Genetic Polymorphisms of Ataxia Telangiectasia Mutated and Breast Cancer Risk

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Abstract

To evaluate the role of genetic polymorphisms of ataxia telangiectasia mutated (ATM) in the etiology of breast cancer, a hospital-based case-control study was conducted in Korea. Nine-hundred ninety-six histologically confirmed incident breast cancer cases and 1,181 cancer-free controls were recruited in Seoul between 1995 and 2003. Genotypes of the ATM polymorphisms -5144A>T, IVS21+1049T>C, IVS33-55T>C, IVS34+60G>A, and 3393T>G were determined by the S-nuclease assay. Individual haplotypes were estimated from genotype data by a Bayesian method. Five ATM alleles were found to be in strong linkage disequilibrium (D' > 0.82; P < 0.001). Haplotype frequencies were significantly different between cases and controls (χ² test, P < 0.001). The ATM IVS21+1049 TC or CC, IVS34+60 GA or AA, and 3393 TG or GG genotypes were associated with increased breast cancer risk, particularly in premenopausal women (odds ratios (OR), 1.51; 95% confidence interval (CI), 1.11-2.05; OR, 1.42; 95% CI, 1.08-1.88; and OR, 1.37; 95% CI, 1.04-1.80, respectively). Compared with diploid of TCCAG:TCCAG, the most common haplotype, the ATTGT:ATTGT was associated with decreased risk of breast cancer with borderline significance (OR, 0.77; 95% CI, 0.58-1.04) and TCCAG:ATCGT and ATTGT:ACCG were associated with increased breast cancer risk (OR, 2.30; 95% CI, 1.18-4.48 and OR, 2.43; 95% CI, 1.10-5.52, respectively) after adjusting for age, education, age at first full-term pregnancy, parity, family history of breast cancer, alcohol consumption, and smoking. As the number of ATTGT haplotype decreased, the risk of breast cancer increased (P for trend <0.01). Our results thus suggest that genetic polymorphisms of ATM play an important role in the development of breast cancer in Korean women. (Cancer Epidemiol Biomarkers Prev 2005;14(4):821–5)

Introduction

Ataxia telangiectasia mutated (ATM) is known as a member of phosphatidylinositol 3-kinase family (1), and it directly phosphorylates p53 and interacts with many other molecules involved in homologous and nonhomologous double strand break repair as well as in cell signaling in response to a critical DNA damage (2). ATM responds to damage caused during meiosis and mitosis or by free radicals generated during the metabolism of estrogens or environmental chemicals (3). Without this surveillance mechanism, cells are prone to replication of damaged DNA templates in S phase and segregation of damaged chromosomes through mitosis (4).

A number of studies investigating the A-T families showed 2- to 3-fold increased risk of breast cancer among obligate female A-T heterozygous carriers (5-10). Therefore, it has been suggested that breast cancer risk in the general population as well as the A-T families is modified by the mutations or polymorphisms of ATM. Thus, ATM is one of the candidate genes that might be involved in breast cancer development.

A number of studies evaluated the association between ATM variants and sporadic breast cancer and generated mixed results (11-17). Several ATM polymorphisms (e.g., S707P, L546V, IVS22--77T>C, and IVS48+238C>G) have been suggested to predispose those with specific genotypes or haplotypes to increased risk of breast cancer (13-15, 17). However, the ATM 707Pro variant was reportedly associated with elevated risk of breast cancer in one case-control study (13) but not in other case-control studies (14, 17). Thus, whether breast cancer risk is modified by the variants of ATM or not is still controversial. Inconsistencies among previous studies might be due to low frequencies of minor alleles of mutations or polymorphisms, moderate sample sizes, and improper subject selection.

In this study, we evaluated the association between five ATM single nucleotide polymorphisms [SNP; with variant allele frequencies more than 10%, based on the SNP500Cancer database (http://SNP500Cancer.nci.nih.gov/home.cfm)] and breast cancer risk in a large case-control study in Korea.

