Garvan's Breakthrough Medical Research 2007 – Neuroscience Research Program Update

Introduction

Researchers in Garvan's Neuroscience Program look at how nerve cells develop and function. They aim to increase our understanding of disorders such as Parkinson's disease, Alzheimer's disease, schizophrenia, eating disorders and hearing loss; and to identify new therapeutic approaches with a special interest in regeneration of the nervous system.

2007 Major Highlights

Hearing Loss

More than half the population over 60 years of age are hard of hearing or deaf. Many forms of hearing loss are due to the degeneration of the sensory receptors for hearing – the hair cells found in the cochlea in the inner ear. This degeneration can be caused by ageing or by exposure to loud noise. Garvan's Hearing Research Group aims to use adult stem cells to replace damaged hair cells with a long-term goal of restoring hearing in many forms of deafness.

Garvan scientists have discovered that adult olfactory stem cells (taken from the lining of the nose) can give rise to new hearing-like cells in culture and so offer the potential to restore hearing in the future. During 2007 the team worked with Ear, Nose and Throat surgeons from St Vincent's Hospital to develop surgical techniques for the accurate transplantation of stem cells and hair cells into the cochlea of mice. Recently they have also begun experiments transplanting stem cells taken from the tongue and vestibular (balance) system into the cochlea and will be subsequently testing the hearing of these mice. During 2007 the team also developed new computer software to aid in analysing the hearing test data.

Neurodegenerative Disease (including Alzheimer's, Parkinson's and other dementias)

The incidence of neurodegenerative disorders, such as Alzheimer's and Parkinson's, is increasing and fuelling the need for new and effective therapies. Dementia now afflicts 1 in 17 people over the age of 65 and there are approximately 100,000 Australians living with Parkinson's.

Recent demonstrations of the isolation of stem cells from the central nervous system, and the ability of nervous tissues to regenerate, highlight the potential of cell-based therapies for these disorders. In particular, the capacity of the olfactory neuroepithelium (the nasal lining) to regenerate throughout adulthood signals this region of the nervous system as an important source of adult neural stem cells. Furthermore, a crucial advantage of this system is that it is one of the only parts of the nervous system that can be biopsied easily. This is an advantage for future auto-transplantation – where one's own cells are transplanted into another part of one's body. Therefore a current major objective of Garvan's work is to understand how olfactory stem cells can be converted into neurons lost in neurodegenerative diseases. In particular to convert olfactory stem cells into the type of neurons (tyrosine hydroxylase-positive dopaminergic neurons) lost in Parkinson's disease.

Following the relatively recent discovery of adult stem cells in the brain, another Neuroscience group (the Neural Plasticity and Regeneration group) has been working on another approach to researching neurodegenerative disease, by investigating the ways the brain naturally regenerates and why this regeneration is blocked in Parkinson's disease for example. The group has shown that the molecule TGF-beta is a critical regulator of new nerve cell growth in the brain and are now systematically exploring the mechanism behind it. The team also analysed dopamine release rates from synapses, furthering knowledge of the mechanisms that are critical in Parkinson's disease.

Cancer and Anorexia

Most cancer patients actually do not die of the cancer itself but of the consequences of cancer induced anorexia leading to extreme weight loss known as chacexia. Garvan scientists have found that most common cancers produce large amounts of the molecule MIC-1, which in turn targets receptors in the brain that switch off appetite. Antibodies against MIC-1 can switch appetite back on, providing people with the strength to survive treatment and improve their chances of recovery. Importantly, this research also opens up the potential treatment of other diseases such as anorexia nervosa as well as the other extreme of eating disorders, obesity. **Click here to read the press release**.

The Brain, Appetite, Obesity and Type 2 Diabetes

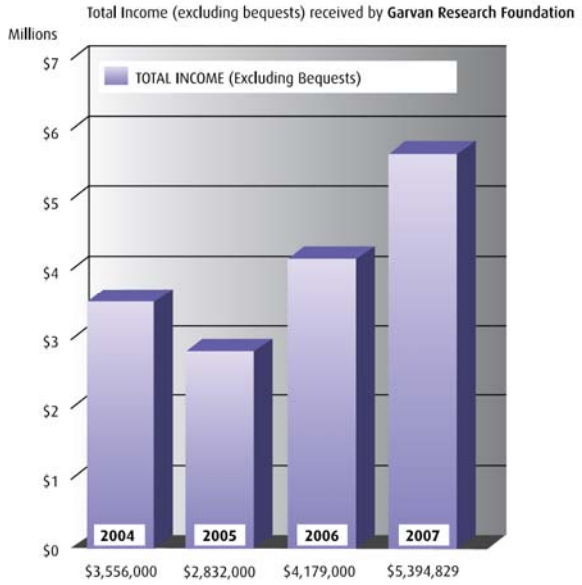
Garvan researchers have demonstrated that a low level of the molecule PYY, a hormone released in the gut after eating a meal and thereby signaling satiety to the brain, is an early predictor for the development of obesity and type 2 diabetes. This will now be further explored in order to develop specific antibodies for a diagnostic kit, which will allow identification of people at risk of developing these diseases, which is currently not possible with any other method. In addition, identifying ways to increase levels of PYY will also be explored to provide a potential treatment of obese people.
Click here to read the press release.

