Letter to the Editor regarding “Identification of the oleic acid ethanolamide (OEA) isomer *cis*-vaccenic acid ethanolamide (VEA) as a highly abundant 18:1 fatty acid ethanolamide in blood plasma from rats and humans”

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Dear Editors, dear authors:

I read with great interest the recent research paper by Röhrig et al. in *Anal Bioanal Chem* 2016 [1], which reported on the unequivocal identification of *cis*-vaccenic acid ethanolamide (VEA) in blood plasma from rats and humans. VEA is an isomer of *cis*-oleic acid ethanolamide (OEA). OEA, palmitic acid ethanolamide (PAE) and stearic acid ethanolamide (SEA) were found to occur physiologically in several biological samples in addition to the endocannabinoid arachidonic acid ethanolamide anandamide (AEA; reviewed in Ref. [2]). OEA, VEA, PAE, and SEA are not endocannabinoids. Previously, we observed by GC-MS/MS in the selected-reaction monitoring (SRM) mode two chromatographic peaks with very similar retention times. We identified the compound eluting at 17.86 min as OEA, yet the peak eluting at 17.92 remained unknown [3]. The findings by Röhrig et al. [1] suggest that the unknown peak we observed in our study [3] is likely to be VEA. Interestingly, the mean peak area ratio of OEA to VEA in plasma samples from our group of about 3.5 is close to the mean value of 2.4 reported by Röhrig et al. for human plasma samples [1]. In plasma of 16 apparently healthy humans, we measured by GC-MS/MS OEA concentrations of 18 ± 6 nM, which suggest an approximate VEA mean concentration of 5 nM. Even this concentration is higher than the plasma AEA concentration of 1.4 nM [3]. Previously, we demonstrated that a considerable fraction of

plasma OEA but not of AEA is due to laboratory contamination [4]. Yet, we did not investigate whether the putative VEA may also originate from laboratory contamination or from OEA derivatization and GC-MS/MS analysis, which require much more drastic conditions compared with UPLC-MS/MS.

Reply by the authors of [1]:

We thank Dr. Dimitrios Tsikas for this highly interesting comment, which provides an important link between our study and Dr. Tsikas' own excellent contributions in this field.

Compliance with Ethical Standards

Conflict of interest The author declares that there is no conflict of interest.

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