Materials and Methods

Study Subjects. The cases consisted of a consecutive series of breast cancer patients admitted to three teaching hospitals (i.e., Seoul National University Hospital, Borame, and Asan) located in Seoul, Korea, between 1995 and 2003. The control subjects consisted of noncancer patients admitted to the same hospitals and healthy women participated in the health checkup program. The study design was approved by the Committee on Human Research of Seoul National University Hospital, and the subjects provided their informed consents before their participation in the study.
We recruited 1,007 eligible patients with histologically confirmed incident breast cancer and 1,232 cancer-free controls from whom DNA samples were available. After exclusion of those with previous history of cancer or previous history of hysterectomy and oophorectomy, the final analysis included 996 breast cancer cases and 1,181 cancer-free controls. The number of healthy controls was 471 (40%) and the other hospital controls (n = 710) had noncancerous diseases including infection or stone of gall bladder/bile duct (25.9%), benign breast disease (17.2%), acute appendicitis (14.0%), hemorrhoid/perforation (7.1%), lipoma (2.2%), and others (22.3%). Risk factors and genotype frequencies were not different between benign breast disease and other diseases among hospital controls, and there was no difference in the results of the analyses that either included benign breast disease in hospital controls or not (data not shown).

Information on demographic characteristics, education, marital status, family history of breast cancer in the first- and second-degree relatives, reproductive and menstrual factors, and lifestyle habits including smoking, alcohol consumption, etc. were collected by trained interviewers using a structured questionnaire. Although some selected characteristics (e.g., age and education) were different between the hospital and healthy controls, the distributions of reproductive/parity factors [e.g., age at menarche and age at first full-term pregnancy (FFTP)] and genotype frequencies were not different (data not shown). The final statistical analysis included adjusting for all significant covariates identified from the initial analysis.

Genotyping. Practically, predicting the haplotype tags (SNP) for genotyping was not possible from the literature, such as the work of Bonnen et al. (18) and Thorstenson et al. (19), which only showed the extensive linkage disequilibrium. Thus, our strategy was to select SNPs with a high frequency of the minor alleles. From the SNP500Cancer database (http://snp500cancer.nci.nih.gov/home.cfm), seven ATM SNPs, of which the variant allele frequencies are more than 10%, were selected. Of these seven SNPs, five were successfully genotyped. Genotypes of ATM −5144A>T (rs228589), IVS21+1049T>C (rs6646477), IVS33−55T>C (rs664982), IVS34+60C>A (rs664143), and 3393T>G (rs4585) were determined by the 5′-nuclelease assay (TaqMan). PCR primers used in the assays and TaqMan Minor Groove Binder (MGB) probes labeled with dyes (FAM or VIC) at 5′ end are listed in Appendix 1.

DNA was isolated using the standard methods from blood drawn into 10-mL heparinized tubes and stored at −20°C until used for DNA extraction. PCR products were obtained in a total volume of 5 μL by using the PCR System 9700 with 384-well blocks (ABI, Foster City, CA). The reaction mixture was composed of 1.0 μL of 20 ng/μL DNA, 2.5 μL of 2× TaqMan Universal PCR master mix (ABI, 430447), 0.1 μL of 5 μmol/L each primer (final concentration, 100 nmol/L), 0.15 μL of 20 μmol/L each probe (final concentration, 600 nmol/L), and 1.0 μL of H₂O. The amplification conditions were decontamination via uracil DNA glycosylase enzyme at 50°C for 2 minutes, initial denaturation at 95°C for 10 minutes, followed by 40 cycles of 15 seconds at 95°C and 60 seconds at 60°C. After PCR, each genotype was determined by the 5′-nuclelease assay in which the fluorescent signals were measured at 60°C by the 7900HT Sequence Detection System (ABI). Genotyping was done blindly to the case-control status and the repeatability tests resulted in a 96.4% concordance rate. The repeatability was tested for five samples with 10 repeats, which were randomly placed in the 384-well plates. Of 250 reactions (i.e., 50 samples for 5 loci) the number of undetermined results was 5 and discordant scoring was 4. When the undermined genotypes were excluded the concordance rate was 98.4%.

Statistical Analysis. The risks were estimated as odds ratios (OR) and 95% confidence intervals (95% CI) by using unconditional logistic regression models adjusting for age, education (at or over high school versus under high school), family history of breast cancer in first- and second-degree relatives, parity, age at FFTP (FFTP < 25, 25 ≤ FFTP < 30, and FFTP ≥ 30), alcohol consumption (<1/mo, ≥1 to 3/mo, and ≥1/wk), and smoking (≥400 versus <400 cigarettes/lifetime).

The missing data with at least one of five polymorphic sites were excluded, and individual haplotypes were then estimated from genotype data by the Bayesian method using PHASE program (ver. 2.0.2) available from a website: http://www.stat.washington.edu Stephens/software.html (20). Only five haplotypes were estimated with the probability lower than 0.95; thus, these haplotypes were excluded from the haplotype or diplotype analysis.

