P1-1S-25  BAG-1 expression in normal endometrium, endometrial hyperplasia and endometrial cancer: Is it prognostic marker?

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Objective: BAG-1 is a BCL-2 binding anti-apoptotic protein that may play a role in carcinogenesis and expressed in breast, prostate, colorectal, lung and esophageal cancer. Our purposes for this study are to compare the expression rate of BAG-1 in normal endometrium, endometrial hyperplasia and endometrial cancer, and to find out the correlation BAG-1 expression and clinicopathological parameters, with furthermore overall survival, so evaluate the possibility for the use as a prognostic marker of endometrial cancer.

Material and Methods: Forty three patients who diagnosed with endometrial cancer, twenty patients with endometrial hyperplasia and twenty normal endometrial tissue in Korea University Hospital, between 1998 and 2005 were included in the study. Immunohistochemical analyses were performed using polyclonal anti-BAG-1 antibody from paraffin-embedded blocks.

Results: Cytoplasmic BAG-1 expression of normal endometrium, endometrial hyperplasia and endometrial cancer were 4/20 (20%), 3/20 (15%) and 34/43 (85%) respectively, higher in endometrial cancer (p<0.05). Nuclear BAG-1 expression were 17/20 (85%), 12/20 (60%) and 16/43 (37%) and lower in cancer. Cytoplasmic BAG-1 expression is correlated with cancer grade (p=0.02) but dose not with other parameters such as stage, ER, PR, and BCL-2. Nuclear BAG-1 expression is not correlated with clinicopathological parameters. The mean survival of positive/negative cytoplasmic BAG-1 expression was 59.4/454 months, and nuclear BAG-1 expression was 54.0/41.1 months, but no difference statistically on survival (log-rank p = 0.31, p = 0.55)

Conclusion: Cytoplasmic BAG-1 is more frequently expressed in endometrial cancer and in high grade cancer, and correlate with cancer grade. Nuclear BAG-1 is more frequently expressed in normal and hyperplasia than endometrial cancer, and is not correlated with clinicopathological parameters. But both cytoplasmic and nuclear BAG-1 expressions are not associated with survival. BAG-1 as a prognostic marker of endometrial cancer is conflicted and further investigation is needed.

Key words: BAG-1, BCL-2, Endometrial cancer.

P1-1S-26  Discovering potential molecular markers and therapeutic targets of endometrial cancer in small RNA world

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[Objective] MicroRNAs (miRNAs) in small RNA world are short, non-coding RNAs that regulate gene expression by inducing cleavage of the targeted messenger or by inhibiting translation, and involved in a wide range of basic processes such as cell proliferation, development, apoptosis and stress response. It has recently been found that they are also abnormally expressed in many types of human cancer. Endometrial cancer is the third most common gynaecologic malignancy in Hong Kong and about 80–90% are endometrioid endometrial adenocarcinomas (EEC). This study was to investigate miRNAs in endometrial tumorgenesis.

[Methods] We examined the expression of 156 mature miRNAs by high through-put real-time RT-PCR assays in laser capture microdissected EECs including 4 advanced- and 9 early-stage tumors, and compared that to 5 normal counterparts.

[Results] Unsupervised clustering analysis of these global miRNA expression profiles showed a distinct separation between cancers and normal controls. Supervised clustering analysis identified 13 miRNAs up-regulated and 3 miRNAs down-regulated, respectively, in EECs. The fold-change observed in cancer in relation to normal controls varied between 2.3 and 425-fold up-regulation and between −2.63 and −5.30-fold down-regulation. In addition, when the miRNA expression profiles in advanced stage tumors were compared to those in early stage tumors, 5 miRNAs were significantly over-expressed and one miRNA under-expressed in advanced stage tumors. We further searched the predicted target genes of these miRNAs on three databases including http://www.microrna.org, http://www.sanger.ac.uk, and http://pic tar.bio.nyu.edu. A total of 38 aberrantly regulated genes that were previously identified by us in a large set of EEC, were predicted as the target genes of 8 miRNAs of most interest in EEC.

[Conclusion] To the best of our knowledge, this is the first report demonstrating miRNA dysregulation as a key event in endometrial cell transformation. Unique miRNA signatures, novel molecular markers and candidate therapeutic targets may be further identified in expanded study of miRNA expression profiling and functional role of miRNAs in EEC.