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TRIPLE SCREENING OF GYNECOLOGY CANCERS USING CERVICAL DNA METHYLATION

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INTRODUCTION

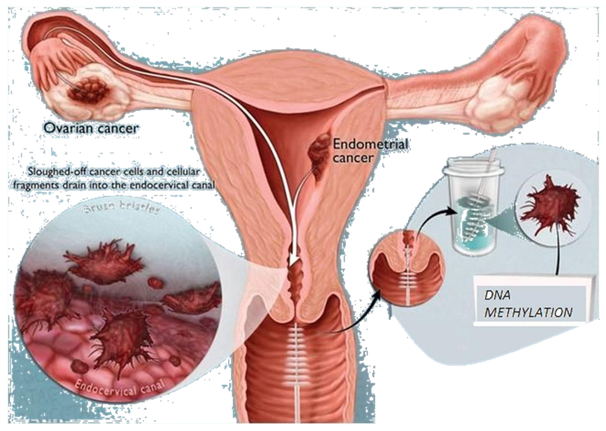
Epigenetic changes play an important role in cancer development. Our previous research on the epigenomics of cervical cancer using genome-wide approaches identified 14 candidate genes that were hypermethylated in cervical cancer tissues. Most of these genes are transcription factors and development-related genes that are common in the development of various cancers. Recent researchers demonstrated that gene mutations in cervical scrapings can reflect the status of endometrial and ovarian cancer tissues.

AIM

We hypothesized that DNA methylation at cervical scrapings could detect the presence of endometrial/ovarian cancers.

MATERIAL & METHODS

We tested the methylation status of these 14 genes in endometrial and ovarian cancer tissues. Genes hypermethylated in cancer tissues were selected for further testing using cervical scrapings from 19 endometrial or 27 ovarian cancer patients and 25 controls. The evaluation of the clinical performance characteristics of DNA methylation, including sensitive, specificity, positive predictive value, and negative predictive value were calculated.



(Modify from the I. Kinde et al., Sci Transl Med, 2013)

RESULTS

Figure1. The flow chart of verification . The methylation status of 14 genes were tested in endometrial and ovarian cancer tissues. Genes methylated in pooled DNA from cancer tissues were further tested in individual samples. Candidate genes derived from tissue results were tested in DNA from cervical swabs.

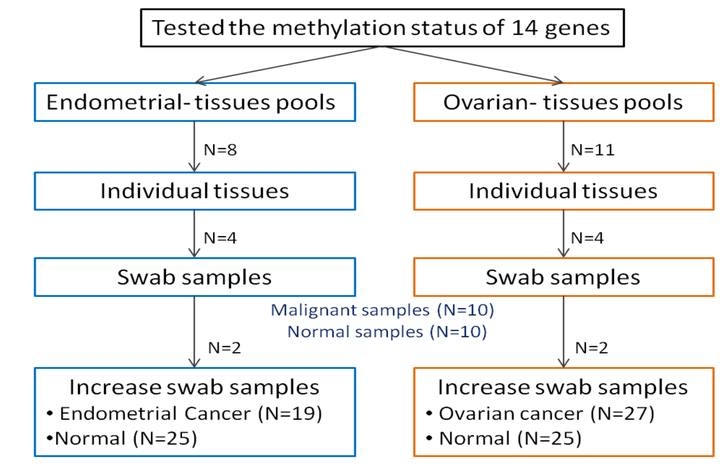


Figure2. The heat map showed the methylation status of 8 and 11 candidate genes in endometrial (a) and ovarian (b) tissues. There are 20 endometrial cancer tissues, 20 normal endometrium tissues, 20 ovarian cancer tissues, and 14 normal ovary tissues. The green and red color represents low and high methylation, respectively .

