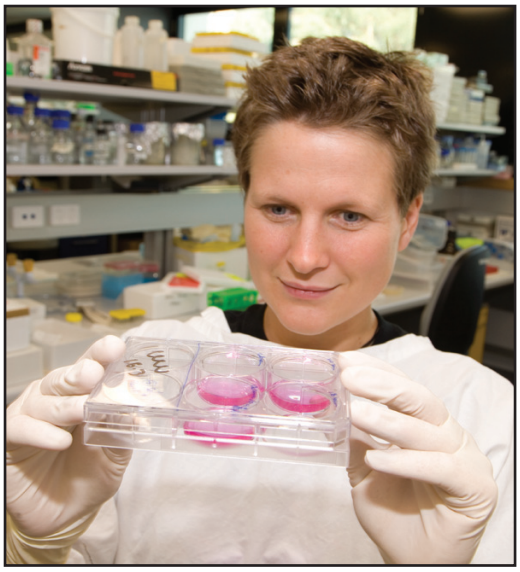
Centre for Women's Health Research



Centre Director: Professor Peter Rogers

The Centre for Women's Health Research (CWHR) encompasses all the research activities of the Monash University Department of Obstetrics & Gynaecology. Located within Monash Medical Centre, CWHR is strategically situated at the interface between fundamental University research and hospital-based clinical practice. The work undertaken by the CWRH focuses on all aspects of women's health, with particular emphasis on pregnancy disorders, uterine fibroids, endometriosis, urogynaecology, ovarian cancer, contraception and infertility. Other major areas of effort include basic studies on angiogenesis (the growth of new blood vessels), the effects of estrogen and progesterone on blood vessels, characterisation of endometrial stem cells, and novel surgical training methods.

The ultimate aim is to reduce illness and improve quality of life for both women and their babies.

There are approximately 40 staff and students actively working in CWHR, including at least 10 PhD and Masters students. A similar number of Monash University, Southern Health and external staff take part in active collaborations with CWHR staff.

Growth and Development of Uterine Fibroids

Project Leader: Prof Peter Rogers
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Project Description:
Uterine fibroids are benign tumours of the smooth muscle of the uterus, and are the most common tumours in women. Fibroids are the commonest cause of hysterectomy in women today, with an estimated annual direct healthcare cost in the USA of 2 billion dollars. This project will build on extensive molecular profiling and protein work undertaken on fibroids over the past several years. A new two-cell model has been created involving both uterine smooth muscle cells and uterine fibroblasts in the development of fibroids.

This project will utilise molecular and protein techniques using human tissues to better understand the processes that lead to the development and continued growth of uterine fibroids.

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Synchrotron radiotherapy for the treatment of cancer

Project Leader: Prof Peter Rogers
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Project Description:
The synchrotron produces near-parallel xray beams that are up to ten billion times more intense than those currently used for radiotherapy in the treatment of cancer. This provides novel opportunities for spatially fractionating the beam to treat tumours. Normal tissues appear to be resistant to spatially fractionated radiation, with survival following doses up to a hundred times greater than with conventional radiation. Conversely, tumours can be readily destroyed using spatially fractionated radiation, although the molecular and cellular mechanisms behind this susceptibility are currently unknown.

This project will utilise the new Australian Synchrotron to investigate the molecular and cellular mechanisms that underpin the response of normal and tumour cells to spatially fractionated radiation in mouse models.

Role of Relaxin in the Mouse Endometrium

Project Leader: Dr Jane Girling
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Project Description:
Relaxin is a hormone with a variety of biological functions. It was initially discovered because of its important roles during reproduction, particularly during the birth process in rodents. It has since been shown to have important functions in lactation, implantation and wound healing. It is essential in the cardiovascular system and is also thought to be a key hormone in the control of angiogenesis (new vessel growth).

