DATA DRIVES PROBE INTO
CANCER CRISIS POINT

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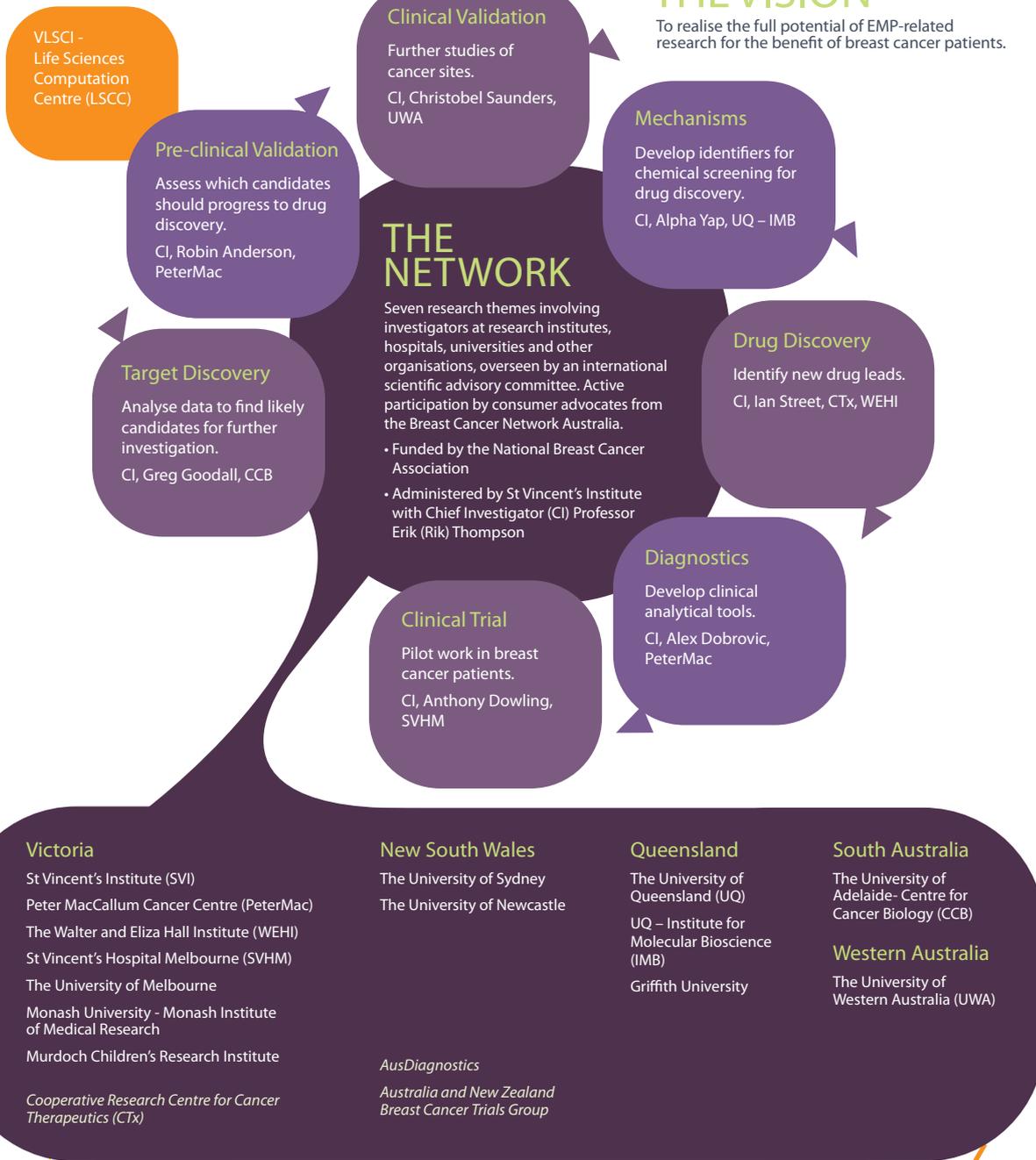
Tim Thwaites, Science Writer

EMP*athy*
Breast Cancer Network

A national collaboration of scientists, surgeons, medical oncologists and consumer advocates investigating the role of epithelial mesenchymal plasticity (EMP) in breast cancer recurrence

THE VISION

To realise the full potential of EMP-related research for the benefit of breast cancer patients.

VLSCI - Life Sciences Computation Centre (LSCC)

Clinical Validation
Further studies of cancer sites.
CI, Christobel Saunders, UWA

Pre-clinical Validation
Assess which candidates should progress to drug discovery.
CI, Robin Anderson, PeterMac

Mechanisms
Develop identifiers for chemical screening for drug discovery.
CI, Alpha Yap, UQ – IMB

THE NETWORK

Seven research themes involving investigators at research institutes, hospitals, universities and other organisations, overseen by an international scientific advisory committee. Active participation by consumer advocates from the Breast Cancer Network Australia.

