Aging, IGF-1, and diet

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Fontana *et al.* (2008) recently reported in *Aging Cell* their interesting findings, based on studies of 46 subjects, of the impact of chronic severe caloric restriction on insulin-like growth factor 1 (IGF-1) and insulin-like growth factor binding protein 3 (IGFBP-3) levels. They concluded that protein intake may be a more important determinant of the circulating levels than energy restriction, and speculated that this may have implications with respect to longevity.

We previously reported (Holmes *et al.*, 2002; Giovannucci *et al.*, 2003) studies of 1037 women and 753 men that explored dietary determinants of IGF-1 and IGFBP-3 levels in a cross-section of subjects on typical North American diets. We observed, in females, a positive association between protein intake with circulating IGF-1 concentration (174, 188, 201, 192, and 196 ng mL^{-1} across quintiles of protein intake; $p = 0.002$), which was stronger than the relationship between energy intake and IGF-1 concentration. Similar findings were seen in men, where the relationship of energy intake to IGF-1 levels was seen only in men with body mass index < 25 kg m^{-2}. Thus, the intervention study involving a small number of subjects by Fontana *et al.* yielded data consistent with the larger observational studies we previously reported.

Caution is required in extrapolating data concerning dietary-induced changes in IGF-1 levels to changes in health outcomes, such as longevity or cancer risk. While there is clear evidence that reduced IGF signalling is associated with increased longevity in model organisms, there is evidence that lower IGF-1 levels are associated with increased cardiovascular disease in humans (Brugts *et al.*, 2008). In addition, recent data (e.g. Ma *et al.*, 2008) suggest that with respect to cancer endpoints, it is important to consider insulin levels as well as IGF-1 levels. The relationships between diet, insulin and IGF-1 levels, and clinical health outcomes is an important topic, but one that appears to be more complex than might have been implied by animal models.

References

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