Horacio Kaufmann
Christopher J. Mathias

Hoeldtke RD (2003) Nitrosative stress in early type I diabetes. *Clin Auton Res* 13:406–421

We received a request to publish a retraction of the above manuscript. What follows is the letter that provides the authors' explanation for this request.

The editors-in-chief

Dear Sirs,

We reported a few years ago that protein bound nitrotyrosine was increased in early Type 1 diabetes and showed a positive correlation with blood pressure and sudomotor function [1]. We measured nitrotyrosine and tyrosine by HPLC followed by electrochemical detection and expressed our results as the ratio of nitrotyrosine to tyrosine, which we found to be $0.34 \pm 0.12 \times 10^{-3}$ in the control subjects and 0.778 ± 0.04 in diabetic patients. Unfortunately at the time we published these data we were unaware of a study by Frost et al. who performed alkaline hydrolysis of the plasma protein followed by mass spectrometry and reported a much lower nitrotyrosine/tyrosine ratio (0.044×10^{-3}) [2]. A few years later Shishehbor et al. performed acid hydrolysis of serum protein and reported a ratio in non-diabetic patients of 5.2×10^{-6} , also much lower (100 fold) than we observed. Because of these discrepancies, we have reassessed our HPLC method and performed a more in depth analysis of the electrical properties of the peaks we have previously identified as nitrotyrosine using a multichannel CoulArray liquid chromatograph (ESA, Chelmsford MA). We observed that the electrical properties of the compound we "identified" as nitrotyrosine on the basis of HPLC retention time differed from the authentic compound in many samples and concluded that interfering substances were obscuring the true nitrotyrosine peaks. We have used a second HPLC

column and eliminated the interferences from some of our samples and this decreased the estimated ratio of nitrotyrosine/tyrosine by approximately a factor of 100. On the basis of these considerations, we have concluded that our previously published nitrotyrosine data [1] are invalid and hereby retracted. Increased nitrotyrosine has been documented in other laboratories in clinical diabetes using other methods [3, 4].

References

1. Hoeldtke RD (2003) Nitrosative Stress in early type I diabetes. *Clin Auto Res* 13:406–421
2. Frost MT, Halliwell B, Moore KP (2000) Analysis of free and protein-bound nitrotyrosine in human plasma by a gas chromatography/mass spectrometry method that avoids nitration artifacts. *Biochem J* 345:453–458
3. Shishehbor MH, Aviles RJ, Brennan ML, Fu X, Goormastic M, Pearce GL, Gokce N, Keaney JF Jr, Penn MS, Sprecher DL, Vita JA, Hazen SL (2003) Association of nitrotyrosine levels with cardiovascular disease and modulation by statin therapy. *JAMA* 289:1675–1680
4. Ceriello A, Mercuri F, Quagliaro L, Assaloni R, Motz E, Tonutti L, Taboga C (2001) Detection of nitrotyrosine in the diabetic plasma: evidence of oxidative stress. *Diabetologia* 44:834–838

Sincerely,

Robert D. Hoeldtke, MD, PhD
Professor of Medicine