- Funded by the National Breast Cancer Association
- Administered by St Vincent's Institute with Chief Investigator (CI) Professor Erik (Rik) Thompson

Target Discovery
Analyse data to find likely candidates for further investigation.
CI, Greg Goodall, CCB

Drug Discovery
Identify new drug leads.
CI, Ian Street, CTx, WEHI

Diagnostics
Develop clinical analytical tools.
CI, Alex Dobrovic, PeterMac

Clinical Trial
Pilot work in breast cancer patients.
CI, Anthony Dowling, SVHM

Victoria
St Vincent's Institute (SVI)
Peter MacCallum Cancer Centre (PeterMac)
The Walter and Eliza Hall Institute (WEHI)
St Vincent's Hospital Melbourne (SVHM)
The University of Melbourne
Monash University - Monash Institute of Medical Research
Murdoch Children's Research Institute

Cooperative Research Centre for Cancer Therapeutics (CTx)

New South Wales
The University of Sydney
The University of Newcastle

AusDiagnostics

Australia and New Zealand Breast Cancer Trials Group

Queensland
The University of Queensland (UQ)
UQ – Institute for Molecular Bioscience (IMB)
Griffith University

South Australia
The University of Adelaide- Centre for Cancer Biology (CCB)

Western Australia
The University of Western Australia (UWA)

vlsci
LIFE SCIENCES COMPUTATION

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The chances of long-term survival with breast cancer plummets if the tumour recurs, or spreads to other parts of the body. After initial treatment for breast cancer that is confined to the breast and/or the draining lymph nodes in the armpit, the chances of surviving five years are at least 50 per cent, even with quite a large tumour, according to figures published by the American Cancer Society. But if the cancer comes back or spreads to a distant place such as a bone, (where it is called a metastasis), that figure drops to about 15 per cent.

In an effort to stop breast cancer spreading around the body, the National Breast Cancer Foundation (NBCF) has funded the EMP*athy* Breast Cancer Network—a five-year, $5-million national program of collaborative research to investigate metastasis and come up with potential drugs to stop or slow it. The program is also geared to finding ways of diagnosing the likelihood of metastasis before it occurs.

Because the work is highly dependent on the latest sequencing technology, it needs a profound understanding of bioinformatics to make it happen. So the EMP*athy* program involves bioinformaticians from the Life Sciences Computation Centre (LSCC), the science consulting arm of the Victorian Life Sciences Computation Initiative (VLSCI).

The research focus is on epithelial mesenchymal plasticity (EMP)—the capacity of cells to change from structured, stay-put, epithelial cells to less organised, mobile, mesenchymal cells and vice versa. EMP is an important underlying mechanism of foetal development. But in cancer it facilitates metastasis.

Led by Professor Erik (Rik) Thompson of St Vincent's Institute (SVI) and the University of Melbourne Department of Surgery at St Vincent's Hospital, the EMP*athy* program brings together an Australia-wide network of researchers and clinicians who are at the forefront of studies into EMP and breast cancer. They will be working almost simultaneously

on seven different parts or themes of the development pipeline of drugs and diagnostics. This strategy has been adopted so that what they discover can be fast-tracked into the clinic.

Much of the initial data generation involves high throughput, next generation DNA and RNA sequencing. The genetic material to be sequenced is replicated and then chopped into millions of small pieces that are analysed in parallel. The result is massive sets of data to be sorted and fitted together into a single sequence, and that's the job of bioinformatics.

EMP*athy* is one of an increasing number of projects across Melbourne's Eastern Hill Precinct in which the LSCC is playing a role. In fact, LSCC research scientist Dr Gayle Philip now spends two days a week at St Vincent's Institute, jointly funded by both organisations. "My job is mainly to help researchers enter this world of next gen. sequencing, so I get to work on a whole range of exciting projects."

"The way a lot of biological [and medical] research is done has changed fundamentally," says A/Prof. Andrew Lonie, LSCC Head, "Ten years ago, it was hypothesis-driven. You thought something, and you went out and tested it, collecting the data to do so—and it was hard work getting that data. Then the technology for gathering data fundamentally changed, particularly in molecular biology. Now it is quite easy and cheap to go out and measure things globally. So experiments are data-driven."

"The big issue for us," says Professor Tom Kay, Director SVI, "is that bioinformatics has become increasingly important, particularly with sequencing, so it really is necessary to have on-site expertise in order to stay at the forefront. I see this as an ongoing relationship, and imagine that it will grow."

The changes that turn epithelial cells into mesenchymal cells occur through the regulation of genes at the molecular level. Specific genes

are switched on and off, some become more active and others less so, some are silenced by small pieces of RNA, known as microRNAs. Microarray screening technology lets scientists look for these changes in hundreds of genes simultaneously.

Initially, different research groups have documented epithelial mesenchymal transition in different species, different cancers and different cell lines. This work is generating huge amounts of microarray and sequencing data.

So Philip, her predecessor Dr Nathan Hall and other members of the LSCC have been asked to come up with efficient ways of using computers to sift through this data, integrating datasets from different sources, and extracting and comparing the results with what has already been published in order to determine what's important and of interest. The eventual aim is to target compounds and biochemical pathways which are the key to controlling the transition, and that potentially can be regulated by drugs.

"We could analyse each data set one by one," EMP*athy* Program Manager Dr Annet Hammacher says, "but that is neither cost, nor time effective."

It's work that takes significant, but not necessarily huge amounts of, computer power, A/Prof. Lonie says. More important is the expertise of bioinformaticians in knowing how to automate the search for patterns in huge data sets, and generate meaningful statistics from massive amounts of information.

Strategic projects such as EMP*athy* should fast-track research in ways which were previously not possible. The more bioinformaticians we can get working on such problems, the faster we can find new treatments", says A/Prof. Lonie.

The EMP*athy* Breast Cancer Network website is at www.empathybcn.org

National Breast Cancer Foundation is at www.nbcf.org.au

VLSCI – www.vlsci.org.au

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