

## P1604

# Validating previously reported Brugada syndrome-associated common variants identified in caucasian population in the Han Chinese BrS cohort in Taiwan: SADS-BrS registry

J.-M. Juang<sup>1</sup>, C.Y. Chen<sup>1</sup>, Y.B. Liu<sup>1</sup>, L.Y. Lin<sup>1</sup>, L.T. Ho<sup>1</sup>, H.C. Huang<sup>1</sup>, L.P. Lai<sup>1</sup>, J.J. Hwang<sup>1</sup>, C.K. Wu<sup>1</sup>, T.T. Lin<sup>1</sup>, C.C. Yu<sup>1</sup>, T.P. Lu<sup>1</sup>, A. Chattopadhyay<sup>2</sup>, Q.Y. Yu<sup>2</sup>, J.L. Lin<sup>1</sup>

<sup>1</sup>National Taiwan University Hospital, Division of Cardiovascular Center and Department of Internal Medicine, Taipei, Taiwan; <sup>2</sup>National Taiwan University, Bioinformatics and Biostatistics Core, Center of Genomic Medicine, Taipei, Taiwan

On behalf of SADS-TW BrS registry

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**Background:** Brugada syndrome (BrS) is a sudden arrhythmic death. The prevalence of BrS is higher in the Southeast Asian populations than that in Caucasian patients. A previous genome-wide association study (GWAS) has reported 13 SNPs significantly associated with BrS. However, no study was performed to validate whether these SNPs are enriched in BrS patients in Han Chinese (HC).

**Purpose:** Evaluating the common variants previously reported in Caucasian BrS patients could be generalized to HC BrS patients in Taiwan

**Methods:** We genotyped 200 unrelated BrS patients using Affymetrix TWB Array (N=653,291 SNPs, a customized array for HC in Taiwan). The controls are obtained from the Taiwan Biobank (N ≈ 16,000) using the same array. An imputation workflow was shown in Figure 1. To confirm the accuracy of the imputed genotype of each variant, Sanger sequencing was performed in 10% of randomly selected cases.

**Results:** Among the 3 most important common variants (rs11708996 in SCN5A, rs10428132 in SCN10A and rs9388451 in HEY2/NCOA7) reported in the previous GWAS mainly conducted in Caucasian BrS patients, 2 of them (rs10428132 and rs9388451) were successfully replicated in the HC population in Taiwan ( $P < 0.01$ ). We also found that the differences of minor allele frequency (dMAF: the MAF of cases minus

the MAF of controls) of the two variants were relatively smaller between the BrS cases and healthy controls in HC population compared with that in Caucasian populations (dMAF, rs9388451: 0.15 (Caucasian) vs -0.07 (HC); rs10428132: 0.28 (Caucasian) vs 0.11 (HC)). For the remaining 10 common variants reaching genome-wide significance ( $P = 5 \times 10^{-8}$ ) in Caucasian BrS patients, 9 of them were also significantly enriched in the HC BrS patients after the Bonferroni correction ( $P < 0.05/12 = 0.0042$ ). We next analyzed the variants identified in the previous GWAS on ECG traits (PR interval, QRS duration, QTc interval, and heart rate) in the Caucasian population. Among the reported 75 variants associated with ECG traits, 5 common variants (rs6798015 (PR), rs1760876 (QRS), rs6795970 (PR/QRS), rs2074238 (QTc) and rs314370 (heart rate)) were significant after Bonferroni correction ( $P < 0.05/75 = 0.00066$ ).

**Conclusions:** The preliminary results indicated that 85% of common variants of SCN10A and HEY2/NCOA7 previously reported in Caucasian BrS patients are replicated in BrS patients in the HC population but not the common variant of SCN5A (rs11708996). Furthermore, the common variants of SCN10A and HEY2/NCOA7 related to cardiac depolarization or repolarization may also contribute to the development of BrS.

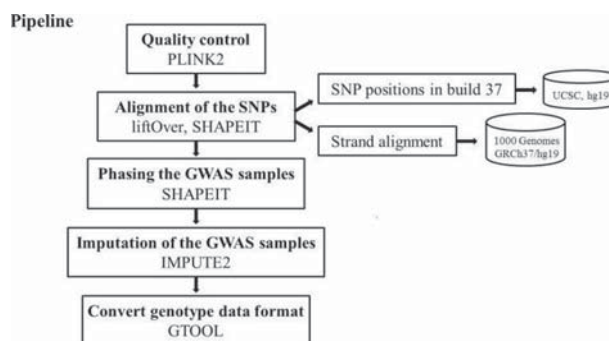


Figure 1