It is well known that most obese individuals have elevated circulating levels of leptin but they do not respond to these increased leptin levels with reduced food intake [4]. Numerous authors have supposed that in obese patients a state of relative leptin resistance may occur [5,6]. This issue has been recently reviewed by Munzberg and Myers [7]. Leptin stimulates the production of anorectic neuropeptides and inhibits the action of orexigenic peptides in the arcuate nucleus through complex mechanisms [7]. When leptin binds to its receptor (LRb) it activates the LRb-associated Jak2 tyrosine kinase, leading to the autophosphorylation of tyrosine residues on Jak2 and the phosphorylation of Tyr985 and Tyr1138 on the intracellular tail of LRb. Phosphorylation of Tyr1138 mediates the activation of the transcription factor STAT3. STAT3 also induces the transcription of SOCS3. SOCS3 binding to the LRb-Jak2 complex attenuates LRb-mediated signalling [7–10].

Munzberg and Myers postulate that when leptin levels are low and thus baseline STAT3 activation is modest, SOCS3 expression is low, and incremental changes in leptin would be almost fully translated into increased LRb signalling. When circulating leptin levels are high (as in obesity), the increased baseline STAT3 activation would lead to an increased expression of SOCS3, mitigating much of the effect of increased leptin binding to LRb.

Taking into account these considerations and the results of our clinical study, it could be suggested that a state of relative leptin resistance may occur also in patients with end-stage renal disease receiving haemodialysis in which circulating leptin levels are significantly higher than in healthy subjects. If further studies in the next future will confirm these hypotheses, the title of the article by Wiecek could be changed in ‘Does leptin really contribute to uraemic cachexia?’.

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