Dear Editor,

We have read the letter from Wagner and Koury (1) concerning our article. We appreciate their concerns and provide our reply to their comments.

First, to determine S-adenosylhomocysteine (AdoHcy or SAH) in mouse plasma, we modified the method of Frantzen et al. (2) that was used to measure homocysteine (Hcy). Although S-adenosylmethionine (AdoMet or SAM) showed a cross-reactivity in concentrations >10μmol/L in the article by Frantzen et al., this is 50–100 times greater than the concentration usually found in human plasma. We eliminated the procedure involving the enzymatic conversion of Hcy to AdoHcy and modified the conditions of constructing the calibration curve (3). To eliminate cross-reaction of the anti-AdoHcy antibody with interfering compounds in plasma, including plasma AdoMet, we prepared the standards for calibration by adding AdoHcy into the control plasma and subjected these controls to the same pretreatment deproteinization procedures as the unknown samples to construct a calibration curve. Another study of hyperhomocysteinemic patients with occlusive vascular disease, by Loehrer et al. (4), showed that a reduced ratio of AdoMet:AdoHcy in both plasma and erythrocytes was due to elevated AdoHcy levels. In kidney failure patients with hyperhomocysteinemia, Perna et al. (5,6) found a 4- to 8-fold increase in intracellular AdoHcy, minimal change in AdoMet. For these reasons, we think that the method reported in our article is suitable to measure the changes of plasma AdoHcy of mice fed diets varying in methionine and B vitamins.

Second, Kerins et al. (7) reported that AdoHcy was elevated in cardiovascular disease in a population with extensive atherosclerosis. However, the authors in this case investigated an epidemiological phenomenon, and concluded that plasma AdoHcy appears to be a more sensitive indicator of atherosclerosis than Hcy in a mouse model by analyzing the correlation between plaque areas and plasma AdoHcy, Hcy concentrations, which seems to be much stronger evidence supporting the concept. We also provided evidence that negative correlations exist between plasma AdoHcy concentration and both DNA methyltransferase activity and global DNA methylation status in the aortic tissue during the development of atherosclerosis in the same mouse model. This suggests that the inhibitory effects of AdoHcy on the methyltransferases may potentially be an important pathogenic mechanism in the development of atherosclerosis.

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Literature Cited

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