouse model of mesothelioma using a small animal PET scanner in the ACRF Cancer Imaging Facility. We have performed a series of preclinical FMISO PET scans and have confirmed we can reproducibly detect hypoxia in the mouse mesothelioma tumour model. We now plan to proceed to looking at ways to modify hypoxia (eg: oxygen therapy), in the preclinical model, with the aim of trying to achieve a better response to radiotherapy.

Mechanisms of fixed airway narrowing in chronic obstructive pulmonary disease (COPD)

Researcher: Alan James

Chronic obstructive pulmonary disease (COPD), which in our community is most often caused by cigarette smoking, is due to injury to the lung, including emphysema (damage of the lung tissue) and/or obstruction to flow through thickened airways.

This project will focus on abnormalities of the airways. In patients with COPD, where the airways are unable to dilate or constrict, thickening of the wall and the smooth muscle layer of the small airways and large airways have been observed and is similar to, but less severe than, that observed in asthma – where the airways can be induced to narrow excessively and to dilate almost to normality.

Our previous work has shown that the increased thickness of the airway smooth muscle (ASM) layer in asthma is related to the severity of the asthma AND that this is due to more and larger smooth muscle cells without a change in the fraction of the matrix between the cells. In contrast, our preliminary work for this project shows that the fraction of matrix is increased in patients with COPD. If this is indeed the case, using asthma treatments for COPD, which is the current practice, can only ever achieve marginal benefits and a completely new approach to treating (and preventing) COPD is required.

This project will use tissue obtained at surgery to follow-up on our preliminary findings in patients with COPD. If confirmed, this will fundamentally change how we manage patients with fixed airway narrowing. We will have to focus on treating the matrix rather than the smooth muscle and inflammation, treatments which to date have been of marginal benefit in this condition.