Some of you were able to attend the ceremony, tour the new laboratories and meet the people who are working here. For those of you who could not attend we have dedicated this issue to showing you some of the laboratory, the research being undertaken and the people who work here.

As you can see from the accompanying photographs, the Microsearch Laboratory is an outstanding modern facility. You can also possibly see that there is plenty of room and few items of equipment to fill it. Our main task at present is to provide the most modern and effective laboratory equipment to allow us to remain at the cutting edge of research. One of our acute needs is to store samples from surgical patients, including transplant patients, as well as from our animal models of surgery and transplantation.

The best way to store these samples is at the lowest possible temperature, well below that of a normal kitchen freezer which only cools to about -20°C. We need to buy a liquid nitrogen storage container, where nitrogen gas (which is the main component of the air we breathe) is maintained in a liquid form at the extremely low temperature of -196°C. At this temperature our specimens can be maintained for years without deterioration.

We also require an ultra-cold freezer, which is a special freezer with an extra cooling system that cools samples down to -80°C. These two items will allow us to store our samples indefinitely prior to analysis.

The Microsearch Laboratories

In our last newsletter we described the opening of the new Microsearch Laboratories at The University of Sydney.

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Progress at Microsearch
– Current Research

Since the opening of the new Microsearch Laboratory at The University of Sydney in April last year we are pleased to report a breakthrough in our work on treatment of organs for transplantation.

Dr Jerome Laurence successfully developed a technique for expressing novel genes in the liver prior to its transplantation. This technique uses a gene therapy approach and allows us to modify organs so that they are less likely to be rejected.

This exciting work was recently featured on the cover of the prestigious international journal “Liver Transplantation”. The cover shows a picture from Dr Laurence’s article depicting a liver from a rat glowing green. It does this because it has been treated to express a gene for green fluorescent protein from a deep-sea jellyfish. The series of pictures on the middle show figures from Jerome’s article. The liver expressing the green fluorescent protein is shown at the top, then a photomicrograph of a section through the liver with individual liver cells (hepatocytes) glowing green. This shows that our method of gene expression is very efficient and targets most cells in the liver. The bottom panel shows the negative control, where there was no green fluorescent protein expression. The hepatocyte nuclei are stained blue.

Although the green fluorescent protein gene was not expected to improve the outcome when the liver is transplanted it graphically demonstrates that the method of gene expression works very well. Subsequently, Dr Laurence used the approach to test the effectiveness of genes that can prevent transplant rejection. He tested a gene called indoleamine dioxygenase that has been shown to be associated with prevention of rejection in a number of animal transplant models. Despite high levels of expression in the liver, it was still rejected after it was transplanted. There are many more genes that are likely to prevent rejection and this method can very quickly test their ability to do so.

Dr Laurence has successfully completed his work at Microsearch and was awarded his Doctoral degree last year. As well as doing ground-breaking research in molecular biology he developed his skills in microsurgery and is currently writing up his results from a rat heart transplant model studying the effect of the drug Probucol on chronic rejection. He is also completing his advanced surgical training and hopes to study at a top international transplant centre for a year or two before returning to Australia.

Left: Microsearch’s findings are showcased on the cover of Liver Transplantation. Center: Gene for green fluorescent protein expressed in liver (A) and a photomicrograph showing expression in hepatocytes (B). Right: Dr Jerome Laurence being presented with a Young Investigator Award at the Annual Scientific Meeting of the Transplantation Society of Australia and New Zealand.
International recognition for Microsearch-supported scientists

Two scientists who have been supported by Microsearch for their research were recently selected to attend the Key Opinion Leaders in Transplantation meeting, held recently in Salvador de Bahia, Brazil. Dr Alexandra Sharland was the new Key Opinion Leader who presented her work on the role of novel natural immunosuppressive molecules. She was introduced by Dr Alex Bishop, who was recognised as a Key Opinion Leader in transplant tolerance. Both Dr Sharland and Dr Bishop have had a long association with the Microsearch Foundation and both are Council members.

Another aspect of Dr Sharland’s research concerns the area of ischaemia-reperfusion injury (IRI). Microsurgical procedures to join blood vessels and nerves are now very successful, but one important factor limiting the success of reattachment of severed body parts is the damage to tissues which occurs while they are deprived of their blood supply (ischaemia). Release of “danger signals” from the ischaemic tissues induces inflammation and further tissue damage, a condition known as ischaemia-reperfusion injury. The importance of IRI is emphasised by the recent incident when a surfer at Bondi Beach had his hand severed in a shark attack. As a result of Microsearch’s advances, the hand was re-connected, something that would not have been possible 30 years ago. Unfortunately, a good functional result was not achieved, and the hand eventually had to be amputated. IRI was almost certainly an important contributing factor to this disappointing outcome. IRI is also a serious problem in organ transplantation. IRI can result in the graft being slow to function and increases susceptibility to transplant rejection. If the damage is severe, the organ may not function at all, sometimes leading to the death of the recipient.

Gerard Adrianus, a recent graduate in Bioengineering from Nanyang Technological University, Singapore, is currently a visiting research intern under Dr Sharland’s supervision. Gerard will utilize the gene transfer methodology pioneered by Jerome Laurence to express a soluble decoy receptor, which can neutralize the effect of the “danger signals” released from ischaemic tissue, thus reducing the severity and consequences of ischaemia-reperfusion injury.

DID YOU KNOW?

Donations to the Microsearch Foundation at the University of Sydney are tax deductible.

The University is endorsed as a deductible gift recipient under subdivision 30-Ba of the Income Tax Assessment Act, 1997.

Your donation will make a real difference to the health of future generations.

GUEST SPEAKER

Dr Alex Bishop will be happy to visit your organisation (within a reasonable distance from Sydney CBD) and address your members on the latest developments at Microsearch.

To request a guest speaker, email us at microsearch@med.usyd.edu.au or phone the office on (02) 9036 7217.
Dr Tay joined Microsearch in October 2007 and we featured a story on her in our last newsletter. One of her projects is to identify genes that might be natural suppressors of rejection. This builds on the work of Dr Jerome Laurence, featured in the article above, to express potentially immunosuppressive genes in the liver.

These genes will reduce the likelihood that the transplanted liver will be rejected. Dr Tay has made rapid progress and has engineered three candidate genes, ready for testing to ensure they function properly. This is an exciting time for her as she will soon be able to confirm whether these genes will reduce the risk of transplant rejection. The genes will be injected into a mouse where they will be rapidly expressed at high levels in the liver. The mouse will then receive a heart transplant and survival of the transplant will be compared with an untreated mouse. Transplantation of hearts, livers or kidneys into rats and mice involves very skilled microsurgery.

One of the ways that our microsurgery students hone their technical skills is to learn organ transplantation in rats and mice. This is the current task of the Myee Codrington Scholarship holder Dr Mitchell Nash. Dr Nash is a young surgeon who has taken some time out from clinical work to develop his microsurgery skills and commence a Master of Surgery degree by research. He is working on a rat kidney transplant model, where he is developing the extremely fine microsurgical techniques that will allow successful outcomes. His project examines whether radiation treatment of the kidney transplant donor, to reduce its stimulation of the rejection response, will improve kidney transplant survival. This could provide a new approach to preventing transplant rejection.

Above: Dr Szun Szun Tay, the Earl Owen Fellowship holder, pictured with the large teaching and research microscope in the Microsearch Laboratory.