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 twofold 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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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-