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Copy number variation in Hong Kong patients with autism spectrum disorder
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Background and aims
When offering chromosomal microarray for patients with autism spectrum disorder (ASD),
as according to international standards, copy number variations of uncertain significance
(CNV VUS) are frequently identified, which leads to challenges in genetic counselling.
We aim to study the CNV findings in children with ASD in Hong Kong, and to gather
information for reclassification of recurrent CNV VUS.

Methods
ASD patients from the Department of Paediatrics and Adolescent Medicine QMH/HKU
were recruited if their Array Comparative Genomic Hybridization (aCGH) were done
anytime from Jan 2011 to August 2014 in Prenatal Diagnostic Laboratory, Tsan Yuk
Hospital. Diagnosis of ASD was made by developmental paediatricians and clinical
psychologists using the criteria from Diagnostic and Statistical Manual of Mental Disorders,
Fourth or Fifth Edition. NimbleGen CGX-135k oligonucleotide array and Agilent CGX 60k
oligonucleotide array were used. Information was summarized from the literature and
existing databases to re-classify CNV VUS occurring in our ASD cohort.

Results
Among 288 patients with ASD in our cohort, we identified 5 patients with pathogenic CNV
(1.74%) and 5 patients with likely pathogenic CNV (1.74%). Among all the CNV VUS, one
variant overlapping DPP10 (hg[19]chr2:116,534,689-116,672,358) was recurrently found
in Chinese individuals. The frequency of this variant in our ASD cohort was 0.35% (1 in
288), and 0.96% (9 in 935) in our controls. (P=0.467, two-tailed Fisher's exact test).
Similar CNVs were suggested to be ASD-related in previous studies recruiting mainly
Caucasians. However, there were Chinese individuals with typical development possessing
similar CNVs identified in independent sources (9 from our internal database, 1 from
Singapore Genome Variation Project, 24 from The Singapore Prospective Study Program).

Conclusions
Our study explored the CNV findings in Hong Kong paediatric ASD patients. The CNV
overlapping DPP10 may be a Chinese-related copy-number variation in Hong Kong
Chinese, and we reclassified it to be likely benign in our locality. Our result emphasized
the need to account for ethnicity to give the most precise interpretation of aCGH data.

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