Last Word on Viewpoint: Epigenetic regulation of the ACE gene might be more relevant to endurance physiology than the I/D polymorphism

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TO THE EDITOR: I read with interest the insightful comments (see Ref. 1) made by readers of the Journal of Applied Physiology in response to my article concerning epigenetic modulation of the ACE gene, the I/D polymorphism, and endurance phenotypes (2).

Professor Danser (see Ref. 1) cites work that shows that ACE genotype does not seem to associate with the conversion of exogenously infused ANG I to ANG II in some human subjects. However, there is contrary evidence that shows higher ANG II levels in individuals with the DD genotype following ANG I infusion (4). Hence I would still suggest that hypermethylation of the ACE promoter could influence endurance performance, assuming that this is the pathway by which ACE and/or the I/D polymorphism is influencing human endurance. This is, of course, is still open to debate.

I agree with Drs Vagula and Rawding’s (see Ref. 1) comments in which they highlight the ACE gene as an important determinant of health-related fitness. This seems well established by those active in the field and it is logical considering the role of ACE in different biological systems as discussed in their commentary. I appreciate the valid points made by Drs. Fraga and Fernandez (see Ref. 1) concerning the availability of human tissue for ACE epigenetic experiments. However, I’m not entirely convinced that using an animal model for investigating the epigenetics of the ACE gene with respect to endurance phenotypes would be beneficial. As there are differences between the CpG sites in humans and rats (3) then this approach might not produce data that could be applied to humans.

Professor Dimitriou (see Ref. 1) raises an important point about the I/D polymorphism and either allele (the I or D) being in linkage disequilibrium with promoter variants that might be susceptible to methylation. I would add that the potentially changeable methylation status of the ACE promoter justifies my assertion that the epigenetic regulation might be more important than the polymorphism.

Finally, I would like to say that I have found the Journal of Applied Physiology’s Viewpoint format an excellent forum for open debate. I also thank each of the authors who have provided commentaries for their valued and expert opinions.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author.

REFERENCES