

ology of AOD remains to be established. Nevertheless, the findings raise a number of questions and identify several areas of future investigation.

Although statistically significant, the association between AOD and the 6A/6A polymorphism is not particularly robust. Less than half of the AOD patients exhibit this polymorphism. The frequency of homozygosity for this polymorphism in AOD patients is only 60% higher than controls (47% of AOD patients versus 29% of control patients). Thus, this MMP-3 polymorphism might contribute to the AOD phenotype in some, but not all, patients. There could exist other genetic polymorphisms or environmental factors that cooperate with this MMP-3 genotype to produce the AOD phenotype, but there is no information at the present time to suggest such a mechanism.

It is possible this polymorphism produces subtle differences in MMP-3 expression that cannot be detected by gene microarray analysis, which in most cases can reliably detect changes of two-fold or greater. The fact that not all AOD patients display the 6A/6A genotype further reduces the likelihood that a difference in expression would be detected by gene microarray analyses that average expression data within groups of patients. This illustrates a potential weakness of large-scale gene microarray analyses, which are not suited to identifying small changes or changes that are variable within a study group. In this regard, it would be informative to compare MMP-3 expression levels in AOD and control patients with 5A/5A and 6A/6A genotypes. This could establish the physiologic effect of the promoter genotype on MMP-3 expression in a physiologic setting and provide information on relative differences in MMP-3 expression between AOD and aortic control tissue.

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REFERENCES

1. Armstrong PJ, Johanning JM, Calton WC, Delatore JR, Franklin DP, Han DC, et al. Differential gene expression in human abdominal aorta: Aneurysmal versus occlusive disease. *J Vasc Surg* 2002;35:346-55.

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Reply

We appreciate the opportunity to reply to this interesting work by Drs Ghilardi and Biondi regarding our article.¹ We utilized gene microarray analysis to compare aneurysmal, occlusive, and control tissue from human aorta. We found a difference in MMP expression only in MMP-9 out of 16 different MMPs evaluated. MMP-3 values were not significantly different between the three groups, but interestingly, the highest values were in the control group.

These investigators have identified a potential association between a polymorphism in the MMP-3 gene promoter and AOD. The importance of this genetic polymorphism to the pathophysi-