N-Acetyltransferase-2 Genetic Polymorphism, Well-done Meat Intake, and Breast Cancer Risk among Postmenopausal Women

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Abstract

Heterocyclic amines found in well-done meat require host-mediated metabolic activation before initiating DNA mutations and tumors in target organs. Polymorphic N-acetyltransferase-2 (NAT2) catalyzes the activation of heterocyclic amines via O-acetylation, suggesting that NAT2 genotypes with high O-acetyltransferase activity (rapid/intermediate acetylator phenotype) increase the risk of breast cancer in women who consume well-done meat. To test this hypothesis, DNA samples and information on diet and other breast cancer risk factors were obtained from a nested case-control study of postmenopausal women. Twenty-seven NAT2 genotypes were determined and assigned to rapid, intermediate, or slow acetylator groups based on published characterizations of recombinant NAT2 allozymes. NAT2 genotype alone was not associated with breast cancer risk. A significant dose-response relationship was observed between breast cancer risk and consumption of well-done meat among women with the rapid/intermediate NAT2 genotype (trend test, P = 0.003) that was not evident among women with the slow acetylator genotype (trend test, P = 0.22). These results suggest an interaction between NAT2 genotype and meat doneness, although a test for multiplicative interaction was not statistically significant (P = 0.06). Among women with the rapid/intermediate NAT2 genotype, consumption of well-done meat was associated with a nearly 8-fold (odds ratio, 7.6; 95% confidence interval, 1.1–50.4) elevated breast cancer risk compared with those consuming rare or medium-done meats. These results are consistent with a role for O-acetylation in the activation of heterocyclic amine carcinogens and support the hypothesis that the NAT2 acetylation polymorphism is a breast cancer risk factor among postmenopausal women with high levels of heterocyclic amine exposure.

Introduction

Heterocyclic amines, such as PhIP, 2-amino-3-methylimidazo[4,5-f]quinoline, and 2-amino-3,4-dimethylimidazo[4,5-f]quinoline, which are formed when meat is cooked at high temperatures until well done, induce mammary gland tumors in the rat (1–3). The consumption of well-done meat has been associated with an elevated risk of human breast cancer in some but not all epidemiological studies (4). Heterocyclic amine carcinogens require host-mediated metabolic activation before initiating DNA mutations that progress to tumors in target organs (3). N-Acetyltransferases catalyze the activation (O-acetylation) of heterocyclic amine carcinogens (5–8) and are subject to genetic polymorphism (9). The NAT2 polymorphism is very common in the human population, and individuals can be subdivided into rapid, intermediate, and slow acetylator phenotypes (9, 10).

Studies investigating the relationship between NAT2 acetylator polymorphism and breast cancer have yielded mixed results. NAT2 acetylator phenotype was not associated with breast cancer in three studies (11–13). However, other studies have suggested that the rapid NAT2 acetylator phenotype is associated with breast cancer risk (14–16) or advanced disease at first presentation (17). Part of the inconsistency may be due to the fact that NAT2 phenotyping assays were performed after cancer diagnosis and/or treatment, and disease status or its sequelae may alter acetylation rate. Furthermore, none of these studies took into consideration the potential modifying effects of heterocyclic amine exposure.

Recent breast cancer studies have used NAT2 genotyping assays to assign acetylation status of study participants (18). Genotype, unlike acetylator phenotype determination, is not influenced by age, diet, disease state, environmental chemical exposures, or concurrent drug therapy. These studies assessed three (19–22), four (23, 24), or six (25) SNPs within the NAT2 coding region.

