

## Increased Adiponectin Levels in Women with Rheumatoid Arthritis After Etanercept Treatment

To the Editor:

We read with great interest the report by Dr. Nagashima, *et al*, "Increase in plasma levels of adiponectin after administration of anti-tumor necrosis factor (TNF) agents in patients with rheumatoid arthritis"<sup>1</sup>. The article is of special importance in regard to accelerated atherosclerosis among patients with connective tissue disease, including rheumatoid arthritis (RA). In the study, the elevation of total and high molecular weight adiponectin was observed in patients with RA treated with both etanercept and infliximab.

To support the observations of those authors, we share our experience with etanercept-related adiponectin changes in a group of 18 women with RA. We determined the plasma adiponectin levels before and after 3 months of treatment with etanercept and compared the results with healthy age-matched women. In patients with RA, the serum adiponectin concentration was measured before treatment and after 3 months. We also measured the total fat mass (TFM) by dual energy x-ray absorptiometry before treatment in patients and compared to controls. The levels of adiponectin were significantly higher in patients before treatment than in healthy controls, and was not related to TFM (there were no significant differences in TFM between the patient and control groups). We observed significant elevation of adiponectin levels after 3 months' treatment with etanercept; that is in agreement with the results of Nagashima, *et al*. We found that increment of adiponectin level was not related to change in disease activity (Disease Activity Score 28-joint count). This suggests that changes in adiponectin level may be caused by the direct influence of proinflammatory cytokine cascades on adiponectin concentration, rather than the general inflammation state<sup>2</sup>.

The role of adiponectin in driving the inflammation in RA is still controversial. Some studies showed a proinflammatory effect of adiponectin with the secretion of interleukin 6 (IL-6) and matrix metalloproteinase-1 from synovial fibroblasts in patients with RA<sup>3,4</sup>. However, others suggest antiinflammatory properties of this adipocytokine instead<sup>5-7</sup>.

We are inclined to recognize an antiinflammatory role for adiponectin, and suggest that TNF- $\alpha$  is a key cytokine that regulates adiponectin level in patients with RA. Huang, *et al*<sup>8</sup> showed that initial TNF- $\alpha$  release from macrophages mediated by the globular form of adiponectin was inhibited by subsequent induction of antiinflammatory IL-10 synthesis. In the study by Yamaguchi, *et al*<sup>9</sup>, the globular form of adiponectin inhibits differentiation of osteoclasts, which may explain the halting of bone resorption observed among patients receiving anti-TNF- $\alpha$  treatment. It is not entirely clear whether all anti-TNF- $\alpha$  agents used in RA have the same effect on

adiponectin level. It seems that contradictory results reported in the literature reflect different levels of TNF- $\alpha$  suppression and subsequent adiponectin changes whose level is higher when TNF- $\alpha$  reduction is not prominent.

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