Pairwise linkage disequilibrium between any two alleles of five polymorphic sites was estimated as relative disequilibrium (D′) from the haplotype data by using the following equations: (A) D = pAB − pApB, (B) D′ = D / Dmax, where Dmax = min(pAB, pA' B, pAB, pA'B') if D ≥ 0, and (C) D′ = −D / Dmax, Dmin = max(−pAB, −pA'B, −pAB, −pA'B') if D < 0, and the statistical significance was evaluated by the Fisher’s exact test. Five alleles were found to be in strong linkage disequilibrium with each other (D′ > 0.82; P < 0.001).

The distribution of haplotypes in the cases and controls was compared by χ² test. The diplotype of the most common haplotype TCCAG was selected as a reference in the diplotype analysis. The risk of breast cancer was estimated for each diplotype compared with TCCAG:TCCAG diplotype with adjustment for other covariates. Diploptype data were treated as categorical variable and were incorporated as dummy variables in the logistic regression models.

Results

As shown in Table 1, increased risk of breast cancer was statistically significantly associated with older age at FFTP (P for trend = 0.05), family history of breast cancer among first- and second-degree relatives (OR, 2.35; 95% CI, 1.53-3.61), alcohol consumption (P for trend <0.01), and smoking (OR, 1.56; 95% CI, 1.12-2.16) after adjustment for other covariates. The allele frequencies of all five loci studied except one (−5144A) were lower (IVS21+1049T, 0.41; IVS33−55T, 0.46; IVS34+60G, 0.47; and 3393T, 0.46) in this Korean population than those in Caucasians (0.66, 0.66, 0.66, and 0.64, respectively). Three of five SNPs studied showed significant differences in their allele frequencies between the cases and controls. The IVS21+1049 TC or CC, IVS33+60 GA or AA, and 3393 TG or GG genotypes were associated with increased breast cancer risk (OR, 1.39; 95% CI, 1.09-1.77; OR, 1.29; 95% CI, 1.04-1.70; OR, 1.24; 95% CI, 1.00-1.54, respectively), particularly in premenopausal women (OR, 1.51; 95% CI, 1.11-2.05; OR, 1.42; 95% CI, 1.08-1.88; and OR, 1.37; 95% CI, 1.04-1.80, respectively; Table 2).

A total of 23 haplotypes were estimated from the genotypic data (Table 3). Haplotype frequencies were also different between the cases and controls (χ² test, P < 0.001). The TCCAG haplotype was the most common (51%) in both cases and controls, and the three most common haplotypes, TCCAG, ATTG and ACTGT, accounted for 91% in the cases and for 96% in the controls. The significant difference was also observed in both premenopausal and postmenopausal women in the stratified analysis by menopausal status (χ² test, P < 0.001 and P = 0.002, respectively).

Compared with the diplotype of TCCAG:TCCAG, the most common haplotype, ATGTG:ATGTG was associated with decreased risk of breast cancer with borderline significance.
Table 1. Selected characteristics for 996 breast cancer cases and 1,181 control subjects

<table>
<thead>
<tr>
<th>Age (mean ± SD)</th>
<th>Body mass index (mean ± SD)</th>
<th>Education</th>
<th>Age at FFTP</th>
<th>Alcohol consumption</th>
<th>Cigarette smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>47.0 (±10.1)</td>
<td>48.2 (±12.4)</td>
<td>23.08 (±3.14)</td>
<td>23.07 (±3.08)</td>
<td>0.95</td>
<td></td>
</tr>
</tbody>
</table>

Family history of breast cancer in first- and second-degree relatives

- No: 929 (93.3) 1,147 (97.1) 1.00 (ref.) 1.00 (ref.)
- Yes: 67 (6.7) 34 (3.0) 2.43 (1.60-3.71) 2.35 (1.53-3.61)

Discussion

Our results suggest that genetic polymorphisms of ATM may play an important role in the development of breast cancer in Korean women, particularly in premenopausal women. The compositions of ATM haplotypes between cases and controls were significantly different, and some specific ATM haplotypes were associated with increased risk of breast cancer.

