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REBUTTAL FROM DRS. O’CONNOR AND PAVLATH

We believe to critically evaluate the contribution of satellite cells to hypertrophy, the following conditions need to be fulfilled: (1) analysis of a complete spectrum of time points (early and late) after application of a hypertrophic stimulus; (2) sufficiently large increases in myofiber cross-sectional area or diameter; (3) enumeration of myonuclear number using a method to clearly delineate the sarcoulemma; and (4) to show cause and effect rather than correlation, ablation of satellite cell activity. The papers cited by McCarthy and Esser in various models of hypertrophy fail to satisfy one or more of these criteria and, therefore, do not provide conclusive evidence against the necessity for satellite cells in hypertrophy. For example, the vast majority of the clenbuterol literature only analyzes muscle weight and content of total protein, RNA, and DNA. Muscle weight and total protein are non-specific measures including both muscle and non-muscle components of the tissue. Total DNA is an inaccurate measure of myonuclei, including fibroblasts, inflammatory cells, etc. Kim et al. (3) analyzed myonuclear number in response to clenbuterol but only at 14 days using inappropriate methods. In contrast, myonuclear number was appropriately analyzed in some studies (5, 6) but only at early time points before the myonuclear domain ceiling of the existing myonuclei was likely to be exceeded. The time points chosen for study in the synergist ablation (2) and stretch overload (4) studies were too early in the hypertrophic process for appropriate interpretations on the role of satellite cells. Not commented on by McCarthy and Esser is that one of their cited studies (1) demonstrated preferential increments in DNA content rather than RNA or protein accretion during the later stages of clenbuterol-induced hypertrophy, thus suggesting a role for satellite cells. The limitations inherent in using DNA content as a measure of satellite cells must be kept in mind though.

In summary, we believe the evidence generated from various models of muscle growth in multiple species support our contention that muscle growth may be viewed as a continuum of temporally regulated responses. We believe that muscle growth consists of multiple phases, including accelerated transcriptional and translational responses followed by satellite cell activation during the later stages of hypertrophy. Satellite cell activation is necessary only if a certain threshold myofiber size is reached.

REFERENCES