Twenty-six NAT2 alleles had been identified in human...
populations when this study was initiated (9, 26). The “wild-
type” allele is denoted as NAT2*4. The other 25 alleles
possess a combination of one to four SNPs at 11 sites within
the 870-bp coding region. Seven SNPs result in amino acid
changes (G191A, T341C, A434C, G590A, A803G, A845C,
and G857A), whereas four do not (T111C, C282T, C481T,
C759T). Based on prokaryotic recombinant enzyme expres-
sion data, 5 NAT2 alleles (NAT2*4, NAT2*12A, NAT2*12B,
NAT2*12C, and NAT2*13) encode proteins with a high
(rapid) O-acetylation capacity toward N-hydroxy amines,
whereas the other NAT2 alleles encode proteins with reduced
capacity (8, 27). Allelic frequency varies with ethnicity (9),
but approximately 50% of Caucasians are rapid/intermediate
acetylators (10).

Many studies examining the joint effects of heterocyclic
amine exposure and enzyme polymorphisms have focused on
colorectal cancer. High meat intake and consumption of fried
meats have been associated with colorectal cancer among rapid
NAT2 acetylators (28–31). However, many heterocyclic
amines are mammary carcinogens, and, in a recent study (32),
we found that another N-acetyltransferase polymorphism
(NAT1) was associated with breast cancer risk in individuals
who consumed consistently well-done meat. This study was
undertaken to investigate whether the NAT2 polymorphism is
associated with breast cancer risk and whether consumption of
well-done meat modifies this risk.

Materials and Methods

Subjects. Human DNA samples were obtained from the nested
case-control study of the Iowa Women’s Health Study, a pro-
spective cohort of 41,836 women, virtually all Caucasian, aged
55–69 years at the 1986 baseline survey. Cohort members have
been followed since 1986 for mortality and cancer incidence.
Detailed descriptions of this cohort study and the nested case-
control study have been published elsewhere (4, 32–35).
Briefly, cohort members diagnosed with breast cancer between
1992 and 1994 were classified as cases (n = 456), and a random
sample of cohort members who were cancer free in 1992 were
classified as controls (n = 876). Each eligible subject (n = 1332)
was asked to complete a food frequency questionnaire
about meat intake habits during the year prior to breast cancer
diagnosis or, for controls, during one of three randomly as-
signed reference years (1991, 1992, or 1993). The questionnaire
assessed usual intake and preparation methods of 15 different
meats. Using a series of color photographs, information on meat
doneness level was obtained for hamburger, beef steak, and
bacon. Of the 930 women who completed this supplementary
survey and to derive adjusted OR and 95% CIs. Because none
lowed by 35 cycles of 1 min at 94°C, 1 min at 55°C, and 1 min
at 72°C, and a 5-min extension step at 72°C.

G191A, A434C, and C481T were detected by digesting 15
µl of the NAT2 PCR product at 37°C (3 h) in a total volume of
30 µl with restriction enzymes Mspl (10 units) and KpnI (5
units) in NEBuffer 1 (New England Biolabs, Beverly, MA)
supplemented with 100 µg/ml BSA. G191A causes loss of a
Mspl site, yielding bands of 416, 384, and 66 bp, whereas
A434C adds an additional Mspl site, yielding bands of 416,
244, 93, 66, and 47 bp. C481T results in loss of the
KpnI restriction site, yielding fragments of 707, 93, and 66 bp.
When neither allele contains G191A, A434C, or C481T, 416–,
291, and 66-bp bands result. T111C, G590A, C759T, and
G857A were distinguished after digestion of the NAT2 PCR
product with TaqI (10 units) and BamHI (10 units) at 37°C (3 h)
followed by 65°C (3 h) in NEBuffer 1 (New England Biolabs)
supplemented with 100 µg/ml BSA. T111C adds a
TaqI restriction site, resulting in 252-, 226-, 170-, 98-, 80-,
and 40-bp fragments. G590A and C759T delete TaqI restriction
sites, yielding bands of 396, 332, 98, and 40 bp and 332, 268,
226, and 40 bp, respectively. G857A causes loss of the
BamHI restriction site, yielding 332–, 226–, 170–, and 138-bp bands.

