Dear Editor,

It is gratifying to read that Liu et al. (1) confirmed our hypothesis regarding the desirability of measuring S-adenosylhomocysteine (SAH or AdoHcy); however, we have 2 concerns about the paper by Liu et al.

First, to determine SAH in mouse plasma, the critical measurement, the authors adapted the method of Frantzen et al. (2) that was designed for the immunoassay of homocysteine (Hcy). This method first converts Hcy to SAH using the enzyme SAH hydrolase and then uses the antibody to SAH in an ELISA assay. The problem with using this method is that the antibody to SAH cross-reacts with S-adenosylmethionine (SAM), as pointed out in the paper by Frantzen et al. and the package insert that accompanies the kit produced by Axis-Shield that was apparently used by Liu et al. Therefore, the values reported by Liu et al. for plasma SAH probably include a contribution from plasma SAM. We recently adapted the method of Frantzen et al. with a modification that eliminates cross-reaction of the anti-SAH antibody with SAM (3). In the article by Liu et al., most of the changes seen in the plasma of mice fed different diets may be due to differences in SAH levels, but one cannot be sure. Other investigators may note the method described by Liu et al. and use it for measurement of plasma SAH in a different setting where it would be completely inappropriate due to increased SAM concentrations.

Second, we believe that the statement “Our results thus suggest for the first time, to our knowledge, that plasma AdoHcy is a far better biomarker of atherosclerosis than Hcy and may be causally linked to the pathogenesis of this vascular disease,” which appears in the Discussion of the Liu et al. article, is incorrect. As Liu et al. noted in their introduction and cited as reference 8, we previously reported that SAH is elevated in cardiovascular disease in a population with extensive atherosclerosis (4). In addition to this paper cited by Liu et al. we have published 2 papers emphasizing the desirability of measuring SAH rather than homocysteine as an indicator of diseases involving vascular dysfunction (5,6). Furthermore, we have provided evidence that increased SAH is likely to be secondary to renal insufficiency that accompanies most vascular disorders (7).

Conrad Wagner*
Mark J. Koury
Vanderbilt University School of Medicine
Nashville, TN 37232

Literature Cited

* To whom correspondence should be addressed. E-mail: conrad.wagner@vanderbilt.edu.