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STRATEGY TO FIGHT CLOPIDOGREL RESISTANCE: A MULTIPLEX GENETIC VARIANTS INVESTIGATION IN CHINESE POPULATION

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Objective Clopidogrel is widely used to treat ischemic heart disease and unexpected resistance could result in severe clinical incidents. Genetic variation has been suggested as the most important factor in intrinsic resistance mechanisms. Hence, a multiplex genetic variation investigation was conducted. The results provided clues for individualised solutions against clopidogrel resistance.

Materials and methods Genomic DNA was extracted from blood samples of 300 CAD patients in 254 hospitals with informed consent. Six single nucleotide polymorphisms (MDR1 C3435T, CYP3A4*18B, CYP3A5*3, CYP2C19*2, CYP2C19*3 and P2Y12 C34T) were genotyped using SNPStream system. Data were statistically analysed.

Result The genotype distribution of all the 6 SNPs fitted Hardy-Weinberg equilibrium test ($p<0.05$). Risk allele frequencies of 4 SNPs, except for CYP2C19*3 and P2Y12 C34T, were different between Chinese and Caucasians ($p<0.05$). The risk allele of CYP2C19*2 was present in 33.8% of Chinese compared to 16% for Caucasians (p=7.7E-4), showing significant difference. According to functional processing, 42 (14%) patients were dysfunctional in transporting; 213 (71%) patients were in metabolism; 19 (6.3%) patients were in receptor binding. Importantly, multiple dysfunctional steps were detected in 63 (21%) patients.

Conclusion This is the first multiplex SNP analysis of clopidogrel resistance in Chinese, investigating key steps in functional processing. The result demonstrated the different distribution of relevant SNPs between Chinese and Caucasians, indicated that native studies are absolutely necessary. The genetic risks and the cumulative effects of multiple variations have to be considered in a backup strategy against clopidogrel resistance. Genotyping will provide convincing basis for treatment selection when complex mechanisms are involved.