Table 2. The distributions of selected ATM genotypes and breast cancer risks by menopausal status

<table>
<thead>
<tr>
<th>All women</th>
<th>Premenopausal women</th>
<th>Postmenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases, N (%)</td>
<td>Controls, N (%)</td>
<td>OR (95% CI)*</td>
</tr>
<tr>
<td>TT 103 (11.3)</td>
<td>91 (8.6)</td>
<td>1.54 (1.12-2.14)</td>
</tr>
<tr>
<td>TA 327 (35.8)</td>
<td>444 (42.1)</td>
<td>1.00 (ref.)</td>
</tr>
<tr>
<td>TA 25 (2.7)</td>
<td>25 (2.1)</td>
<td>1.24 (1.00-1.54)</td>
</tr>
<tr>
<td>TA 103 (11.3)</td>
<td>91 (8.6)</td>
<td>1.54 (1.12-2.14)</td>
</tr>
</tbody>
</table>

AA 277 (28.0) | 323 (27.9) | 1.11 (0.87-1.42) |
| AA 103 (11.3) | 91 (8.6) | 1.54 (1.12-2.14) |
| AA 277 (28.0) | 323 (27.9) | 1.11 (0.87-1.42) |

CT 132 (13.4) | 198 (17.8) | 1.00 (ref.) |
| CC 374 (37.9) | 398 (35.8) | 1.40 (1.01-1.82) |
| CT 856 (86.6) | 914 (82.2) | 1.39 (1.09-1.77) |

TT 277 (28.0) | 323 (27.9) | 1.11 (0.87-1.42) |
| CC 374 (37.9) | 398 (35.8) | 1.40 (1.01-1.82) |
| CT+CC 856 (86.6) | 914 (82.2) | 1.39 (1.09-1.77) |

GTA 183 (18.6) | 248 (22.8) | 1.00 (ref.) |
| GTA 513 (52.2) | 524 (48.2) | 1.30 (1.03-1.63) |
| GTA 799 (81.4) | 839 (77.2) | 1.29 (1.04-1.60) |

Discussion

Our results suggest that genetic polymorphisms of ATM may play an important role in the development of breast cancer in Korean women, particularly in premenopausal women. The compositions of ATM haplotypes between cases and controls were significantly different, and some specific ATM haplotypes were associated with increased risk of breast cancer.

*Adjusted for age, education, family history of breast cancer, age at FFTP and parity, alcohol consumption, and smoking.
The association between intronic SNPs and breast cancer risk found in the present study is consistent with the result of a previous study, in which the tightly linked ATM polymorphisms IVS22–77T>C and IVS48+238C>G in the homozygous state were associated with increased breast cancer risk (15). On the other hand, Bretsky et al. (14) evaluated the association between 20 missense SNPs of ATM in exon regions and breast cancer risk and found that only one variation (L546V) was associated with the high-stage breast cancer among the African-American subgroup.

All five polymorphic sites in this study located in noncoding region might influence the splicing process as the IVS10–6T>G does. The IVS10–6G mutation was shown to lead to incorrect splicing of exon 11 and to exon skipping, resulting in a frame shift and subsequent truncation of the protein at amino acid residue 419 (12). From the results for each genotype, the IVS21+1049C>T allele seemed to be the most critical among the five polymorphic sites. However, there is the possibility that (an)other critical variation(s) might exist in the state of tight linkage disequilibrium with the five SNPs in this study, and thus the five sites may just be the proxies of that site(s). Despite this possibility, the fact that relatively rare alleles were more common in the cases than in the controls supports the hypothesis that these ATM variants are associated with breast cancer risk.

Pairwise linkage disequilibrium (D') among the five polymorphisms of ATM genotyped in this study was very high (D' > 0.8). This result is also consistent with the results from studies by Bonnen et al. (18) and Thorstenson et al. (19), in which they reported that 14 and 17 biallelic variants showed similar extensive linkage disequilibrium at the ATM locus, respectively.

Remarkable differences were found in allele frequencies between Korean (−5144A, 0.48; IVS21+1049T, 0.41; IVS33–55T, 0.46; IVS34+60G, 0.47; and 3393T>G) and Caucasians (0.33, 0.66, 0.66, 0.66, and 0.64, respectively), African or African American, Hispanic, and Pacific Rim [http://snp500cancer.nci.nih.gov/home.cfm]. These results confirm the ethnic diversity in genetic composition. Bretsky et al. (14) also found a wide variation in the frequencies of 20 missense SNPs across diverse ethnic groups (i.e., African American, Latino, Japanese, and Caucasian).

