Last Word on Point:Counterpoint: IGF is the major physiological regulator of muscle mass

C. E. Stewart1 and J. M. Pell2

1Institute for Biomedical Research into Human Movement and Health, Manchester; 2The Babraham Institute, Babraham Research Campus, Babraham, Cambridge, United Kingdom

TO THE EDITOR: The authors proposing the Point of the Point:Counterpoint debate entitled “IGF is/is not the major physiological regulator of muscle mass” (6) would like to thank our colleagues for their insightful responses (5) pertaining to this topic. The extent of the commentaries on the debate underscores the importance of gaining a better understanding of the role of IGF in muscle physiology. What, however, is evident is the general consensus, in line with our reported view, that IGF is central to pre- and postnatal muscle growth as was first compellingly reported almost two decades ago by Liu et al. (4). Controversy, however, remains pertaining to the role of IGF in load-induced hypertrophy. Given the complexities of all multicellular organisms, it is important to acknowledge that one factor alone is unlikely to work in isolation; rather responses are likely to be multifactorial, influenced by niche, environmental, biophysical, and hormonal cues. This is eloquently portrayed in the observations and earlier work of Ameredes et al. (1) who suggest, as do others in the commentaries linked to this debate (5), that IGF may not drive the growth response associated with load, but acts to amplify or optimize the impact of a chronic repetitive activity. Studies focusing on extremes of exercise responses between individuals (e.g., as detailed in Refs. 2, 3) may provide insight into the mechanisms essential to or supporting load-induced hypertrophy. What has also become apparent through the course of the reported reflections (and may constitute the foundations for future debates) is the focus that we exert on J) Akt/mTOR and their roles in hypertrophy, at the expense, perhaps of other critical signaling pathways and 2) the need to develop and implement the most appropriate human (and animal or cell) models to further establish the extent of the contribution of IGF, not only in relation to hypertrophy (load induced or otherwise) but also in influencing muscle loss, damage, repair, and inflammation. What is clear, in the absence of unequivocal data, is that considerable work remains to be undertaken to clarify the effects of the IGFs in skeletal muscle—considerations relating to the kind of stimulus (hormonal vs. mechanical), the quantity and duration of exposure to IGF, the extent of a response, the age/health of the model, and the mechanisms/timing of sampling must not be ignored. In summary, both hormonal and mechanical factors can elicit hypertrophic responses. The quantitative/qualitative roles of either will be difficult to ascertain because of their close interactions; it is therefore essential that we continue to report and to challenge the roles of the IGFs in muscle physiology.

REFERENCES