The team has also shown that stress can strongly influence weight and increases the rate of fat gain when combined with a high caloric/ high fat diet. The mechanism behind this is a receptor called Y2, located on fat cells, which when activated increases the accumulation of fat. Therefore research is now on the way to find agents that will block that Y2 receptor to help reducing fat mass. This might also open up the possibility to manipulate particular fat tissues in the abdominal region known for their critical role in developing type 2 diabetes.

GARVAN AT A GLANCE - 2007

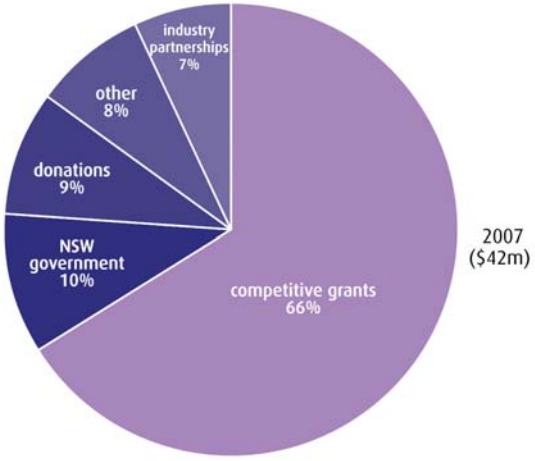
Garvan Research Foundation Income Growth

Garvan Research Foundation is the marketing and fundraising arm of Garvan Institute. In 2007 donations from the public (excluding bequests) increased by **30%** to over **$5.3 million.** In 2008 Garvan Research Foundation must raise at least **$7.6 million** from the public to help fund the Institute's planned research program.



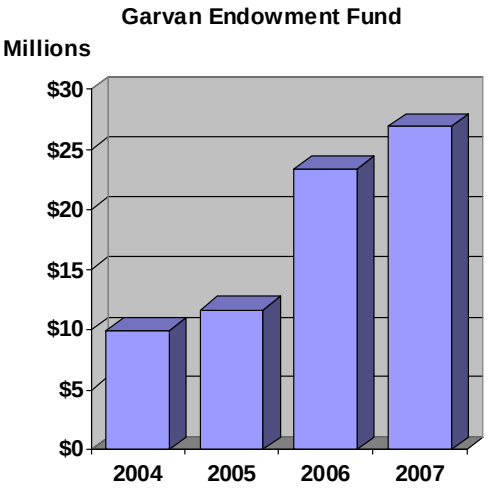
Garvan Institute Sources of Income

Donations from the public constituted **9%** of the Institute's total income for 2007. This excludes earnings from our Endowment Fund.



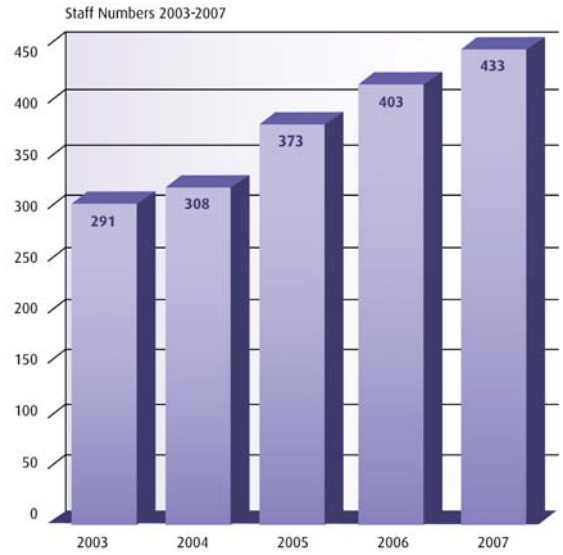
Endowment Fund Growth

Garvan's Endowment Fund gives Garvan the security of predictable funding into the future. The fund has grown from $10 million in 2004 to **$27million** in 2007.



Growth of the Institute's Research Capacity

Over the past 5 years the Garvan has significantly increased our research capacity across our 5 program areas. Our staff numbers have grown by almost 50% since 2003.



Garvan Publications

Breakthrough research by Garvan scientists appeared in **153** publications in 2007. Each paper published constitutes a **new piece of knowledge**, and scientists aim to publish in the most highly regarded journal in their research field. Each journal has an "impact factor" which is a common measure of its relative importance within a specific discipline. Research organisations use "average impact factor" measurements to determine the overall significance of their research output. For example, in 2007 Garvan achieved an **"average impact factor" of 8.2 for the top 80% of its publications**. This is an excellent result, well above the international benchmark.