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DNA microarrays: Ability of DNA microarrays to predict cancer outcomes.

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PRIORITISING SUMMARY

REGISTER ID: **0000004**

NAME OF TECHNOLOGY: **DNA MICROARRAYS**

PURPOSE AND TARGET GROUP: **ABILITY OF DNA MICROARRAYS TO PREDICT CANCER OUTCOMES**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☐	Experimental	☐	Established
☒	Investigational	☐	Established *but* changed indication or modification of technique
☐	Nearly established	☐	Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number	
☒	No	☐	Not applicable

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway	Limited Use	Widely Diffused
Systematic review, Greece	✓		
Case series, breast cancer outcomes, Taiwan	✓		
Case series, breast cancer, Sweden	✓		

IMPACT SUMMARY:

DNA microarrays are a relatively new technology that is widely used in the research environment. They allow the simultaneous, rapid, characterisation of thousand of genes and as such are useful tools in categorising diseases such as cancer by determining the presence or absence of particular genes, which may provide important biological, diagnostic and prognostic information. It is believed that DNA microarrays may be able to predict individual outcomes in cancer patients and research in this area is being undertaken (Haviv & Campbell 2002, Ntzani & Ioannidis 2003). DNA microarrays are not currently used for *diagnostic* purposes in Australia.

There are two microarray technologies currently in use: spotted arrays, first developed at Stanford University in 1996, and oligonucleotide arrays, pioneered by the US based company Affymetrix. The Affymetrix system is based on the use of short oligonucleotides produce in-situ by a photolithographic process, with each gene represented by many oligonucleotides. Specificity is increased using the Affymetrix system (Haviv & Campbell 2002).

The spotted array system involves the binding of the target DNA, either a gene or a portion of the gene sequence of interest, to a glass slide in a grid-like arrangement (Figure 1). These grids may contain hundreds or thousands of genes but are presently unlikely to contain the entire human genome (Haviv & Campbell 2002). Target DNA may be a “home-made” polymerase chain reaction (PCR) product or may be purchased commercially as sets of up to 20,000 human genes (personal communication, Institute of Medical and Veterinary Science,

Microarray Facility). In the spotted array system, mRNA is isolated from 2 samples and converted into fluorescently tagged cDNA (single stranded DNA complementary to mRNA): the sample of interest may be tagged red (eg breast cancer sample) and a normal sample, tagged green. The 2 populations are mixed and hybridised to the DNA microarray. Unbound cDNA is washed away and a laser scanner measures the intensity of the remaining spot bound with cDNA. The data is translated to give a relative level of a particular gene transcript in both the test and normal samples (Haviv & Campbell 2002, Campbell 2003).

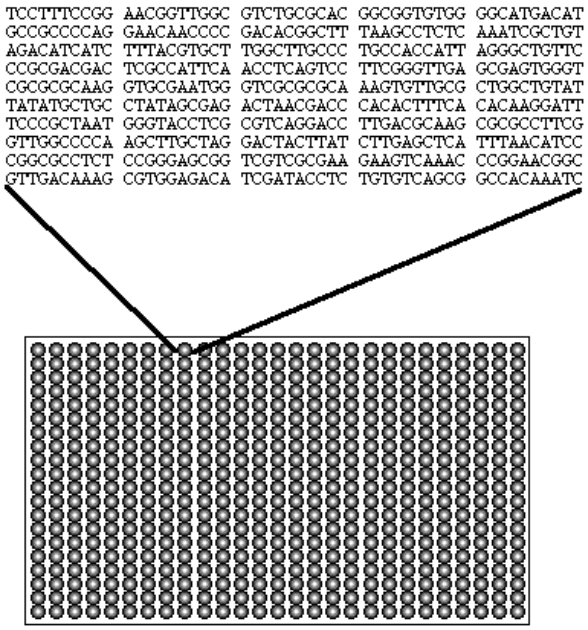

Figure 1. Example of a DNA microarray or chip, with a single gene sequence highlighted (Campbell 2003)

The systematic review by Ntzani & Ioannidis (2003) assessed the ability of DNA microarrays to predict major clinical outcomes such as death, recurrence and response to therapy, in malignant disease. They assessed 84 case series studies and found the predictive performance of microarrays to be variable due to a lack of validation and clinical design. However, they did find that significant associations were 3.5 (95% CI 1.5-8.0) times more likely with a doubling of the sample size and 9.7 (95% CI 2.0-47.0) times more likely with a 10-fold increase in microarray probes.

Huang et al (2003) used DNA microarrays in a case series to predict breast cancer outcomes. Breast cancer is highly heterogeneic due to the genetic complexity of individual tumours, therefore lymph node status at diagnosis is used as a surrogate measure for predicting breast cancer recurrence. Unfortunately lymph node status is not always detectable in all patients and 22-33% of these patients may go on to develop a recurrence of breast cancer. Huang et al (2003) identified patterns of gene expression, associated with lymph node status, and used DNA microarrays to detect these meta-genes. They were 90% accurate in predicting outcomes in individual patients.

The AIHW reported 85,231 new cases of cancer (excluding skin cancers other than melanoma) in Australia in the year 2000. Of these, there were 11,400 new cases of breast cancer in Australia with a crude mortality rate of 26.1 per 100,000 in the year 2000. Breast cancer is the most common registered cancer and the leading cause of mortality for women in Australia (AIHW 2004).

Estimated costs for spotted DNA microarrays are estimated to be A$200 per DNA chip. DNA chips are produced by a robotic spotter and read by a laser scanner, which costs approximately $280,000 and A$80,000 respectively. A complete Affymetrix system would

cost approximately A$250,000 with each Affymetrix slide costing A$700 (personal communication, Institute of Medical and Veterinary Science, Microarray Facility).

CONCLUSION:

This technology is currently in use in the Australian research environment, with the low level evidence on prognostic accuracy in the clinical field. However, the level of clinical need is high in the Australian health system.

HEALTHPACT ACTION:

Therefore it is recommended that this technology be monitored.

SOURCES OF FURTHER INFORMATION:

Campbell, M. A. (2003). *Introduction to DNA microarrays* [Internet]. Department of Biology, Davidson College. Available from: http://www.bio.davidson.edu/Biology/macampbell/strategies/chipsintro.html [Accessed 14th January 2004].

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Pusztai, L., Ayers, M. et al (2003). 'Clinical application of cDNA microarrays in oncology', *Oncologist,* 8 (3), 252-258.

Schena, M. (1996). 'Genome analysis with gene expression microarrays', *Bioessays,* 18 (5), 427-431.

Schena, M., Heller, R. A. et al (1998). 'Microarrays: biotechnology's discovery platform for functional genomics', *Trends Biotechnol,* 16 (7), 301-306.

Vigano, A., Dorgan, M. et al (2000). 'Survival prediction in terminal cancer patients: a systematic review of the medical literature', *Palliat Med,* 14 (5), 363-374.

SEARCH CRITERIA TO BE USED:

Neoplasms/*genetics/pathology/surgery/*mortality/diagnosis
Gene Expression Profiling/methods
*Oligonucleotide Array Sequence Analysis/*methods
Predictive Value of Tests
Prognosis
Gene Expression Profiling
Gene Expression Regulation