Letters to the Editor

Candidate gene association analysis of thoracic aortic aneurysm and dissection

To the Editor:

In their recent article, Chen and colleagues¹ have described the association of three single-nucleotide polymorphisms of the matrix metalloproteinase 9 gene, with thoracic aortic aneurysm and dissection. One of the three single-nucleotide polymorphisms (A-8202G) was found to be associated with the disease phenotypes of aortic aneurysm and aortic dissection. Such genetic association studies are based on the presence of linkage disequilibrium in the human genome and can be a powerful tool to dissect the genetic basis of diseases. A fundamental aspect of this approach, however, is the meticulous selection and matching of unrelated study subjects (case and control subjects). We believe that this study has some basic weaknesses; hence the results should be viewed with caution.

First, Chen and colleagues¹ compared the prevalence of alleles and genotypes at the three loci between patients recruited from the United States and their control subjects from Australia. In our opinion, the case and control subjects belong to two very distinct populations, and their comparison cannot yield any meaningful evidence. It is a common observation in genetic association studies that genetic markers have diverse, and in some cases even opposite, associations in different ethnic groups.²⁻⁴ The strength of linkage disequilibrium between any two loci will not be equal in any two different ethnic groups, hence the importance of ethnicity-matched control subjects.

Second, Chen and colleagues¹ should comment on the presence of Hardy-Weinberg equilibrium in the genotype distributions at the three loci separately for the case and control groups. Hardy-Weinberg equilibrium in the genotype distributions provides evidence of random selection of subjects, which is an important pillar of the case-control genetic association study design. Furthermore, if the genotypes at the

three loci are in Hardy-Weinberg equilibrium in case and control subjects, then it will be interesting to see the prevalence of the various haplotypes in the study population and also their associations with the diagnoses under study. This may provide additional information about the role of matrix metalloproteinase polymorphisms in thoracic aortic aneurysm and dissection.

Usman Ahmad, MBBS

Muhammad A. Javed, MD

Saulat H. Fatimi, MD, FACS

Department of Surgery

Division of Cardiothoracic Surgery

Faculty of Health Sciences

Aga Khan University

Karachi, Pakistan

References

1. Chen L, Wang X, Carter SA, Shen YH, Bartsch HR, Thompson RW, et al. A single nucleotide polymorphism in the matrix metalloproteinase 9 gene (-8202A/G) is associated with thoracic aortic aneurysms and thoracic aortic dissection. *J Thorac Cardiovasc Surg*. 2006;131:1045-52.
2. Cao K, Hollenbach J, Shi X, Shi W, Chopek M, Fernandez-Vina MA. Analysis of the frequencies of HLA-A, B, and C alleles and haplotypes in the five major ethnic groups of the United States reveals high levels of diversity in these loci and contrasting distribution patterns in these populations. *Hum Immunol*. 2001;62:1009-30.
3. Sanghera DK, Saha N, Aston CE, Kamboh MI. Genetic polymorphism of paraoxonase and the risk of coronary heart disease. *Arterioscler Thromb Vasc Biol*. 1997;17:1067-73.
4. Wang X, Fan Z, Huang J, Su S, Yu Q, Zhao J, et al. Extensive association analysis between polymorphisms of PON gene cluster with coronary heart disease in Chinese Han population. *Arterioscler Thromb Vasc Biol*. 2003;23:328-34.

doi:10.1016/j.jtcvs.2006.05.050

Reply to the Editor:

We appreciate the comments by Ahmad and colleagues regarding our initial investigation of single nucleotide polymorphisms (SNPs) involving the matrix metalloproteinase 9 gene (*MMP9*) in patients

The Editor welcomes submissions for possible publication in the Letters to the Editor section that consist of commentary on an article published in the Journal or other relevant issues. Authors should:

- Include no more than 500 words of text, three authors, and five references
- Type with double-spacing
- See <http://jtcvs.ctsnetjournals.org/misc/ifa.html> for detailed submission instructions.
- Submit the letter electronically via jtcvs.editorialmanager.com.

Letters commenting on an article published in the JTCVS will be considered if they are received within 6 weeks of the time the article was published. Authors of the article being commented on will be given an opportunity to offer a timely response (2 weeks) to the letter. Authors of letters will be notified that the letter has been received. Unpublished letters cannot be returned.