Multi-site Evaluation of the AmplideX® PCR/CE TOMM40 Kit (RUO) for Rapid and Accurate Genotyping of Poly-T Length Polymorphisms at rs10524523 of the TOMM40 Gene

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Introduction

There is increasing interest in identifying Alzheimer’s disease (AD) populations that can benefit from early intervention. Poly-T polymorphisms at rs10524523 (‘523) of the TOMM40 gene have been reported to influence age of onset in late-onset AD (LOAD) and the rate of cognitive decline2. Studies that have examined this locus, 60-80% of all dementias and impacting 5.4M Americans.

Materials and Methods

The AmplideX® PCR/CE TOMM40 Kit (RUO) achieved rapid and reliable genotyping and/or other prognostic information.

Conclusion

The AmplideX® PCR/CE TOMM40 Kit (RUO) enabled single-base poly-T resolution, reproducible genotyping, and unambiguous data interpretation from cell-line, blood, buccal, and brain DNA.

References


TOMM40 Genotypes by APOE Subgroup
AD Cohort

TOMM40 Poly-T Distribution
AD Cohort

TOMM40 Poly-T Distribution
Control Cohort

Figure 6. Distribution of TOMM40 genotypes across 93 patient samples. Distribution of TOMM40 genotypes in a cohort of neuropathologically confirmed AD cases (AD cohort), and a control cohort without AD neuropathology (control cohort).

Figure 4. TOMM40 genotypes generated at two different laboratories are identical across 16 cell-line and whole-blood samples.

Figure 5. TOMM40 genotypes in matched brain and whole-blood samples. One demonstrated full agreement in the number of poly-T repeats for 11 paired samples, with a median time difference between paired collections of 30 days. Sample 1 and Sample 2 electropherograms are shown as an example of the genotyping profile. A separate sample set revealed genotype concordance for matched buccal and whole-blood samples at Site 1 (p > 0.05).

Figure 3. The AmplideX® PCR/CE assay produces reproducible poly-T genotypes across multiple operators and days. DNA samples with 16-36 Ts were assessed by three operators across two sites, three different days and three 384-well instruments. All results were in agreement within ±1 nucleotide repeat. Representative electropherograms are shown for each sample. A call of 16/29 Ts and 8b as 11/11 sample of 30/36 Ts.

Figure 2. Time-motion for the AmplideX PCR/CE assay workflow, highlighting the rapid turnaround time of ~2.5 hours from gDNA to answer. Total Hands-on Time = 15 min; Time-motion for the AmplideX PCR/CE assay workflow.

Figure 1. The TOMM40 gene and risk alleles. TOMM40 (Translocase Of Outer Mitochondrial Membrane 40) is a gene that codes for TOMM40, a variable poly-T tract, which is associated with age of onset in late-onset AD (LOAD) and the rate of cognitive decline. The TOMM40 gene is associated with age-of-onset risk of AD and the potential to improve patient management in the future.