Invited Speaker Plenary 1: Functional Foods

**Role of whey and whey components in regulating adipose tissue and skeletal muscle metabolism**

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**Background** - Thermodynamics and energy balance are clearly core factors involved in the obesity epidemic, with small increases in energy intake coupled with declining physical activity resulting in net positive energy balance and progressive weight and fat gain. Consequently, the obesity epidemic is often reduced to a simple question of energy balance, and proposed strategies accordingly focus upon best approaches to induce negative energy balance. However, obesity is a complex genetic trait, with multiple genes interacting to confer relative resistance or susceptibility to positive energy balance. Similarly, dietary components and patterns may affect the same metabolic pathways affected by genetic susceptibility and thereby alter energy portioning and obesity risk. A growing body of evidence, discussed in this review, suggests that dairy whey contains compounds that exert such effects and thereby contribute to healthy weight management.

**Review** - We have found dairy-rich diets to attenuate body fat accumulation and weight gain during periods of over-consumption of an energy dense diet and to increase fat breakdown and oxidation while preserving lean tissue during energy restriction. The underlying theory is that the calcitriol released in response to sub-optimal calcium intakes stimulates lipogenic gene expression and lipogenesis and inhibits lipolysis and fat oxidation, resulting in increased adipocyte triglyceride storage and excess adiposity, while the higher levels of calcium contained in dairy suppress calcitriol and exert the opposite effect. In addition, calcitriol inhibits adipocyte mitochondrial uncoupling and apoptosis, resulting in increased efficiency of energy storage on low calcium diets, while greater adipocyte uncoupling, energy dissipation and apoptosis occurs on dairy-rich diets. While these effects are attributable, in part, to calcium suppression of calcitriol, dairy is more than twice as effective as calcium *per se* in inhibiting adiposity, and this additional bioactivity resides in the whey fraction. Moreover, calcium is without effect on preserving lean mass during energy restriction, while whey confers significant protection. The angiotensin converting enzyme (ACE) inhibitory activity of whey contains a portion of this additional activity, as it attenuates autocrine angiotensin II-induced adipocyte lipogenesis. However, combining calcium and whey-derived ACE inhibitors produces an effect that is significantly less potent than that of intact whey, indicating the presence of other anti-obesity factors in whey; the identity of these factors is presently under investigation. Moreover, this combination does not retain the ability of intact whey to protect lean mass. Instead, the branched chain amino acid (BCAA) content of whey appears to contribute significantly to preservation of lean mass during energy restriction and expansion of lean mass in the absence of energy restriction; this effect is likely due to leucine stimulation of muscle protein synthesis and may also contribute to reduced adiposity as a result of the additional energetic cost of muscle protein synthesis. However, whey-free diets containing BCAA confer less lean mass protection than intact whey.

**Conclusions** - Whey components have the potential to play a significant role in weight management and protection of lean mass during dieting. While the calcium content of whey accounts for a portion of this effect (<50%), there are clearly other bioactive whey components which also contribute. However, although both ACE-inhibitory peptides and BCAA contribute to this additional bioactivity, they cannot fully account for the anti-obesity and muscle-protective properties of whey, indicating that there are other, as of yet unidentified, whey components which contribute to these effects.