Response to Comment on: Tikhonenko et al. (2010) Remodeling of Retinal Fatty Acids in an Animal Model of Diabetes: A Decrease in Long-Chain Polyunsaturated Fatty Acids Is Associated with a Decrease in Fatty Acid Elongases Elovl2 and Elovl4. Diabetes;59:219–227

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We thank Byeon and Chu (1) for initiating the discussion about potential mechanisms of decreased docosahexaenoic acid (DHA) levels in diabetic eyes. The authors refer to their recent case report from two diabetic patients showing lower ratios of DHA in retinal hard exudates relative to plasma phospholipid levels. They speculate that lower levels of DHA in hard exudates are the result of higher DHA degradation; however, no direct evidence for DHA oxidation is provided in the study. Although we cannot speak to the mechanism of low DHA levels in hard exudates, we would like to point out that our study measured retinal phospholipids at an early time point in diabetes, before the formation of retinal hard exudates. We demonstrated at that very early time point that the diabetic retina is unable to remodel long-chain n-3 fatty acids (2). The decrease in DHA that we observed in the diabetic retina could be due to this remodeling deficiency, lower uptake from plasma, or fatty acid oxidation. Our study was, however, specifically focused on the decline in retinal fatty acid remodeling in diabetes and presented compelling data to demonstrate importance of this mechanism in the retina.

Byeon and Chu further speculate that increased oxidation of DHA and eicosapentaenoic acid (EPA) could lead to cytotoxicity and inflammation and refer to work by Lyons et al. (3). A number of oxidized lipids, indeed, have demonstrated proinflammatory and pro-atherogenic properties. The study by Lyons et al. clearly demonstrated toxic effects of oxidized LDL in the retina. On the contrary, oxidized lipid products of DHA and EPA denoted as resolvins, protectins, and maresins (4) have potent anti-inflammatory properties at physiological concentrations. Thus, oxidation of DHA and EPA in the diabetic retina may be beneficial, not pathological. Indeed, our recent study demonstrated that a DHA-rich diet inhibited the increase in retinal inflammatory markers and prevented the development of acellular capillaries in diabetic retinas (5). Our data are in agreement with a previously published study concerning the beneficial effect of DHA on retinal microvasculature in a model of retinopathy of prematurity (6).

Byeon and Chu suggest that increased dietary DHA intake may increase susceptibility to oxidative modification of plasma or tissue lipids. However, recent studies show the opposite, as dietary DHA may actually prevent oxidation of LDL (7).

In conclusion, although Byeon and Chu raise a valuable question about the oxidation of DHA as a possible mechanism for the decrease in DHA observed in the diabetic retina, it does not undermine the potential beneficial properties of DHA in diabetes.

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