

# TITLE

**Relationship Between TOMM40  
and APOE Genotypes in the  
Wisconsin Registry for  
Alzheimer's Prevention**

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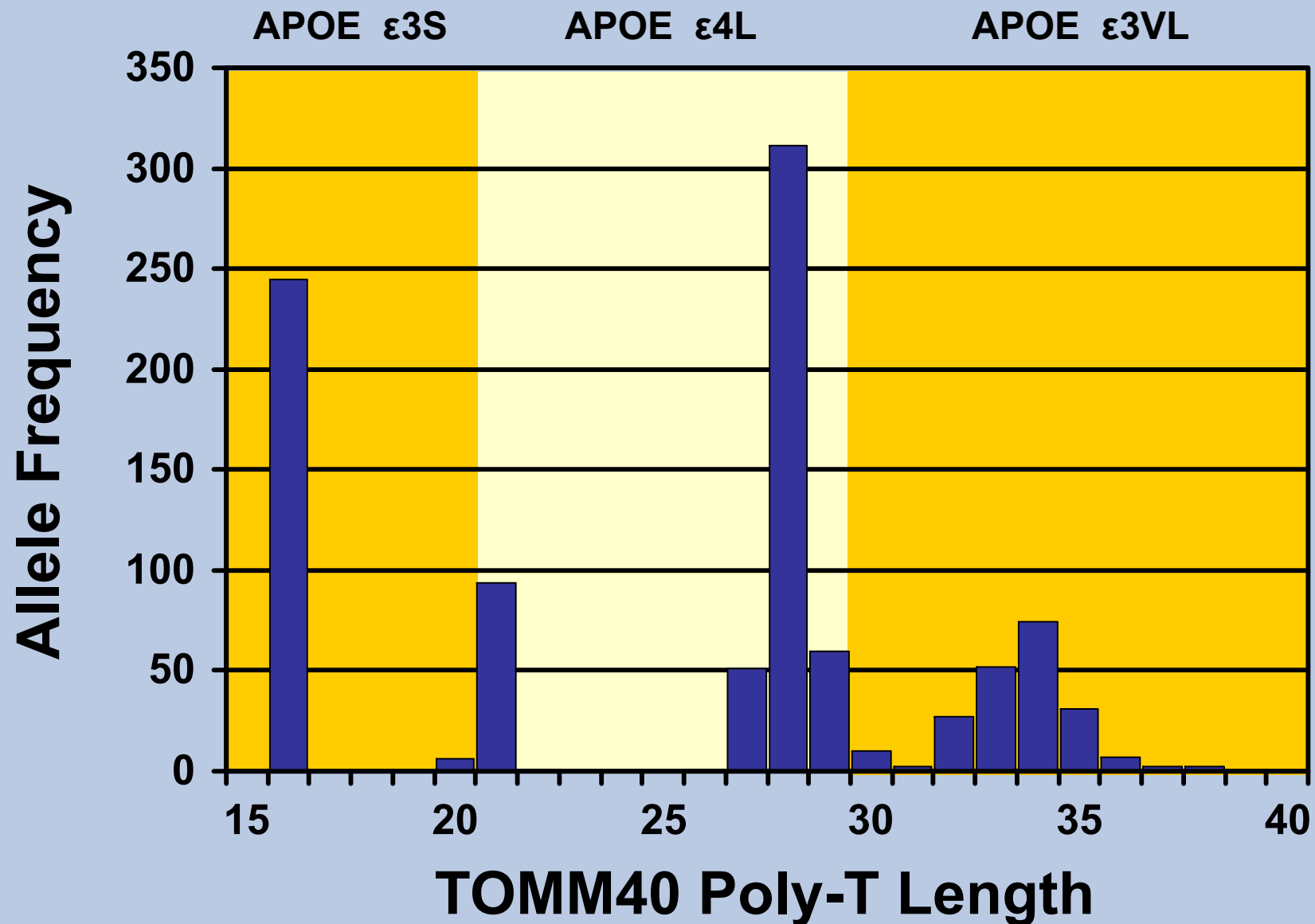
# BACKGROUND

The TOMM40 gene is a poly thymine (T) repeat located within intron 6 of chromosome 19 and is inherited with APOE. Studies have implicated a role for TOMM40 in Alzheimer's disease (AD) pathogenesis, but these studies are few in number and have involved small sample sizes. For this reason, little is known about the relationship between TOMM40 poly T length and APOE genotypes. The purpose of this study is to better define this relationship in a large sample enriched with parental history of AD.

# METHODS

1,318 asymptomatic middle-aged adults with both TOMM40 and APOE genotyping enrolled in WRAP were eligible for this study. 71% of the study population had a parental history of AD, 70% were female, 94% were non-Hispanic Caucasian and 40% possessed at least one APOE  $\epsilon$ 4 allele. TOMM40 and APOE genotyping were performed by Polymorphic DNA Technologies, Alameda, CA. Poly T lengths were classified as short (<20), long (20-30) or very long (>30) as in Lutz et al., 2010.