When neither allele contains T111C, G590A, C759T, or
G857A, 332–, 226–, 170–, 98–, and 40-bp bands result. C828T
and A845C were detected by digesting PCR-amplified NAT2
with the restriction enzymes FokI (2 units) and DraIII (1.5
units) at 37°C (3 h) in NEBuffer 3 (New England Biolabs)
supplemented with 100 µg/ml BSA. C828T causes loss of a
FokI site, yielding bands of 667 and 199 bp. A845C adds a
DraIII site, resulting in 429–, 238–, 153–, and 46-bp bands.
When neither allele contains C828T or A845C, 249-, 199-, and
199-bp fragments result.

T341C and A803G were detected with nested PCR reactions.
One µl of amplified NAT2 was used as the template in a 20-µl
reaction containing 10 mM Tris-Cl (pH 8.3), 50 mM KCl, 1.5 mM
MgCl2, 0.2 mM of each deoxynucleotide triphosphate, 220 ng
of primer 5′-CACCCTTCCTGAGGTCGAG-3′ and primer 5′-
TGTCACAGCAAGAAATGCAAGG-3′ or 240 ng of primer
5′-TGAAGAGAGGTGAAAGATGCT-3′ and 290 ng of 5′-
AAGGGTTTATTTTGTTCCTTATTCTAAAT-3′, respectively,
and 0.5 unit of Taq DNA polymerase (bold indicates the nucleo-
tide change made in the primer sequence to generate a partial AcII
restriction site, which is underlined.) The mixture was pretreated
at 94°C for 5 min, followed by 30 cycles of 30 s at 94°C, 30 s at
58°C, and 30 s at 72°C, and a 5-min extension step at 72°C.

To distinguish between C341 and T341, 20 µl of the
nested PCR product were digested at 37°C (3 h) in a total volume of
35 µl with 5 units of AcII in NEBuffer 3 (New England Biolabs).
Samples homozygous for T341C yield bands of 121 and 20 bp instead of 141 bp. A803G was detected after
digestion of the nested PCR product with the restriction enzyme
DdeI (10 units) as described above for AcII. When both alleles
contain A803G, the 120-bp band was cut into 97- and 23-bp fragments.

Statistical Analysis. Individuals possessing two NAT2 alleles
associated with high acetylation activity (NAT2*4, NAT2*12A,
NAT2*12B, NAT2*12C, and NAT2*13) were classified as rapid
acetylators; individuals with one of these alleles were classified
as intermediate acetylators, and individuals possessing none of
these alleles were identified as slow acetylators. ORs were used to
measure the strength of the association between exposures
and cancer risk. Unconditional logistic regression was used to
control for potential confounders assessed at the 1986 baseline
survey and to derive adjusted OR and 95% CIs. Because none

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of the previously identified breast cancer risk factors contributed the association between NAT2 genotype and breast cancer, only age was adjusted in the model. Trend tests for dose-response relationships were performed by treating ordinal-score variables as continuous variables in the logistic regression model. Tests for interaction were based on the difference in the likelihood ratios from models with and without interaction terms of genotype and exposure. Intake levels of red meat were estimated by summing the grams of hamburgers, cheeseburgers, beef steaks, pork chops, bacon, breakfast sausage links and patties, other sausages, bratwurst, and hot dogs consumed. Meat doneness levels were classified as 1, 2, or 3 for rare/medium, well-done, and very well-done meat, respectively. A doneness score was calculated by summing the doneness levels of hamburger, beef steak, and bacon, the three meats for which information on doneness was obtained. Thus, a person who reported consuming very well-done hamburger, beef steak, and bacon received a doneness score of 9.

