

## *Null Results in Brief*

# A Prospective Study of Cytochrome P450 1A1 Polymorphisms and Colorectal Cancer Risk in Men<sup>1</sup>

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### Introduction

Positive associations with increased red meat intake and colorectal cancer have been reported consistently (1), particularly with the consumption of broiled and grilled meats (2). This may be attributable to PAH<sup>4</sup> formation. Cigarette smoking is another source of PAH exposure, and an association of early onset of smoking with adenomatous polyps (3), and less consistently, with colon cancer has been reported (3, 4).

*CYP1A1* codes for a protein (5) that converts PAHs to their ultimate DNA-binding forms. The only published study on the association between *CYP1A1* and colorectal cancer risk reported a 7-fold increase in *in situ* colorectal cancer risk for the *MspI* variant genotype among Asians but not in Caucasians (6).

In this prospective study, we tested whether Caucasian men with the variant *CYP1A1* genotypes are at increased risk of developing colorectal cancer and whether the associations of red meat intake and smoking with colorectal cancer were modified by *CYP1A1*.

### Materials and Methods

The 212 cases and 221 controls in this report have been described previously (7). *CYP1A1-MspI* and *exon 7* genotypes were identified by PCR-RFLP methods described previously (5, 8). Conditional logistic regression models were used to estimate the association of potential risk factors such as red meat consumption, physical activity, body mass index (kg/m<sup>2</sup>), and alcohol intake with colorectal cancer. Red meat intake was estimated by combining consumption of the three main meat items on the questionnaire: hot dogs, beef in sandwiches, and beef as a main dish. To calculate ORs and 95% CIs, heterozygous and homozygous variant individuals were combined to form the “high-risk” group. In addition to

the matching variables, body mass index, physical activity, alcohol intake, and red meat consumption were included. Interactions between dietary and other lifestyle variables with the *CYP1A1* genotypes were assessed by using the likelihood ratio test by comparing the model with indicator variables for the cross-classified variables to the reduced model with indicator variables for the main effects only.

### Results

Except for pipe smoking, none of the variables were significantly associated with colorectal cancer risk. Red meat intake was observed to be a risk factor for colorectal cancer among cases  $\geq 60$  years of age (7). Neither polymorphism was associated with colorectal cancer risk (Table 1), with or without adjustment for potential confounders. *CYP1A1* polymorphisms did not modify the associations between colorectal cancer and cigarette smoking or red meat intake.

### Discussion

In this prospective study of Caucasian men, we did not observe an association between these *CYP1A1* genotypes and *in situ* colorectal cancer. Sivaraman *et al.* (6) reported an increase in colorectal cancer risk with the variant polymorphisms among individuals of Asian descent only. These findings are similar to those observed between *CYP1A1* and lung cancer, where associations have been reported in Asian populations but not in Caucasian (5, 9). Given power limitations, these estimates do not exclude modest associations between these polymorphisms and colorectal cancer risk.

The modest red meat effect overall may be attributable to an insufficient variation in red meat intake in this cohort. Red meat intake was a risk factor for colorectal cancer among older cases, similar to that observed in the prospective Health Professionals' Follow-up Study.<sup>5</sup> Environmental exposures may have a greater effect among older individuals because of longer exposure time. Nonetheless, we did not observe any effect modification by *CYP1A1* genotype of this association with red meat. Because of the absence of information on cooking methods, frequency of red meat intake may be a relatively poor surrogate for dietary PAH exposure. Further study involving a larger number of individuals is warranted, particularly in populations with higher allele prevalence (*i.e.*, Asians).

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<sup>4</sup> The abbreviations used are: PAH, polyaromatic hydrocarbon; OR, odds ratio; CI, confidence interval.

<sup>5</sup> E. Giovannucci, personal communication.

Table 1 Association between colorectal cancer risk and *CYP1A1* polymorphisms

	<i>n</i>	<i>Msp</i> 1			Adjusted <sup>a</sup> OR (95% CI)
		WT/WT	WT/Var	Var/Var	
Controls	221	169 (76.5%)	47 (21.3%)	5 (2.2%)	1.00 (ref)
Cases	211	170 (80.6%)	37 (17.5%)	4 (1.9%)	0.79 (0.49–1.28) <sup>b</sup>
	<i>n</i>	Exon 7			Adjusted <sup>a</sup> OR (95% CI)
		WT/WT	WT/Var	Var/Var	
Controls	221	186 (84.2%)	31 (14.0%)	4 (1.8%)	1.00 (ref)
Cases	212	176 (83.0%)	31 (14.6%)	5 (2.4%)	1.08 (0.65–1.80)

<sup>a</sup> Logistic regression adjusted for the matching variables of age and smoking history at baseline.

<sup>b</sup> Estimates calculated by combining both heterozygotes and homozygous variant individuals in comparison to homozygous wild-type subjects.

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