

‘A Decade of Discovery’ 1994-2004

Highlights of VCCRI Achievements

- 1994** **The VCCRI Officially launched by the Prime Minister the Hon Paul Keating, MP with Mr Kerry Packer, AC as Patron**
Gh: A GTP-binding protein with transglutaminase activity and receptor signaling function
 Reports for the first time that an enzyme involved in forming protein polymers is also able to function as a critical molecule linking the activation of cells, such as those in the heart, with enhanced functioning of these cells in response to stress. *Science* 1994; 264:1593-96
- 1995** **The VCCRI incorporated as an Independent Research Facility with the Hon Neville Wran, AC, QC as Chairman of the Board. The VCCRI accredited by the National Health & Medical Research Council as an independent research organization; major papers published in the Lancet and the New England Journal of Medicine (NEJM)**
Ketoconazole to reduce the need for cyclosporine after cardiac transplantation
 A major finding demonstrating how the metabolism of an expensive immunosuppressant drug widely used in transplant patients can be slowed (and therefore costs saved) by the use of another much cheaper drug used to prevent infections in these patients. *New England Journal of Medicine* 1995; 333: 628-33
- 1996** **Diana, Princess of Wales visits the Institute and opens the VCCRI in its new premises**
- 1997** **Inhibition of red cell aggregation prevents spontaneous echocardiographic contrast formation in human blood**
 Demonstrates how clumping of red blood cells results in changes that can be observed non-invasively with an echocardiogram and used to diagnose patients with an increased risk for blood clots and strokes. *Circulation* 1997; 96: 889-96
- 1998** **VCCRI reports major advances in the NEJM, Cell, Lancet & the Proceedings of the National Academy of Sciences (USA) (PNAS)**
- 1999** **Victor Chang posthumously recognized as Australian of the Century, Luciano Pavarotti guest of honour at fundraiser. Scientific advances by the VCCRI reported in Nature, Genes & Development (G & D), and Circulation, NEJM, Journal of Clinical Investigation (JCI), and Cell**
Epigenetic inheritance at the agouti locus in the mouse
 An entirely unexplained but important phenomenon is the fact that even in identical twins disease severity can vary markedly. Thus, one twin may have very severe disease whereas the other is only mildly affected or normal. Given that such twins have identical genes, the difference cannot be in the genes themselves, but rather, as discovered in this paper, to differences in the functioning of their genes. Furthermore, these differences can be inherited. *Nature Genetics* 1999; 23: 314-318
- 2000** **Further advances reported in the EMBO Journal, Circulation Research, Circulation, G & D, and Nature Reviews Molecular Cell Biology (NRMCB)**
Cardiac septal and valvular dysmorphogenesis in mice heterozygous for mutations in the homeobox gene Nkx2.5
 Documents the involvement of an important cardiac specification gene, Nkx2.5 in the development of a hole in the heart (atrial septal defects) the commonest form of heart disease present at birth. When both copies of the gene are not functioning the heart fails to develop, but if only one copy of the gene is defective this results in a higher rate of atrial septal defects. *Circulation Research* 2000; 9:127-27
- 2001** **Major papers published in Nature Genetics, Circulation Research and Journal of Cell Biology**
A radiation hybrid transcript map of the mouse genome
 Since the human genome has been sequenced we now know the order of millions of DNA bases—the chemicals that make up our genes as well as the extra material between the genes. What cannot be fully predicted from this sequence is where all the genes lie compared to all the extra DNA material. This paper describes for the first time the precise location of thousands of genes that are active in the developing embryo – information that is extremely critical for reading our genome map. *Nature Genetics* 2001; 29: 194-200
- 2002** **Institute discoveries published in Physiological Reviews, PNAS, NEJM, Nature Reviews in Genetics, Cell, American Journal of Human Genetics (AJHG)**
- 2003** **Discoveries report in Development Cell, Genome Research, NRMCB, Molecular Cell and PNAS**
A despecialization step underlying evolution of a family of serine proteases
 How enzymes and other proteins have evolved is critical to understanding how they function and how they may be altered to advantage, to produce ‘designer’ enzymes with new functions. In this paper, a Jurassic enzyme (over 170 million years old) is recreated and studied, revealing a major new understanding of how it evolved and functions. *Molecular Cell* 2003; 12: 343-54
- 2004** **VCCRI continues to make major advances reported in JCI, Nature Genetics, Nature, Nature Reviews in Drug Discovery, AJHG & Circulation. Review of the VCCRI by the international panel of experts finds ‘the institute well on its way to becoming a world class institution...the quality of the scientific output is excellent’**

