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Genetic variations of *MUC17* are associated with endometriosis development and related infertility

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Abstract

Background: Genetic alterations of mucin genes, such as *MUC2* and *MUC4*, were previously identified to be associated with endometriosis and related infertility. Additionally, gene expression profiling has confirmed MUC17 to be overexpressed in mucinous ovarian carcinoma; however, its associated risk for endometriosis remains unclear. This study was focused on the potential impact of genetic variations in *MUC17* on endometriosis development and associated clinical features.

Methods: The study subjects included 189 female Taiwanese patients with pathology-proven endometriosis and 191 healthy Taiwanese women as controls. Five single-nucleotide polymorphisms (rs4729645, rs10953316, rs74974199, rs4729655, and rs4729656) within the *MUC17* gene were selected and genotyped using the *Taqman* genotyping assay to examine the allele frequency and genotype distributions of *MUC17* polymorphisms.

Results: Genotyping revealed that the A allele at rs10953316 in *MUC17* was a protective genetic factor in endometriosis development ($p = 0.008$; OR = 0.53; 95 % CI: 0.36-0.79). Genetic variation of rs4729655 protected patients against endometriosis-induced infertility, but was associated with a higher cancer antigen 125 (CA125) level. Base-pairing analysis, called MaxExpect, predicted an additional loop in the mRNA structure caused by rs10953316 polymorphism, possibly influencing ribosome sliding and translation efficiency. Such predictions were confirmed by immunohistochemistry that patients with AA genotype at rs10953316 showed low MUC17 levels in their endometrium, patients with GA genotype showed moderate levels, and strong staining could be found in patients with GG genotype.

Conclusions: *MUC17* polymorphisms are involved in endometriosis development and the associated infertility in the Taiwanese population.

Background

Endometriosis is a common chronic gynecological disease described as the presence of endometrial glands and stroma located outside the uterine cavity, ovaries, fallopian tubes, and even on the bladder or intestines [1, 2]. It occurs in approximately 10 % of women or teenage girls at reproductive age. Up to 50 % of patients also suffer from infertility [3, 4]. Clinical symptoms of endometriosis include several types of pain, such as excessive menstrual pain, pelvic pain with defecation, and chronic pelvic pain [5]. Epidemiological studies revealed a higher risk for endometriosis patients to develop different types of ovarian cancers [6, 7]. Molecular pathological analyses have provided strong evidence to support the histological transition from benign endometriosis to ovarian malignancy [8, 9].

Mucins are high-molecular-weight o-glycoproteins that function as the protective and lubricative layers on epithelial surfaces, such as the respiratory, gastrointestinal, and reproductive tracts [10–13]. Gene expression analyses have indicated that MUC1 ~ 4 are the major mucins constitutively expressed in endometrial epithelium, and their levels can be controlled by the menstrual cycle [14, 15]. With potent roles in cellular proliferation,

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