**Results**

NAT2 amplification was successful in 99% of DNA samples obtained from all 488 blood samples and the 79 buccal samples in which other genes had been successfully amplified. As shown in Table 1, our study subjects (176 cases and 391 controls) were similar to all eligible subjects for most demographic and breast cancer risk factors. Ten of 26 known NAT2 alleles were identified in our Caucasian study population (Table 2). The relative NAT2 allelic frequency was NAT2*5B > NAT2*6A > NAT2*4 > NAT2*5A > NAT2*5C and NAT2*7B in both cases and controls. In contrast, NAT2*13 was present in seven controls but was absent in cases. NAT2*14 alleles were rare in both cases and controls, as was expected in the Caucasian population. Twenty-seven different NAT2 genotypes were determined (Table 3) and assigned to slow, intermediate, and rapid acetylator groups based on recombinant expression of NAT2 allozymes (8). NAT2 genotype frequencies were similar between cases and controls, although the most frequent NAT2 genotype in cases was NAT2*4/*5B (an intermediate acetylator genotype), whereas it was NAT2*5B/*6A (a slow acetylator genotype) in the controls. The relative frequencies of slow, intermediate, and rapid genotypes were similar between cases (52.9%, 41.4%, and 5.7%) and controls (55.0%, 39.0%, and 5.9%).

In stratified analyses (Table 4), meat doneness score was associated with an elevated risk of breast cancer in a dose-dependent manner among women with rapid/intermediate NAT2 genotype (P = 0.003) but not among women with the slow NAT2 genotype (P = 0.22). These results suggest an interaction between NAT2 genotype and meat doneness, although a test for interaction based on a multiplicative model was not statistically significant (P = 0.06). Breast cancer risk appeared to increase with level of meat intake in women with rapid/intermediate acetylator genotype, but the trend was not significant (P = 0.11). Meat intake level was not associated with breast cancer risk in the slow NAT2 acetylator genotype group (trend test, P = 0.30).

To enhance the stability of risk estimates for the association between breast cancer risk and meat doneness score stratified by both genotype and breast cancer risk factors, we applied a multiplicative model.
identified by NAT2 genotypes, the doneness level was collapsed into three groups (Table 5). Compared with women who consumed consistently rare or medium-done meat, breast cancer risks were elevated with increasing meat doneness, particularly among women with the rapid/intermediate NAT2 genotype (P < 0.01). A similar pattern was found in analyses stratified by cigarette smoking, indicating that smoking is unlikely to explain the observed association.

**Discussion**

Metabolic activation of carcinogenic heterocyclic amines is a multistep process catalyzed by both phase I and phase II enzymes. One working hypothesis suggests initial N-oxidation by hepatic CYP1A2 (38, 39), followed by transport of the hydroxy-heterocyclic amine to tumor target organs, where it undergoes O-acetylation catalyzed by N-acetyltransferase(s) that ultimately leads to DNA adducts and mutations (9, 40, 41). This hypothesis suggests that, compared with women with the slow NAT2 genotype, women with the rapid/intermediate NAT2 genotype may more readily activate heterocyclic amines present in well-done meat to reactive metabolites that initiate DNA adducts and tumors. An alternative hypothesis suggests that activation occurs in situ because CYP1B1 and CYP1A1 are expressed in human mammary cells and can metabolize PhIP to N-hydroxy-PhIP (42–44). Regardless of whether N-hydroxy-PhIP is formed in the liver, mammary gland, or both, it undergoes further activation (via O-acetylation) by all known human NAT2 allozymes (5, 7, 27). In addition to acetyltransferases, the human mammary gland may activate dietary mutagens by prostaglandin hydroperoxidase(s) (41). Additional studies investigating the relative contribution of each of these and other enzyme systems are needed.