A main research area within our laboratory is the study of blood vessel growth in the endometrium (lining of the uterus). Although it has been suggested that relaxin has important roles in angiogenesis, this possibility has not been investigated in detail in the endometrium. The aim of these studies is to investigate the expression of relaxin during the oestrus cycle, early pregnancy and following hormone treatment in the mouse endometrium. These are models which we regularly use in our laboratory and in which the angiogenic response has been characterised. We will also extend these models to examine the angiogenic response of the endometrium following relaxin treatment.

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Endometrial angiogenesis and vascular maturation

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Project Description:
The development of new blood vessels (angiogenesis) is important for normal functioning within the endometrium (lining of the uterus) during the menstrual cycle. It is also an essential component of numerous clinically important processes, including wound healing and tumour growth and spread. A further component of blood vessel development is the recruitment of vascular mural cells including pericytes and vascular smooth muscle cells. Mural cells provide physical support for the vessels, as well as having an important role in regulating angiogenesis and vessel function. There is emerging evidence that endometrial angiogenesis and vessel maturation occur by different mechanisms when driven by oestrogen as opposed to progesterone. There is also evidence that abnormal angiogenesis contributes to endometrial breakthrough bleeding, a common and troublesome gynaecological disorder suffered by many women, particularly those using progestin-only type contraception. Three mouse models have been developed to examine the effects of oestrogen, progesterone and long-term progestin treatment on endometrial angiogenesis and vessel maturation. Projects will be available to manipulate these models and further investigate the different mechanisms controlling endometrial vascular development.

Lymphatics in the Endometrium

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Project Description:
While the location of various blood vessel types has been well characterized in the endometrium, the scientific literature on uterine lymphatics is not extensive. This is despite the known and hypothesised importance of lymphatic vessels to pathologies such as endometrial cancer, endometriosis and adenomyosis. Using recently developed markers specific to lymphatic endothelial cells, we have accurately described the location and density of uterine lymphatic vessels in human and mouse uterine tissue. Large numbers of lymphatics were observed in the basalis region (adjacent to the muscle layers) of the human endometrium, with only small numbers of vessels in the functionalis. In contrast, few if any lymphatics were observed in the mouse uterus.

Projects will be available to investigate the mechanisms by which oestrogen, progesterone and progestins regulate endometrial lymphatic vessel growth and the interaction of these steroids with the key lymphangiogenic growth factors VEGF-C and VEGF-D.

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Endometriosis

Project Leaders: Prof. Peter Rogers, Dr Caroline Gargett, Dr Jane Girling
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Project Description:
Endometriosis is a disease where endometrial tissue grows outside the uterus, most commonly on the organs and tissues of the peritoneal cavity. Endometriosis can cause severe pain, associated with peritoneal inflammation, fibrosis and adhesions. It has been estimated that 8-10% of women in their reproductive years suffer from endometriosis. Endometriosis is a complex disease that is difficult to study.

The aim of this project is to develop a mouse model of endometriosis that can then be used as part of ongoing studies with endometrial stem cells, as well as for functional studies of genes identified as playing a role in endometriosis through genetic studies.

Molecular response to radiation cancer treatment

Project Leader: Dr Carl Sprung
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Over 50% of cancer patients will receive radiotherapy, therefore, investigation into advances of this modality is critical. Radiotherapy dose has to be measured against unpredictable severe reactions that a small percentage of individuals develop. As a consequence, the dose limits imposed by these radiosensitive individuals lead to a reduction in the optimal treatment for most patients (95%). Our hypothesis is that we will be able to predict an individual's susceptibility to radiosensitivity based on molecular expression profiles and thus individualize radiotherapy resulting in higher cancer cure rates.

Our approach is to employ the latest high throughput technologies to interrogate gene expression on a genome-wide scale to understand the biological effect of radiation at the molecular level. Techniques for this project will include microarray analysis, real-time PCR, sequencing, RNA and protein analysis, siRNA knock-downs and other avenues of gene and protein expression regulation to identify predictive genes and proteins.