

Genes and drugs team up to lower blood pressure

September 13 2007

Patients with high blood pressure respond very differently to antihypertensive medication, making treatment selection tricky for physicians. But new research published in the online open access journal, *BMC Medical Genetics*, pinpoints a number of gene-drug interactions that could allow medication to be tailored to individual patients based on their genetics.

Sharon Kardia from the University of Michigan together with a US team drawn from the University of Texas, Houston and the Mayo Clinic, Rochester, studied siblings with hypertension participating in a Genetic Epidemiology Network of Arteriopathy study. The team took blood pressure readings and details of the subjects' drug regimens. Using these data, the authors found a new set of single nucleotide polymorphisms (SNPs) on the adducin 2 (ADD2) gene that may influence the regulation of blood pressure among people with hypertension.

Variation in blood pressure was affected by genotype, drugs and interactions between the two. The researchers used cross-validation methods to test the predictive power of their findings on individuals outside the study group, eliminating false positive findings.

Three SNPs were associated with differential blood pressure responses in beta-blocker users versus diuretic users while two other SNPs were associated with differential responses in renin-angiotensin-aldosterone system (RAAS) inhibitor users versus diuretic users. The findings also provide initial evidence that the effects of genetic variation on blood

pressure in people with untreated hypertension may be very different compared with those taking medication. Although the authors looked at individual SNPs, it is also likely that SNPs interact.

"We suspected that ADD2 could be associated with differences in response to different antihypertensives because adducins have been proposed to regulate renal tubular transport of Na⁺ reabsorption and the development of hypertension," says Kardia.

Today's drugs target the body's systems for regulating blood pressure, so understanding individuals' differing responses to hypertensive drugs based on genetic and environmental factors is particularly worthwhile to create tailored drug regimens. Prospective studies with individuals selected based on their genotype, along with further SNP investigations, are the next steps toward translating these findings into clinical practice.

Source: BioMed Central

Citation: Genes and drugs team up to lower blood pressure (2007, September 13) retrieved 30 April 2024 from

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