Novel Marker for Diagnosis of Ovarian Cancer

Using whole genome techniques to directly profile DNA methylation aberrations in cancer, Garvan scientists have identified a novel diagnostic biomarker for the detection of ovarian cancer.

▶ Hyper-methylation of LOC134466 indicative for the presence of many forms of cancer, including epithelial ovarian cancer & colon cancer.

▶ Can be determined in clinical (blood/plasma) samples, potentiating widespread application

▶ Ideal candidate marker for post-surgical surveillance or monitoring the success of treatment and relapse/recurrence of disease.
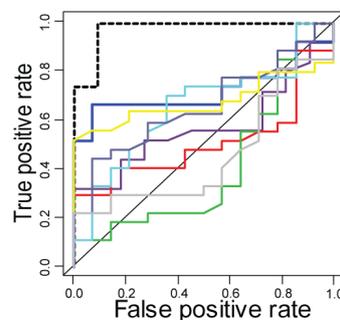
LOC134466 hypermethylation in Ovarian Cancer

Ovarian cancer is the fifth leading cause of cancer death in women and the second most commonly diagnosed gynecological malignancy. More than 50% of women with ovarian cancer are diagnosed in the advanced stages of the disease because no cost-effective screening test for ovarian cancer exists.

Using whole genome techniques to directly profile DNA methylation aberrations in cancer, Garvan scientists have identified a novel diagnostic biomarker for the detection of ovarian cancer.

Initially discovered in ovarian cancer cell lines, the LOC134466 gene was found to be hypermethylated in 81% (81/100) of ovarian tumour samples relative to 7.7% (1/13) of normal ovarian tissue.


Figure 1. *Validation by Sequenom massARRAY methylation analysis confirmed a panel of six gene promoters where hypermethylation discriminated 27 serous ovarian cancer clinical samples versus 12 normal ovarian epithelial cells.*

| Gene	AUC	p
ARMXC1	0.57	0.75
ICAM4	0.51	0.24
LOC134466	*0.73*	*0.02*
PEG3	0.66	0.13
PYCARD	0.66	0.08
SGNE1	0.68	0.07
6 Gene Model	*0.98*	

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- Analysis of archival tumour DNA using 6-gene methylation panel (including LOC134466) showed high sensitivity and specificity for ovarian cancer detection.

- 2-gene methylation panel (LOC134466 and SGNE1) also showed high predictive values.

- LOC134466 is a zinc finger protein 300 pseudogene1 (ZNF300P1).

Gene	AUC
SGNE1	**0.93**
LOC134466	*0.78*
ARMXC1	0.75
ICAM4	0.63
PEG3	0.61
PYCARD	0.54
2 Gene Model	**0.97**
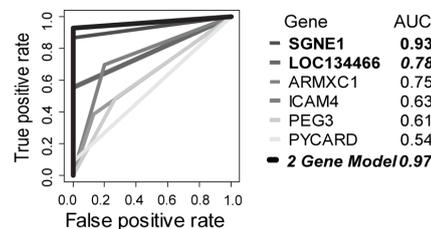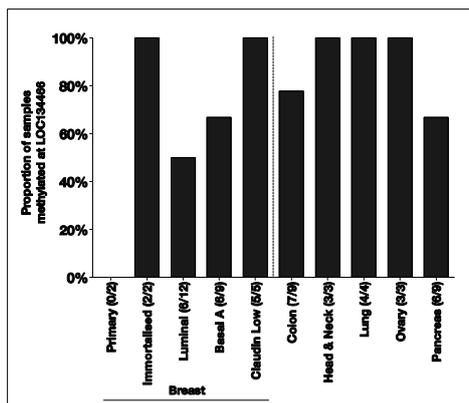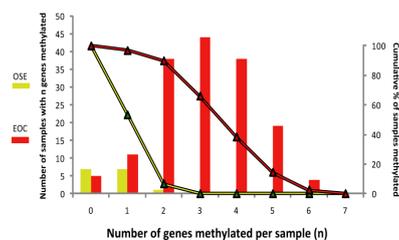
- MSH-PCR assay of LOC134466 in plasma samples can successfully distinguish cancer from normal samples.

- LOC134466 is hypermethylated in various other cancers, including breast cancer, and is indicative of metastatic potential.
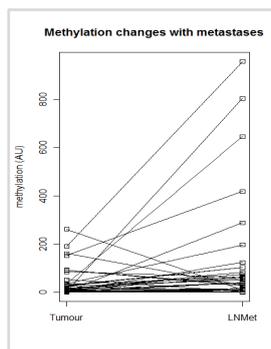
Gene/model	EOC Positive	OSE Positive	Sensitivity	Specificity	AUC	p value
LOC134466	88/159	0/11	59%	100%	0.777	0.0002269
ARMCX1	111/159	3/15	70%	80%	0.749	0.000223
ICAM4	61/159	2/15	38%	87%	0.625	0.0885
PEG3	78/159	4/15	49%	73%	0.612	0.1117
PYCARD	14/159	0/15	9%	100%	0.544	0.6136
SGNE1	138/159	0/15	87%	100%	0.934	3.34E-12
SGNE1+LOC134466	**148/159**	**0/11**	**93%**	**100%**	**0.965**	**1.14E+11**

Intellectual Property: PCT/AU2012/000397

Publication: Gloss, B.S., et al. Cancer Letters 2012, 318(1): 76-85.

Opportunity: Available for licensing or collaborative research & development

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Garvan Institute of Medical Research

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