Most previous association studies focused on rare mutations or polymorphisms with low allele frequencies (less than 10%) of ATM (11-14, 16) or conducted with moderate sample sizes (15). Therefore, those studies might have limited power to detect the increasing or decreasing effect of genetic variants in ATM on the risk of breast cancer. All studies (11-16) except for one (14) have been conducted in Caucasians. Also, all previous association studies except for Spurdle et al. (17) have not considered nongenetic risk factors (i.e., the results of genetic factors were not adjusted for other covariates as we did in the present study).

The advantages of this study include the high frequencies of SNP studied (about 50%) and large sample size (991 cases and 1,181 controls). The validity of haplotype or diplotype analysis in this study is supported by the relatively high repeatability of genotype data (>96%) and the minimal ambiguity for most of haplotype data (precision ≥ 0.95). The failure of concordance under undetermined genotyping and the haplotype was not estimated when at least one missing value for genotype data exists in this study. Thus, we expect bias in the concordance.

### Table 3. The distributions of haplotypes in cases and controls

<table>
<thead>
<tr>
<th>Haplotype*</th>
<th>All women</th>
<th>Premenopausal women</th>
<th>Postmenopausal women</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case, N (%)</td>
<td>Control, N (%)</td>
<td>P (χ² test)</td>
</tr>
<tr>
<td>TCCAG</td>
<td>990 (50.7)</td>
<td>1,090 (50.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ATTGG</td>
<td>668 (34.2)</td>
<td>839 (38.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACTGT</td>
<td>125 (6.4)</td>
<td>129 (6.0)</td>
<td>11.9</td>
</tr>
<tr>
<td>ATCGT</td>
<td>43 (2.3)</td>
<td>51 (2.4)</td>
<td>7.0</td>
</tr>
<tr>
<td>TCTAG</td>
<td>33 (1.7)</td>
<td>15 (0.7)</td>
<td>2.0</td>
</tr>
<tr>
<td>ATTGT</td>
<td>125 (6.4)</td>
<td>129 (6.0)</td>
<td>11.9</td>
</tr>
<tr>
<td>Others</td>
<td>57 (2.9)</td>
<td>31 (1.4)</td>
<td>2.0</td>
</tr>
</tbody>
</table>

Total: 1,954 (100) 2,156 (100) 1,146 (100) 594 (100) 1,000 (100)

### Table 4. ATM diplotype and breast cancer risk

<table>
<thead>
<tr>
<th>Haplotype pairs*</th>
<th>All women</th>
<th>Controls, N (%) OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case, N (%)</td>
<td>Control, N (%)</td>
</tr>
<tr>
<td>TCCAG TCCAG</td>
<td>241 (24.7)</td>
<td>282 (26.2)</td>
</tr>
<tr>
<td>TCCAG ATTGT</td>
<td>353 (36.1)</td>
<td>405 (37.6)</td>
</tr>
<tr>
<td>ATTGT ATTGT</td>
<td>119 (12.2)</td>
<td>181 (16.8)</td>
</tr>
<tr>
<td>TCCAG ACTGT</td>
<td>69 (7.1)</td>
<td>69 (6.4)</td>
</tr>
<tr>
<td>ATTGT ACTGT</td>
<td>46 (4.7)</td>
<td>53 (4.9)</td>
</tr>
<tr>
<td>TCCAG ACCAG</td>
<td>16 (1.6)</td>
<td>19 (1.8)</td>
</tr>
<tr>
<td>TCCAG ACGC</td>
<td>19 (1.9)</td>
<td>9 (0.8)</td>
</tr>
<tr>
<td>TCTAG TCTAG</td>
<td>10 (1.0)</td>
<td>7 (0.7)</td>
</tr>
<tr>
<td>ACTGT ACTGT</td>
<td>61 (6.2)</td>
<td>34 (3.2)</td>
</tr>
</tbody>
</table>

Total: 977 (100) 1,078 (100)

### Table 5. Combined diplotypes of ATM (ATTGT) and breast cancer risk

<table>
<thead>
<tr>
<th>Haplotype pairs*</th>
<th>All women</th>
<th>Controls, N (%) OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATTGT ATTGT</td>
<td>119 (12.2)</td>
<td>181 (16.8)</td>
</tr>
<tr>
<td>ATTGT Others</td>
<td>430 (44.0)</td>
<td>477 (44.3)</td>
</tr>
<tr>
<td>Others Others</td>
<td>428 (43.8)</td>
<td>420 (39.0)</td>
</tr>
</tbody>
</table>

P for trend <0.01

*Composed of five polymorphic sites: −5144A>T, IVS21+1049T>C, IVS33–55T>C, IVS34+60G>A, and 3393T>G.

