# BASIC SCIENCE

## PP-107

### Is Alzheimer's Disease Risk Factor, Apolipoprotein E Polymorphism, A Risk Factor of Type-2 Diabetes Mellitus?

https://doi.org/10.15605/jafes.034.S119

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**INTRODUCTION**
Individuals with Type-2 Diabetes Mellitus (T2DM) are known to have higher risk of developing Alzheimer's Disease (AD). One of the most prominent risk factors of AD is Apolipoprotein E (ApoE) polymorphisms. While ε2 allele is known to have suppression effect, ε4-carriers have 5-30-fold increased risk of developing AD compared to ε3-carriers. In this study, we have developed an efficient blood-based APOE genotyping method to investigate if APOE polymorphism plays roles in T2DM.

**METHODOLOGY**
Whole blood were collected from 409 participants (88 pre-diabetes, 202 diabetes, 119 healthy) under approved study protocol NMRR-15-980-26563. Four allele-specific primers were designed with intentional mismatches at each single nucleotide polymorphism (SNP) sites at rs429358 and rs7412, and two common primers flanking the non-allele-specific region. Single plex polymerase chain reaction (PCR) was carried out using a panel of 5 primer sets, whole blood 2 μL/reaction and KAPA Biosystem's Blood PCR Mix. Analysis of APOE genotypes against T2DM status were compared using ANOVA tests and chi-square tests ($\alpha$=0.05).

**RESULTS**
Definitive APOE genotype were obtained for 407 participants (99.5% of total subjects). Genotype of two participants were further confirmed using follow-up samples. As expected, ε3 allele (84.23%) is the most common, followed by ε2 (9.05%) and ε4 (6.72%). Interestingly, ε4 is significantly linked to Malays (10.69%, p-value=0.0035). However, no statistical difference is found in the allele distribution across pre-diabetic, diabetic, and healthy participants (p-value=0.763), suggesting there is no direct association of ApoE genotype and T2DM in our cohort. Further analysis also found no particular links of fasting blood glucose, HbA1c and BMI with ε2-, ε3- and ε4-carriers.

**CONCLUSION**
ApoE polymorphism is not directly indicative of T2DM in our cohort. However, given that ε4-carriers have increased risk of developing AD, it is imperative to follow up with T2DM ε4-carriers, especially the Malay ethnic, who has a significant prevalence as ε4-carrier.

## PP-108

### Identification of Chromosome Conformation Signatures involved in Progression of Type-2 Diabetes Mellitus Using EpiSwitch™

https://doi.org/10.15605/jafes.034.S120

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**INTRODUCTION**
Prevalence of Type-2 Diabetes Mellitus (T2DM) has increased more than 50% in 2006-2015 (National Health and Morbidity Survey, 2015). Oxford Biodynamics has demonstrated using Chromosome Conformation signatures (CCS) (Salter M. et al, 2018), as the most informative molecular entity in epigenetics for stratification of phenotypes. The proprietary EpiSwitch™ biomarker discovery platform is employed to find markers informative of T2DM progression.

**METHODOLOGY**
We have recruited a total of 409 subjects and categorised them into 4 groups, i.e. healthy, pre-diabetes, diabetes treatment naïve and treated diabetes; n=122, 90, 77, 120, respectively, based on glycated haemoglobin (HbA1C), fasting blood glucose (FBG) and oral glucose tolerant test. HbA1C, FBG and relevant clinical data of these subjects were followed up for 2 years at a 6-month interval. Five pre-diabetes, 6 diabetes treatment naïve and 6 treated diabetes samples were selected based on baseline data and compared against a pool of 16 healthy controls using proprietary microarray.

**RESULTS**
Follow-up blood tests showed 2 pre-diabetes samples progressed to diabetes. After comparing against samples regressing either from pre-diabetes to healthy, diabetes to pre-diabetes, diabetes to healthy and samples that are constantly diabetes, 59 unique progression markers have been identified. Functional analysis of the 59 markers