

## Volume 69, Number 3, March 2011

### Lead Article

#### 123 **Impact of conjugated linoleic acid on bone physiology: proposed mechanism involving inhibition of adipogenesis**

Steven W Ing and Martha A Belury

*Conjugated linoleic acid (CLA) supplementation decreases adipose mass and increases bone mass in mice. Recent clinical studies demonstrate a beneficial effect of CLA on reducing weight and adipose mass in humans. This article reviews possible biological mechanisms of action of CLA on bone metabolism, focusing on modulation of nuclear receptor peroxisome proliferator-activated receptor gamma activity to steer mesenchymal stem cell differentiation toward an adipose and away from an osteoblast lineage. Clinical studies of the effects of CLA on bone mass and clinical implications of the effects of CLA on bone health in humans are summarized and discussed.*

### Special Articles

#### 132 **Effects of maternal malnutrition and postnatal nutritional rehabilitation on brain fatty acids, learning, and memory**

Amanda Santos de Souza, Flávia Spreafico Fernandes, and Maria das Graças Tavares do Carmo

*Undernutrition still affects mothers and children in developing countries and thus remains the major focus of nutritional intervention efforts. Neuronal development, which classically includes neurogenesis, migration, maturation, and synapse refinement, begins in utero and continues into the early postnatal period. These processes are not only genetically regulated but also clearly susceptible to environmental manipulation. Dietary deprivation during early life is known to have adverse effects on brain anatomy, physiology, and biochemistry, and may even lead to permanent brain damage. Although all nutrients are important for the structural development of the central nervous system, lipids such as long-chain polyunsaturated fatty acids, especially docosahexaenoic acid (22:6 n-3) and arachidonic acid (20:4 n-6), are important for normal brain development. The purpose of this literature review is to examine how early undernutrition involving a deficiency in long-chain polyunsaturated fatty acids can affect brain development and function and produce deficits in spatial cognitive learning ability.*

#### 145 **Reliability of leptin, but not adiponectin, as a biomarker for diet-induced weight loss in humans**

Monica C Klempel and Krista A Varady

*Calorie restriction (CR)-induced weight loss has been shown to lower the risk of chronic disease in obese individuals. Although the mechanisms that link weight loss to disease risk reduction remain unclear, evidence suggests adipokines may play a role. What has yet to be determined, however, is the dose-response effect of body weight loss and visceral fat mass loss on adipokines. Accordingly, this review examines how varying degrees of CR-induced weight loss (i.e., >10%, 5–10%, and <5% from baseline) impact plasma levels and expression of adiponectin, leptin, resistin, interleukin 6 (IL-6), interleukin 8 (IL-8), monocyte chemoattractant protein 1 (MCP-1), and retinol-binding protein 4 (RBP-4). The dose-response relationship between visceral fat mass loss and adipokine profile improvement will also be explored. Results from this review demonstrate that even mild weight loss induced by CR may have beneficial effects on leptin levels, but it has no clear impact on adiponectin, resistin, IL-6, IL-8, MCP-1, or RBP-4 concentrations.*

### Emerging Science

#### 155 **Vitamin E and adiponectin: proposed mechanism for vitamin E-induced improvement in insulin sensitivity**

Brianna Gray, Jennifer Swick, and Alayne G Ronnenberg

*Insulin resistance and type 2 diabetes have been treated with the PPAR $\gamma$  agonists thiazolidinediones, or TZDs, since the 1990s. One mechanism by which these drugs may work is through PPAR $\gamma$ -mediated upregulation of adiponectin, an endogenous adipokine that has been shown to increase insulin sensitivity. Interestingly,  $\alpha$ - and  $\gamma$ -tocopherol, two vitamin E vitamers, have structural similarities to the TZDs and have also been linked to enhanced insulin sensitivity. A recent study identified a novel function of  $\alpha$ - and  $\gamma$ -tocopherol in 3T3-L1 preadipocytes: upregulation of an endogenous ligand involved in activating PPAR $\gamma$ . This study also found that tocopherols dramatically enhanced adiponectin expression and that this effect was mediated through  $\alpha$  PPAR $\gamma$ -dependent process. These findings illustrate a possible mechanistic link between vitamin E and insulin sensitivity.*

#### 162 **Bone quality and vitamin K<sub>2</sub> in type 2 diabetes: Review of preclinical and clinical studies**

Jun Iwamoto, Yoshihiro Sato, Tsuyoshi Takeda, and Hideo Matsumoto

*Type 2 diabetic patients are at high risk of bone fractures even if their bone mineral density is normal or high. This is likely explained by poor bone quality and extraskeletal factors. The present review was conducted to provide an overview of the currently available preclinical and clinical evidence on the effect of vitamin K<sub>2</sub> on bone quality in persons with type 2 diabetes. Vitamin K<sub>2</sub> stimulates  $\gamma$ -carboxylation of osteocalcin and can increase bone formation through steroid and xenobiotic receptors. Clinical studies of type 2 diabetic patients have shown detrimental collagen cross-links in bone; low serum insulin-like growth factor-1 and osteocalcin concentration are associated with an increased risk of fractures. A therapeutic strategy for preventing fractures in type 2 diabetic patients remains to be established. One recent preclinical study showed that vitamin K<sub>2</sub> administration in a type 2 diabetic rat model had the following skeletal benefits: increased serum osteocalcin, improved collagen cross-link profiles, and increased bone strength. These new findings suggesting a possible beneficial effect of vitamin K<sub>2</sub> supplementation on bone quality in type 2 diabetes warrant further investigation.*

#### 168 **Nutrition Updates**