

Letter to the Editor

Comment on: Harmancey et al. (2007) Adrenomedullin Inhibits Adipogenesis Under Transcriptional Control of Insulin: *Diabetes* 56:553–563

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I have read with great interest the article by Harmancey et al. (1) on inhibition of adipogenesis by adrenomedullin. Previous studies, including ours (2–4), have shown that adrenomedullin is produced and secreted by adipocytes and adipose tissues, whereas the reported effects of adrenomedullin on lipolysis are conflicting (5,6). Harmancey et al. (1) have clearly shown inhibition of adipogenesis by adrenomedullin using small interfering RNA technology. However, I have several concerns regarding this article. First, the concentration of exogenously added adrenomedullin (100 nmol/l) was very high in the experiment on the inhibitory effects on adipogenesis (Fig. 1 in article). The adrenomedullin concentrations in the medium of cultured adipocytes rarely exceed 1 nmol/l (2,4). Second, the authors used 3T3-F442A preadipocytes but not adipocytes in the transfection study (Fig. 6 in article). There is a considerable difference in the adrenomedullin promoter activity between preadipocytes and adipocytes, probably due to the presence of another promoter sequence in the adrenomedullin gene named ADRE-AR, as shown in our previous study using 3T3-L1 cells (3). Third, the authors placed too much emphasis on the inhibition of adrenomedullin expression by insulin in adipocytes. Adrenomedullin expression was rather increased, however, during adipocyte differentiation of human mesenchymal stem cells, which was induced by the

medium containing insulin (4). Finally, the authors showed a high negative correlation between plasma adrenomedullin and insulin levels in 10 obese subjects. (Table 1 in the article shows seven male and six female subjects.) Plasma insulin levels in these obese subjects were not elevated, however, when compared with 10 lean subjects. (Table 1 in the article shows six male and seven female subjects.) If the authors had included obese subjects with increased plasma insulin levels in this analysis, the results may have been different. I agree with the inhibitory effect of adrenomedullin on adipogenesis shown by the small interfering RNA technology but cannot agree with the proposed manner of the insulin involvement in this phenomenon.

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