



## ORAL PRESENTATIONS

### OP-1-1

#### ASSOCIATION OF HIF1A rs142179458 WITH BODY ADIPOSITY IN MULTI-ETHNIC ASIANS WITH TYPE 2 DIABETES

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#### OBJECTIVES

Hypoxia is known to contribute to obesity and its related metabolic disorders. Our preliminary data derived from whole-exome sequencing suggested an association of the hypoxia-inducible factor 1  $\alpha$  (HIF1 $\alpha$ ) rs142179458 variant with type 2 diabetes (T2D). However, the impact of this HIF1 $\alpha$  variant on adiposity remains unclear. The study sought to identify the relationship between the HIF1 $\alpha$  rs142179458 and the obesity phenotype.

#### METHODOLOGY

The study involved participants from the Singapore study of macro-angiopathy and microvascular reactivity in type 2 diabetes (SMART2D) study (n = 2010; age = 57  $\pm$  11; 51.3% males). The subjects were screened for the possibly damaging HIF1 $\alpha$  rs142179458 (c.1045g>a [p. asp349asn]) variant [minor allele frequency: 0.00459 (all), 0.02719 (East Asians)] in genome-wide genotyping. The association of the HIF1 $\alpha$  genotype with anthropometric variables was assessed using Chi-square test, Pearson's correlation, and regression analyses.

#### RESULTS

Among the subjects, 2.5% (n=50) carried the HIF1 $\alpha$  variant (ag/aa) and displayed higher body mass index (BMI) than the wildtype genotype (29.8  $\pm$  6.9 versus 27.6  $\pm$  5.2 kg/m<sup>2</sup>; p=0.004). Hip circumference and percentage body fat were also markedly higher in the former group. A positive correlation was observed between the HIF1 $\alpha$  variant and the anthropometric parameters analyzed (all p<0.05). HIF1 $\alpha$  variant was associated with BMI using the Asian BMI cut-off of 23.5 kg/m<sup>2</sup> even after adjusting for age, gender, and ethnicity (odds ratio:1.21, 95% CI:0.99-1.47, p=0.020).

#### CONCLUSION

HIF1 $\alpha$  rs142179458 variant is associated with increased adiposity in adults with T2DM. We postulate that alteration in HIF1 $\alpha$  gene may cause dysregulation of the adaptive response to hypoxia, resulting in body mass index gain and potentially aggravating diabetes.