*Adjusted for age, education, alcohol consumption, and smoking.

*Other than ATTGT combination.
rate if the haplotype data should be small. Also, the results of haplotype estimation by expectation maximization methods (EH program) were similar to those by the Bayesian methods adopted in this study.

In conclusion, despite several limitations, such as hospital-based study design and limited numbers of SNPs in the large ATM gene, the results of this study suggest that genetic polymorphisms of ATM might play an important role in the development of breast cancer in Korean women. However, further studies with more comprehensive genotyping and evaluation of genotype-phenotype relationship need to be conducted.

### References


### Appendix 1. Oligonucleotide sequences of PRC primers and probes labeled with FAM or VIC for each polymorphisms

<table>
<thead>
<tr>
<th>SNP Class</th>
<th>5’ Sequence</th>
<th>3’ Concentration (nmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>−5144A&gt;T (rs228589)</td>
<td>1. Primer_S AGG TCC TTC TGT CCA GCA TAG C</td>
<td>600</td>
</tr>
<tr>
<td>2. Primer_AS CCG GCT TGT ATT AGG TAA GC</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>3. TaqMan probe FAM ACC TTC CCT CCC GGT</td>
<td>MGBNFQ 100</td>
<td></td>
</tr>
<tr>
<td>4. TaqMan probe VIC CCC TTC ATC CCG GT</td>
<td>MGBNFQ 100</td>
<td></td>
</tr>
<tr>
<td>IVS21+1049T&gt;C (rs664677)</td>
<td>1. Primer_S TGA CAA ATA AGT TTA GCA CAG AAG GA</td>
<td>600</td>
</tr>
<tr>
<td>2. Primer_AS TTC TGA TAA AAG CAC TCA GAA AAC TCA</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>3. TaqMan probe FAM TGG AAG TAA CTT ACA ATA A</td>
<td>MGBNFQ 100</td>
<td></td>
</tr>
<tr>
<td>4. TaqMan probe VIC TGG AAG TAA CTT ATA ATA AC</td>
<td>MGBNFQ 100</td>
<td></td>
</tr>
<tr>
<td>IVS33+55T&gt;C (rs664982)</td>
<td>1. Primer_S TCA CAG CAT CTA GAG TCA AAC ACA TT</td>
<td>600</td>
</tr>
<tr>
<td>2. Primer_AS TGG TCT AAA GCA AAT AAA AGC AAA GA</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>3. TaqMan probe FAM TGG ACA TCG TAA AGA CTA MGBNFQ</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>4. TaqMan probe VIC TGG AAG TAA CTT ATA ATA AC</td>
<td>MGBNFQ 100</td>
<td></td>
</tr>
<tr>
<td>IVS34+60G&gt;A (rs664143)</td>
<td>1. Primer_S TGA AGC AGT GCT CTT CAC ATC AG</td>
<td>600</td>
</tr>
<tr>
<td>2. Primer_AS AGT GAT GAG AAA CTC TCA GGA AAC TCT</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>3. TaqMan probe FAM TGT CAA CAT ATC TTT ATC T</td>
<td>MGBNFQ 100</td>
<td></td>
</tr>
<tr>
<td>4. TaqMan probe VIC TGT TGT CAA CGT ATC TTT AT</td>
<td>MGBNFQ 100</td>
<td></td>
</tr>
<tr>
<td>3393T&gt;G (rs4585)</td>
<td>1. Primer_S TGG TCT AAA GCA AAT AAA AGC AAA GA</td>
<td>600</td>
</tr>
<tr>
<td>2. Primer_AS CTA TAT TTC AAA CCA ATA TAC TGG TTT TCT</td>
<td>600</td>
<td></td>
</tr>
<tr>
<td>3. TaqMan probe FAM TGG ACA TCG TAA AGA CTA</td>
<td>MGBNFQ 100</td>
<td></td>
</tr>
<tr>
<td>4. TaqMan probe VIC TTT GGA CAG CGT AAA GA</td>
<td>MGBNFQ 100</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: MGBNFQ, minor groove binder non-flourescence quencher.
Genetic Polymorphisms of Ataxia Telangiectasia Mutated and Breast Cancer Risk

Kyoung-Mu Lee, Ji-Yeob Choi, Sue Kyung Park, et al.


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