**NAT2 Polymorphism and Breast Cancer Risk**

### Table 3 Distribution of NAT2 genotype among incident breast cancer cases and controls

<table>
<thead>
<tr>
<th>NAT2 genotype</th>
<th>Cases (n = 174)</th>
<th>Controls (n = 387)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percentage</td>
</tr>
<tr>
<td>Slow acetylator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NAT2*5A/*5A</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>NAT2*5A/*5B</td>
<td>7</td>
<td>4.0</td>
</tr>
<tr>
<td>NAT2*5B/*5B</td>
<td>28</td>
<td>16.1</td>
</tr>
<tr>
<td>NAT2*5B/*5C</td>
<td>2</td>
<td>1.2</td>
</tr>
<tr>
<td>NAT2*5B/*5D</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>NAT2*5A/*6A</td>
<td>4</td>
<td>2.3</td>
</tr>
<tr>
<td>NAT2*5B/*6A</td>
<td>32</td>
<td>18.4</td>
</tr>
<tr>
<td>NAT2*5C/*6A</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NAT2*5A/*7B</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NAT2*5B/*7B</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NAT2*6A/*6A</td>
<td>16</td>
<td>9.2</td>
</tr>
<tr>
<td>NAT2*6A/*7B</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>NAT2*7B/*14B</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total slow acetylator</td>
<td>92</td>
<td>52.9</td>
</tr>
<tr>
<td>Intermediate acetylator</td>
<td>52</td>
<td>30.1</td>
</tr>
<tr>
<td>NAT2*4/*5A</td>
<td>5</td>
<td>2.9</td>
</tr>
<tr>
<td>NAT2*4/*5B</td>
<td>34</td>
<td>19.5</td>
</tr>
<tr>
<td>NAT2*4/*5C</td>
<td>2</td>
<td>1.2</td>
</tr>
<tr>
<td>NAT2*4/*6A</td>
<td>27</td>
<td>15.5</td>
</tr>
<tr>
<td>NAT2*4/*7B</td>
<td>3</td>
<td>1.7</td>
</tr>
<tr>
<td>NAT2*5B/*12A</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NAT2*6A/*12A</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>NAT2*5B/*13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NAT2*6A/*13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>NAT2*7B/*13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total intermediate acetylator</td>
<td>72</td>
<td>41.4</td>
</tr>
<tr>
<td>Rapid acetylator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NAT2*4/*4</td>
<td>9</td>
<td>5.2</td>
</tr>
<tr>
<td>NAT2*4/*12A</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>NAT2*4/*13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total rapid acetylator</td>
<td>10</td>
<td>5.7</td>
</tr>
</tbody>
</table>

*(Participants with genotype/total cases or controls) × 100.

### Table 4 Adjusted ORs for the association of breast cancer risk with well-done meat intake stratified by NAT2 genotype

<table>
<thead>
<tr>
<th>Meat doneness score</th>
<th>Cases/controls OR (95% CI)</th>
<th>Cases/controls OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 and 4</td>
<td>24/71 1.0 (reference)</td>
<td>13/65 1.0 (reference)</td>
</tr>
<tr>
<td>5</td>
<td>20/51 1.2 (0.6–2.3)</td>
<td>25/39 3.2 (1.5–7.0)</td>
</tr>
<tr>
<td>6</td>
<td>26/26 3.0 (1.4–6.1)</td>
<td>17/28 3.0 (1.3–7.0)</td>
</tr>
<tr>
<td>7</td>
<td>5/33 4.4 (0.2–13)</td>
<td>12/19 3.0 (1.2–7.7)</td>
</tr>
<tr>
<td>8</td>
<td>3/4 2.2 (0.5–10.8)</td>
<td>4/5 4.0 (0.9–17.0)</td>
</tr>
<tr>
<td>9</td>
<td>4/3 3.9 (0.9–18.9)</td>
<td>3/2 7.6 (1.1–50.4)</td>
</tr>
<tr>
<td>Trend test</td>
<td>P = 0.22</td>
<td>P = 0.003</td>
</tr>
<tr>
<td>Test for interaction</td>
<td>P = 0.06</td>
<td></td>
</tr>
</tbody>
</table>

### Table 5 Association of well-done meat intake and breast cancer risk stratified by NAT2 genotype and cigarette smoking

