Investigations for methylation status of genomic DNA in endometrial carcinogenesis

2003 Fiscal Year Final Research Report Summary

Investigations for methylation status of genomic DNA in endometrial carcinogenesis

Research Project

Project/Area Number

14571547

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Obstetrics and gynecology

Research Institution

KANAZAWA UNIVERSITY

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Project Period (FY)

2002 – 2003

Keywords

DNA methylation / Endoiuetrial cnacer / hMLH1 / Metvlation Snecific PCR / Bisulfite sequencing / PTEN mutation / Microsatellite instability / Microdissection

Research Abstract

The results previously cleared in this study are four points as follows ;
1.The hyperinethylation of hMLH1 promoter is found about 40% of endometrial cancers.
2.Protein expression is decreased with hyperinethylation of hMLH1 promoter.
3.The hypermethylation is already found in normal endoinetrium adjacent to endometrial cacers.
4.Genetic instability is also found both in cancer and normal endometrium with hypermethylation of hMLH1.
With the above-mentioned results, the followings are cleared in 2003.

1.Quantitative methylation analysis of hMLH1 promoter
Methylation specific PCR(MSP)was used as qualitative analysis, however, quantitative analysis for hMLH1 promoter hypermetylation is required.For this purpose, we used bisulfite sequencing to investigate metylation status within 700-bp promoter area of hMLH1.With the 56 endometrial cancer cases, 16 cases (29%) are fully methylated in promoter, 14 cases(25%) are partially methylated, and 14 cases (46%) are non-methylated.
2. Relation between hMLH1 methylation and PTEN mutation
It is reported that PTEN mutations are found in early stage of endometrial carcinogenesis.In this study, PTEN mutations are recognized in 40% of endometrial cancers, and in particular, insertion/deletion mutations of PTEN are significantly related with hMLH1 promoter hypermethylations.
3.Laser capture microdissection : LCM
LCM is used to distinguish carcinoma or precancerous lesion with normal stromal tissue.Methylation analysis was technically difficult with LCM because of the small amount of DNA, but we solved this problem by the combination of PCR and methylation sensitive restriction enzymes.As a result, methylation frequency of the endoinetrial hyperplasia and cancer was almost equal, While the methylation frequency of the normal endometrium was zero.
With these results, our future plans are elucidation of endometrial carcinogenesis, and clinical application of endometrial cancer screening.

Research Products (11 results)

All Other

All Publications

[Publications] Taro Kanaya et al.: "Frequent hypermethylation of MLH1 promoter in normal endometrium of patients with endometrial cancers"Oncogene. 22. 2352-2360 (2003)

[Publications] Satoru Kyo, Taro Kanaya et al.: "Role of MLH1 gene hypermethylation in endometrial carcinogenesis"Cell and Molecular Biology of Endometrial Carcinoma, Kuramoto H, Nishida M (Eds.) (Springer-Verlag, New York). 1. 232-244 (2003)

[Publications] Satoru Kyo, Taro Kanaya et al.: "Significance of immunological detection of human telomerase reverse transcriptase : re-evaluation of expression and localization of human telomerase reverse transcriptase."American Journal of Pathology. 163. 859-867 (2003)

[Publications] Masaaki Tanaka, Taro Kanaya et al.: "Evidence of the monoclonal composition of human endometrial epithelial glands and mosaic pattern of clonal distribution in luminal epithelium."American Journal of Pathology. 163. 295-301 (2003)

[Publications] Yoshiko Maida, Taro Kanaya et al.: "Is the telomerase assay useful for screening of endometrial lesions?"International Journal of Cancer. 100. 714-718 (2002)

[Publications] 金谷 太郎 他: "子宮体癌の遺伝子診断"産婦人科治療. 85. 637-641 (2002)

[Publications] Kanaya T, Kyo S, Maida Y, Yatabe N, Tanaka M, Nakamura M, Inoue M.: "Frequent hypermethylation of MLH1 promoter in normal endometrium of patients with endometrial cancers."Oncogene.. 22(15). 2352-2360 (2003)

[Publications] Kyo S, Kanaya T, Inoue M.: "Role of hMLH1 gene hypermethylation in endometrial carcinogenesis."Cell and Molecular Biology of Endometrial Carcinoma, (Kuramoto H, Nishida M(Eds.)(Springer-Verlag, New York). 232-244 (2003)

[Publications] Kyo S, Masutomi K, Maida Y, Kanaya T, Yatabe N, Nakamura M, Tanaka M, Takarada M, Sugawar I, Murakami S, Taira T, Inoue M.: "Significance of immunological detection of human telomerase reverse transcriptase : re-evaluation of expression and localization of human telomerase reverse transcriptase."Am J Pathol.. 163(3). 859-867 (2003)

[Publications] Tanaka M, Kyo S, Kanaya T, Yatabe N, Nakamura M, Maida Y, Okabe M, Inoue M.: "Evidence of the monoclonal composition of human endometrial epithelial glands and mosaic pattern of clonal distribution in luminal epithelium."Am J Pathol.. 163(1). 295-301 (2003)

[Publications] Maida Y, Kyo S, Kanaya T, Wang Z, Tanaka M, Yatabe N, Nakamura M, Inoue. M.: "Is the telomerase assay useful for screening of endometrial lesions?"Int J Cancer.. 100(6). 714-718 (2002)

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