# Figure 2. TOMM40 Poly T Lengths for APOE $\epsilon$ 4 Carriers

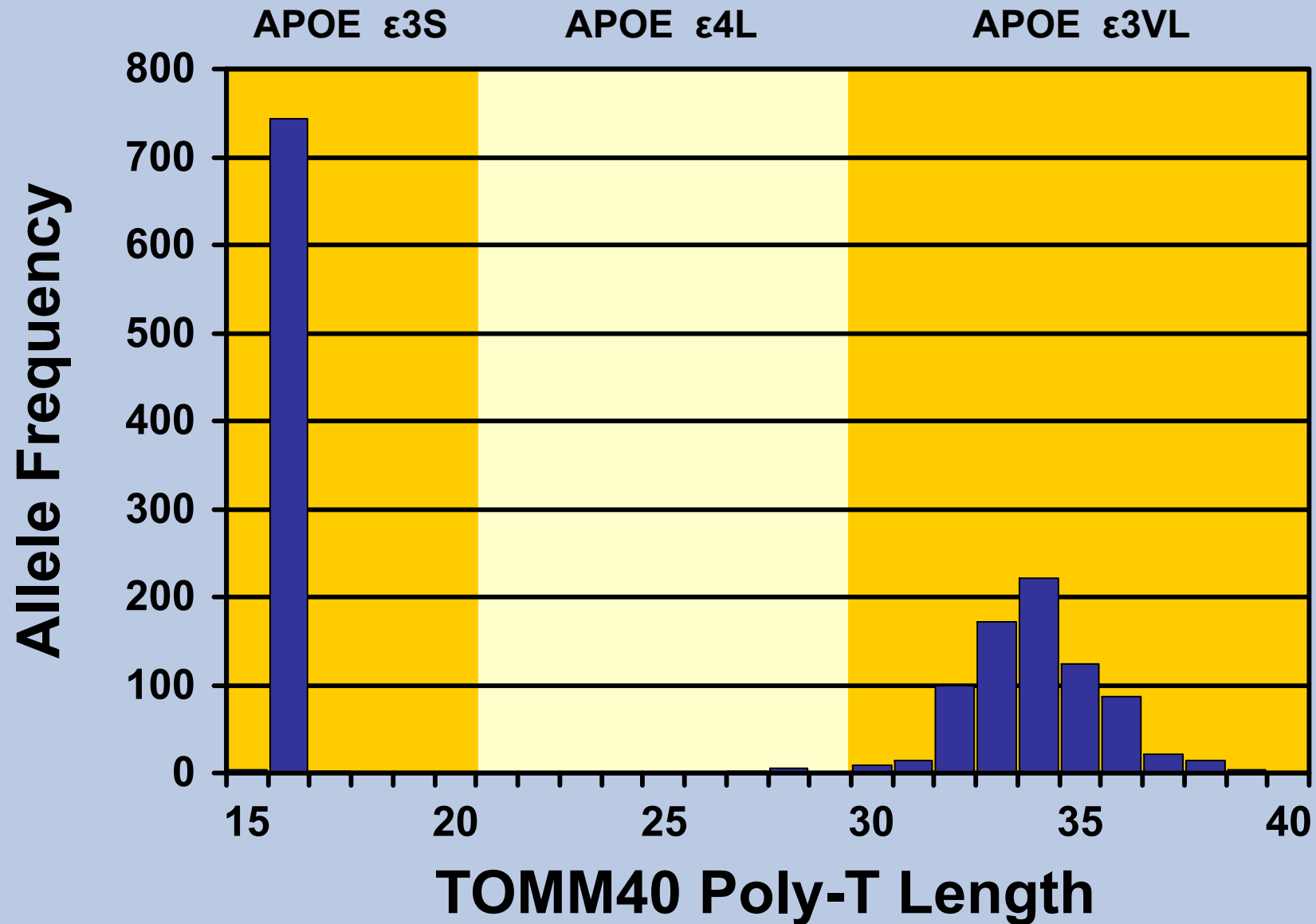




# TOMM40 Poly T Lengths in APOE $\epsilon$ 4 Carriers and Noncarriers

TOMM40	APOE $\epsilon$ 4- N (%)	APOE $\epsilon$ 4+ N (%)
S/S	183 (24)	4 (2)
S/L	3 (<1)	229 (47)
S/VL	379 (50)	15 (3)
L/L	0 (0)	51 (10)
L/VL	4 (1)	187 (38)
VL/VL	191 (25)	3 (1)
Total N (%)	760 (100)	489 (100)

# Figure 1. TOMM40 Poly T Lengths for APOE $\epsilon$ 4 Noncarriers





# RESULTS

- Among non-Hispanic Caucasians without an  $\epsilon 4$  allele, poly T lengths were bi-modally distributed, either  $<20$  or  $>30$  with few exceptions. See Figure 1.
- For non-Hispanic Caucasians with an  $\epsilon 4$  allele, poly T lengths for  $\epsilon 4$  alleles were uniformly between 20 and 30 with 8% of poly T lengths between 20 and 22 and 92% between 27 and 30. See Figure 2.

# RESULTS

- Poly T lengths associated with APOE genotypes did not vary for persons with and without a parental history of AD.
- Poly T lengths for  $\epsilon 4$  alleles in African-Americans were significantly shorter than seen in Caucasians. 43% of  $\epsilon 4$  alleles in African-Americans had a poly T length  $<20$  vs.  $<1\%$  for Caucasians (not shown).

# CONCLUSIONS

These findings are consistent with results reported from smaller samples and with few exceptions, indicate a consistent relationship between TOMM40 poly T length and APOE genotype for non-Hispanic Caucasians. The presence of two distinct poly T lengths (20-22 and 27-30) in persons with  $\epsilon 4$  alleles has not previously been reported. The biologic significance of TOMM40 poly T length in persons with different APOE genotypes remains to be determined.

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