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COMMENTARY

ADIPOKINES AND BONE: ENIGMA OR PARADIGM?

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Despite years of intense research in the field of adipokines and musculoskeletal system (1), there is still an open debate over the effect of certain adipokines, particularly leptin and adiponectin, on this system. Though, adipokine effects on bone turnover and density are still under deep investigation (2).

The review by Kanazawa in this issue of *Adipobiology* affords insights into the effect of adipokines in the skeleton (3). It is becoming increasingly evident that the role of adipokines in skeletal physiology should be considered in a broad context of bone-cartilage-fat- brain- immune interactions. Actually, musculoskeletal system, immune response and energy metabolism are functionally related by a complex neuroendocrine circuit involving a plethora of factors and cells (4). Kanazawa's review points the finger initially on leptin, the forerunner of adipokine superfamily (5) and outline clearly the difficult to understand the effects of leptin on skeleton. This interpretation is in part due to discrepant findings observed in studies carried on in rodents, depending on the strains. Depending on the administration route of leptin (centrally *versus* peripherally). Depending on dosage, body mass index, gender etc… What else might account for these discrepancies in the literature regarding leptin's action on bone? It is also evident that while each of these elements may be contributory, none can explain fully the current state of conflicting evidence. To further complicate the situation, human clinical studies do not shed any light on these questions. In any case, there is a clear consensus that leptin modulates bone metabolism although there is a "healthy" debate regarding its influence on bone formation *versus* resorption (6). Kanazawa focuses also on adiponectin, the other "godfather" of the family. In this case, also, the reader is making his logical deduction: adiponectin is sometimes good and sometimes bad. This conclusion is due to the fact that during long time adiponectin has been viewed as a "positive" adipokine for its insulin-sensitizing, anti-inflammatory (at least at cardiovascular level) and anti-atherogenic effects in metabolic diseases. However, various recent studies have clearly indicated that the axiom adiponectin = healthful adipokine, which was generally assumed a few years ago seems to be incorrect (7-9). Finally, Kanazawa reviewed also other so-called young members of the family, although they are, at present, not so young as they were. This review is a comprehensive work that will help Adipobiology readers to familiarize with intriguing and amazing effects of adipokines on musculoskeletal system. Beyond any doubt, the discovery of leptin initially and next of the other members of adipokine superfamily, has remarkably revolutionized our narrow view of adipose tissue as a simply and passive energy storage reservoir. Since the first publication on leptin by Friedman's group in 1994 (10), thousands of articles on adipokines have documented that adipose tissue is a dynamic endocrine organ contributing to systemic feedback loops integrating multiple peripheral organs with the

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central nervous system and immune system. However, understanding of the actions of adipokines dealt with in this review is generally still too incomplete to generate well-supported therapeutic hypotheses. The rate at which their roles are being clarified nonetheless makes it certain that they, too, will soon be central to pharmacotherapeutic approaches to bone metabolism diseases.

Regardless, the current issue of *Adipobiology* moves us at least a step forward in our understanding of the complex role of adipokines in controlling the dynamics between bone and adipose tissue. This work outline that the topic of adipokines as mediators of bone biology is under active investigation as attested to by an increasing number of articles recently published. The moral of the story, as usual in scientific stories, is that future studies will be necessary to further dissect the intricate feedback loops existing among adipose tissue, bone and brain.

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