<table>
<thead>
<tr>
<th>Study participants</th>
<th>Meant Test for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–4</td>
<td>24/71 1.0 (reference)</td>
</tr>
<tr>
<td>5</td>
<td>20/51 1.2 (0.6–2.3)</td>
</tr>
<tr>
<td>6–9</td>
<td>38/66 1.7 (0.9–3.1)</td>
</tr>
<tr>
<td>Trend test</td>
<td>P = 0.154</td>
</tr>
<tr>
<td>Test for interaction</td>
<td></td>
</tr>
</tbody>
</table>

### Adjusted for age.

### Adjusted for tertile.
of the samples in our study would have been assigned an incorrect NAT2 genotype using an assay that detects only three SNPs. The frequency of the major NAT2 alleles in our controls was very similar to that observed in a large Caucasian (i.e., German) population (48). However, NAT2 allelic frequency varies with ethnicity (9), and this may also account for the disparity between studies.

A study reporting that NAT2 activity was below the limit of detection in human mammary cytosols (40) suggests that NAT2 may not be important for in situ activation of N-hydroxy-heterocyclic amines. However, a role for NAT2 is supported by studies reporting detection of NAT2 mRNA in human mammary cells (40, 49), as well as by studies that found higher levels of NAT2 activity (50) and N-hydroxy-PhIP metabolic activation (51) in mammary cytosols from rapid NAT2 acetylator rather than slow NAT2 acetylator congenic Syrian hamsters. In addition, in recombinant NAT2 studies have shown that human NAT2 has a higher selectivity for some N-hydroxy-heterocyclic amines, including PhIP, than does NAT1 (5, 7).

Finally, human mammary cells from rapid NAT2 acetylators exhibit higher levels of heterocyclic amine DNA adducts than cells derived from slow acetylators (52). Each of these findings is consistent with the results from our study suggesting that women with the rapid/intermediate NAT2 acetylator genotype activate heterocyclic amines to DNA-adducting metabolites to a greater extent than do women with the slow NAT2 acetylator genotype. In summary, our results suggest that the NAT2 polymorphism may be a breast cancer risk factor among women exposed to heterocyclic amines through the consumption of well-done meat. The findings should be interpreted with caution, due to the limitations of our study. Although our results suggest an interaction between rapid/intermediate NAT2 genotype and meat doneness, a test for interaction based on a multiplicative model was not statistically significant. Another consideration may be the low response rate for blood sample collection and the low amplification rate of buccal DNA. There is little reason, however, to suspect that these rates would be associated with both case-control status and NAT2 genotype. As shown in Table 1, our study subjects were similar to all eligible subjects in the associations of breast cancer risk with well-done meat intake and in virtually all other breast cancer risk factors. The high comparability between study participants and nonparticipants strongly suggests that potential selection bias in our study, if any, is unlikely to be substantial. The sample size of 174 cases and 387 controls is small, limited to Caucasians in Iowa, and heterocyclic amine exposure was determined indirectly via dietary survey. Because the dietary information was obtained retrospectively, problems of differential recall between cases and controls in this cohort are possible. Nevertheless, the results of this study, in addition to our recent study investigating the NAT1 acetylation polymorphism and well-done meat consumption in breast cancer risk (32), provide mechanistic support for the role of well-done meat consumption in breast cancer risk (4).

These results, as well as additional gene-gene-environmental interactions, need to be confirmed in studies with a larger sample size and other ethnic populations.

Acknowledgments

We thank Dr. R. Sinha for help in developing the meat section of the food frequency questionnaire and for providing copies of food photographs for assessing meat doneness level. The food frequency questionnaire used in the study was modified from one developed by Drs. R. Sinha and K. Anderson. We thank Drs. D. Campbell, J. Cerhan, W. Otting, L. Kush, K. Anderson, and T. Sellers for their contributions to the Iowa Women’s Health Study.

References


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