

## Centre for Women's Health Research



### Centre Director Acting Director, Prof David L Healy

The Centre for Women's Health Research (CWHR) encompasses all the gynaecological 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 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.

### Clinical studies in In Vitro Fertilisation (IVF)

**Project Leaders:** Dr. Luk Rombauts, Dr. Gareth Weston & Prof. David Healy

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#### **Project Description:**

Monash University is famous for many advances in IVF. Projects into egg freezing, or vitrification, are available to help couples have a baby. Healthier IVF research protocols are examining single versus double embryo transfer, and differences between fresh versus frozen-thaw embryo transfer. Other projects include low cost IVF programs. Prof Healy is President, International Federation of Fertility Societies (IFFS) from 2010.

### Endometriosis

**Project Leaders:** Dr. Caroline Gargett & Dr. Gareth Weston

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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.

## Centre for Women's Health Research

### Human uterine mesenchymal stem cells for tissue engineering

**Project Leader:** Dr. Caroline Gargett  
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#### **Project Description:**

We have identified a small population of mesenchymal stem-like cells (MSC) in human endometrium (lining of the uterus) by their co-expression of 2 markers that gives a 10 fold enrichment for cells with capacity to differentiate into fat cells, smooth muscle cells, chondrocytes and bone cells in vitro. Several projects are available to examine the potential use of endometrial MSC in a tissue engineering application for autologous treatment to augment pelvic organ prolapse surgery in women.

In this project we wish to

1. study endometrial MSC differentiation to smooth muscle cells and connective tissue in vitro and in vivo by transfection of cells with appropriate transcription factors
2. optimize scale up culture of endometrial MSC using High Content Screening as the assessment tool
3. develop a tissue engineering construct comprising endometrial MSC attached to novel scaffold materials developed by CSIRO and expanded in 3D culture for delivery to target tissues
4. test the efficacy of several tissue engineering constructs in a rat hernia model of pelvic organ prolapse

These projects involve human tissue dissociation, FACS sorting, 2D and 3D culture methods, cell transfection, high content screening assays, qRT-PCR, immuno-histochemistry, and small animal surgery. This research involves working in collaboration with researchers at CSIRO Medical Health Technologies at the Clayton Campus. Knowledge gained from this project has application for use in tissue engineering for pelvic organ prolapse surgery, a very common surgical treatment required by 10% of women.

### Molecular characterisation of reproductive stem cells for tissue engineering

**Project Leaders:** Dr. Gayathri Rajaraman & Dr. Caroline Gargett  
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#### **Project Description:**

Mesenchymal stem cells (MSC) are rare populations of undifferentiated cells found in many tissues that are capable of self renewal and differentiating into multiple mesodermal lineages. We first discovered a novel MSC population in the endometrium, the highly regenerative lining of the uterus, (eMSC) and can isolate them using two specific markers. We have also isolated a population of MSC from the human placenta decidua basalis (dbMSC) using eMSC markers. Potential use of reproductive stem cells for tissue engineering and cell-based therapies is attractive as it may be possible to use a patient's own stem cells to repair reproductive organs. However, the molecular characterisation of eMSC/dbMSC has not been done and is necessary prior to their application in regenerative medicine. This study will identify candidate genes that may control eMSC/dbMSC function.

**Techniques:** Gene array, Real-time PCR, Western immunoblotting.

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### Molecular response to radiation

**Project Leader:** Dr. Carl Sprung  
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**Project Description:**

Nearly every person will be exposed to radiation for medical procedures in some form during their life, for example, X-ray imaging or radiotherapy. Radiotherapy is an example of a medical treatment that uses relatively large doses of ionizing radiation as a means to control cancer cells and is received by about one in six people. Understanding the molecular mechanism underpinning the radiation response is essential for optimizing radiotherapy. Occupational exposure in both the medical and non-medical fields will also benefit from understanding the radiation response.

My laboratory has a number of exciting projects that focus on the molecular responses to radiation at the transcriptional and translational levels. Using our approach to employ the latest high throughput technologies to interrogate gene and protein expression on a genome-wide scale, we have found a number of novel mechanisms involved in the response to radiation which provide exciting project opportunities for graduate students. The knowledge gained from the proposed studies will undoubtedly result in more effective treatment strategies in the form of radioprotectors, radiosensitizers and/or biodosimeters.

### Cancer treatment individualisation

**Project Leader:** Dr. Carl Sprung  
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**Project Description:**

Most cancer patients will receive radiotherapy which is proven to be effective. However, the effectiveness is limited by individuals who have severe reactions to this treatment. Our goal is to identify these individuals using molecular and cellular techniques to provide a basis for radiotherapy individualization. This has the potential to improve cure rates for many types of cancers, including breast, prostate, cervical and many other cancer types.

My laboratory has a number of exciting projects that focus on improving this treatment. We are especially interested in gene and protein expression differences in these radiosensitive patients. Our approach is to use the latest high throughput technologies to interrogate gene and protein expression on a genome-wide scale to determine why some individuals show increased radiosensitivity and to develop strategies to apply results to the clinic.

Techniques for this project will include cell culture, microarray analysis, quantitative real-time PCR, sequencing, RNA and protein analysis, siRNA and the latest molecular and cellular assays to decipher gene and protein expression regulation to identify predictive factors.

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### Biological responses to synchrotron microbeam radiation

**Project Leader:** Dr. Carl Sprung  
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**Project Description:**

The majority of cancer patients will receive radiotherapy, therefore, investigations into advances into this modality are important. Currently, conventional RT dose intensities are limited by a small fraction of the population that react adversely to the prescribed radiation regime. Therefore, a primary goal in radiation oncology is to find a RT strategy that would increase the therapeutic index (the ratio of curative effects to adverse normal tissue effects).

One strategy is to investigate the use of novel improved radiotherapy methods. One such advance is the use of an array of thin planar high intensity X-ray microbeams. We make use of the Australian Synchrotron that is capable of generating the high dose-rate microbeams with the necessary properties that conventional sources do not possess. Microbeam radiotherapy (MRT) in animal models has shown great promise with the ablation of tumours without serious effects to normal tissues. Therefore, the use of MRT has the potential to revolutionise cancer treatment.

Projects suitable for PhD candidates will focus on understanding the molecular and cellular responses to microbeam radiotherapy, including the bystander effects that these microbeams may confer on unirradiated adjacent cells. This will advance the understanding of this remarkable phenomenon with the goal of facilitating application of MRT into the clinic.

### Growth and development of uterine fibroids

**Project Leader:** A/Prof. Beverley Vollenhoven  
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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.