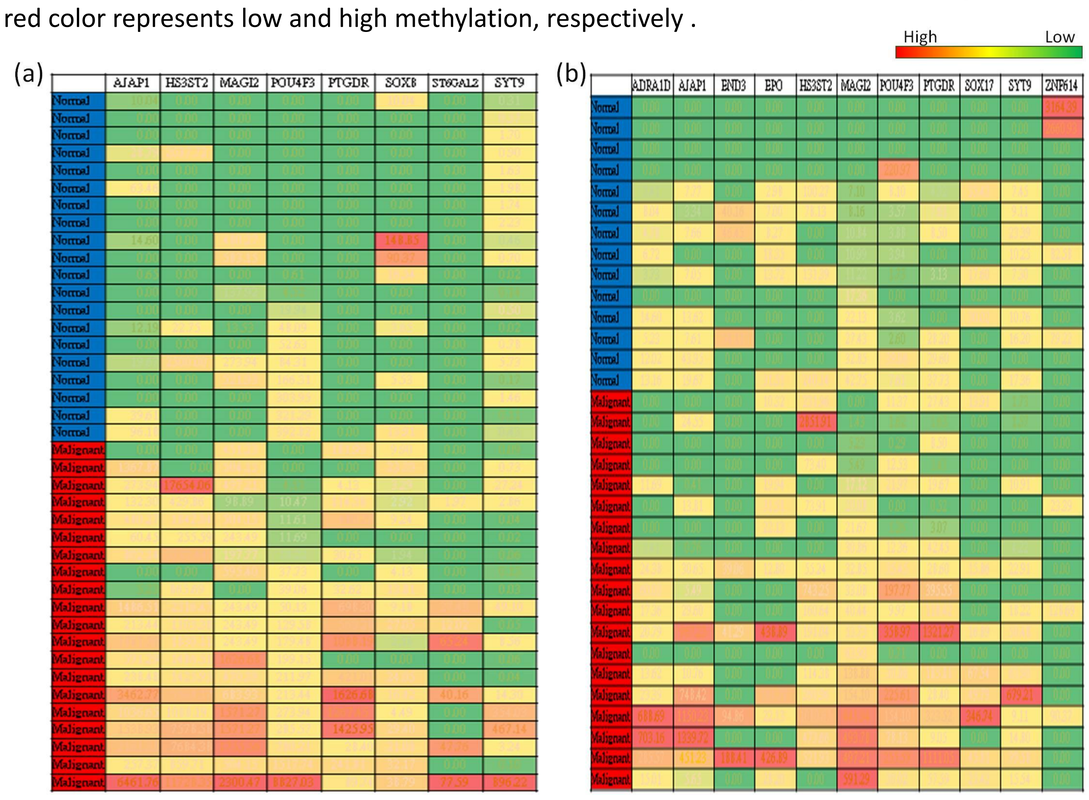


Figure3. Four (*PTGDR*, *HS3ST2*, *POU4F3*, *MAGI2*) genes showed hypermethylation in cervical swabs of endometrial (a) and ovarian (b) cancers. Ten samples of each group were tested.

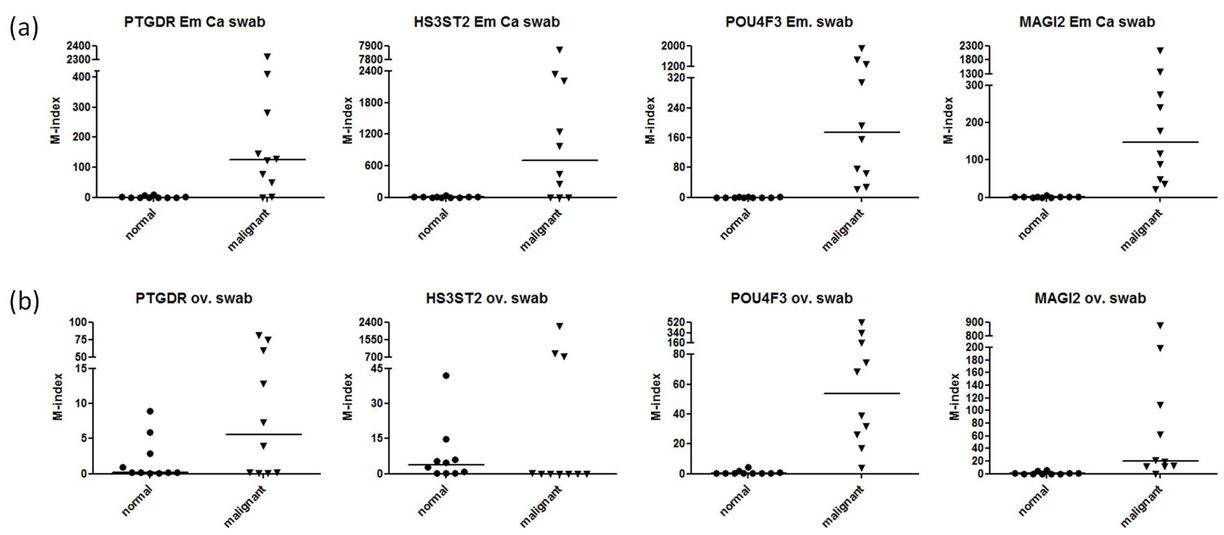
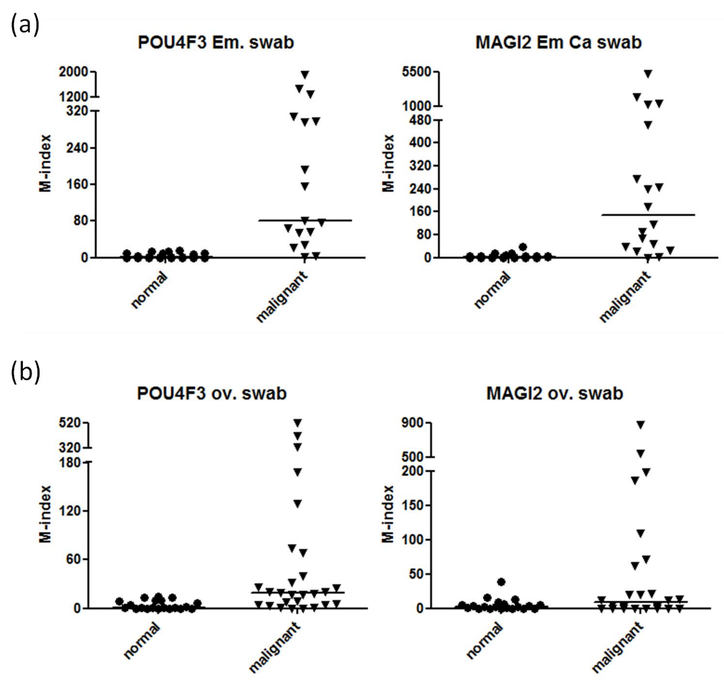


Figure4 . The performance of *POU4F3* and *MAGI2* hypermethylation in cervical swabs for the detection of endometrial (a) and ovarian (b) cancers.



	Em Cancer (N=19)	Normal (N=25)
Gene name	Sensitivity (%)	Specificity (%)
POU4F3	88.2	100
MAGI2	88.9	95

	Ovarian cancer (N=27)	Normal (N=25)
Gene name	Sensitivity (%)	Specificity (%)
POU4F3	62.7	100
MAGI2	57.7	85

SUMMARY / CONCLUSION

POU4F3 revealed the clinical performance with sensitivity and specificity of 88% and 100% for detecting endometrial cancers, 63% and 100% for detecting ovarian cancers, respectively. The proof of concept has lead us to the analysis of epigenomics of endometrial cancer and ovarian cancer individually (Manuscript in preparation; patent pending). Those results shed a new light on the triple screening of gynecological cancers in the future.

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