Analysis of Mismatch repair gene methylation for Gynecologic cancer screening

2006 Fiscal Year Final Research Report Summary

Analysis of Mismatch repair gene methylation for Gynecologic cancer screening

Research Project

Project/Area Number

16591649

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Obstetrics and gynecology

Research Institution

Department of Clinical Research, National Hospital Organization Kanazawa Medical Center (2005-2006)
Kanazawa University (2004)

Principal Investigator

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Project Period (FY)

2004 – 2005

Keywords

Gynecologic cancer / Cancer screening / DNA methylation / Mismatch repair gene / Gene mutation

Research Abstract

We already reported the methylation of MLH1 promoter and the decrease of its protein expression in endometrial cancer, and the mutations of downstream genes with microsatellite instabilities. With this funds, we provided more details as shown.
1. Analysis of MLH1 promoter methylation in endometrial hyperplasia
Because of a very small amount for clinical sample of the endometrium hyperplasia, as a cancer precursor, it was difficult to perform methylation analysis. We developed the method of methylation analysis of the MLH1 promoter from the very small amount of endometrial sample, using PCR after restriction enzyme processing and Bisulfite modification. As a result, 11 of 27 endometrial hyperplasia examples (41%) were methylated, and the methylation frequency was approximately equal with endometrial cancers.
2. Relation with the PTEN mutation
PTEN is a cancer suppressor gene which has mutations in the early stage of endometrial cancers. As a result of PTEN mutation analysis, 38% of the endometrial cancers

and 19% of the endometrial hyperplasias have PTEN mutations. We also found complex hyperplasias have more frequent PTEN mutations than simple hyperplasias. We recognize the methylation of MLH1 promoter is upstream of histological changes, and the PTEN mutation is a next step.
3. The methylation and mutation analysis with cytological specimen
In this study, the purpose is gynecologic cancer screening with the combination of cyto-histology and genetic analysis. With our preliminary experiments, cytological specimen has enough samples for methylation and mutation analysis. In future, we have to distinguish the high risk patients for gynecologic carcinogenesis with methylation and mutation analysis of cytological specimens for clinical application.

Research Products (6 results)

All 2005

All Journal Article

[Journal Article] Association of mismatch repair deficiency with PTEN frameshift mutations inendometrial cancers and the precursors in a Japanese population 2005

[Journal Article] Aberrant expression and mutations of TGF-beta receptor type II gene inendometrial cancer 2005

[Journal Article] Efficient inhibition of human telomerase reverse transcriptase expression by RNA interference sensitizes cancer cells to ionizing radiation and chemotherapy 2005

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