

Epigenetic alterations associated with aggressive phenotype ovarian cancer

Woong Ju, M.D., Ph.D. M.P.H.

Professor
Department of Obstetrics and Gynecology
College of Medicine, Ewha Womans University
Korea

Despite progress in cancer therapy, a lack of reliable biomarkers for early detection and risk of metastatic recurrences makes ovarian cancer the most lethal gynecological cancer.

To understand the molecular mechanisms involved in ovarian cancer metastasis *in vivo*, we analyzed genome-wide interplay between promoter CpG DNA methylation and gene expression in a mouse model of metastatic ovarian cancer to identify genes whose expression was regulated by abnormal changes of DNA methylation during metastatic ovarian tumor formation. The GABRP, CA9, SLC6A12, and MAL showed increased mRNA expression and hypomethylation of promoter CpG in metastasized tumor tissues. The DNA methylation-dependent transcriptional regulation of those genes was confirmed by treatment of demethylating agent. We also found that overexpression of those genes caused increased migration and invasiveness in SK-OV-3 cells via activation of extracellular signal-regulated kinase (ERK). Conversely, silencing of those genes decreased phosphorylation of ERK1/2 and selective inhibition of ERK1/2 significantly decreased migration and invasiveness in SK-OV-3 cells.

Our result also revealed that hypomethylation of GABRP and other genes within promoter CpG is associated with advanced stage and metastasis to the lymph node in patients with ovarian cancer. Receiver operating characteristics analysis showed good discrimination between patients at early and advanced stage.

In this study, we provide novel evidence for epigenetic regulation of relevant genes in ovarian cancer. We herein suggest that the DNA methylation status within GABRP, CA9, SLC6A12, and MAL promoter region may be a potential biomarker that can indicate the aggressive behavior of ovarian cancer.



Woong Ju, M.D., Ph.D. M.P.H.

Professor
 Department of Obstetrics and Gynecology
 College of Medicine, Ewha Womans University
 Korea

Personal information

Department of Obstetrics and Gynecology, Mok-Dong Hospital, Ewha Womans University School of Medicine,
 911-1 Mok-Dong, Yang Chun-Ku, 158-710, Seoul, Korea
 Tel: 82-2-2650-2779, 5274, Fax: 82-2-2647-9860
 E-mail: goodmorning@ewha.ac.kr, woongju@post.harvard.edu, Certification number 59948

Scholarship

1996. 2. 27 Graduated from Seoul National University, School of Medicine
 2004. 8. 30 Graduated from Seoul National University, School of Medicine, Master's degree (MS) for Medicine
 2007. 2. 26 Graduated from Seoul National University, School of Medicine, PhD for Medicine
 2012. 5. 30 Graduated from Harvard University, School of Public Health, Master of Public Health (MPH)

Career

1996. 3 - 1997. 2 Internship in Seoul National University Hospital, Seoul, Korea
 1997. 2 - 2000. 4 Military Service as a Primary physician (National Duty)
 2000. 5 - 2004. 2 Residency in Seoul National University Hospital (Dept of Obstetrics and Gynecology), Seoul, Korea
 2004. 3 - 2005. 2 Fellowship in Seoul National University Hospital (Dept of Obstetrics and Gynecology, Division of Gynecologic Oncology), Seoul, Korea
 2005.3 – 2011.2 Assistant Professor in Obstetrics and Gynecology, Ewha Womans University Mok-Dong Hospital, Seoul, Korea
 2011.3 – 2016.2 Associate Professor in Obstetrics and Gynecology, Ewha Womans University Mok-Dong Hospital, Seoul, Korea
 2016.3 – Professor in Obstetrics and Gynecology, Ewha Womans University Mok-Dong Hospital, Seoul, Korea
 2013.6- 2013.8 Research Intern, Center for Connected Health, Massachusetts General Hospital
 2015.8- 2017.7 Director, Ewha Womans University Mok-dong Hospital, Referral Center
 2015.8- 2017.7 Director, Center for Gynecologic Oncology, Ewha Womans University Cancer Center for Women