Investigating the Cellular Actions of BPC-157 on Skeletal Muscle Precursor Cells In Vitro

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INTRODUCTION:
BPC-157 is a synthetic pentadecapeptide (15 amino acids) originally isolated from a partial sequence of a protein found in human gastric juice. It has recently attracted attention for its regenerative and cytoprotective actions in multiple tissues, particularly within the musculoskeletal system. BPC-157 is not approved by the FDA for human use and is listed by the World Anti-Doping Agency (WADA) as a prohibited substance in competitive sports, including the Olympics. At the same time, numerous preclinical studies showed that BPC-157 accelerates repair of injured skeletal muscle, tendon, ligament, and bone, while also exhibiting protective effects on vascular endothelium and peripheral nerves. These effects have been attributed to overlapping signaling pathways, including activation of VEGFR2, stimulation of the Akt–eNOS axis that promotes angiogenesis, upregulation of growth hormone receptor (GHR), and activation of ERK1/2 signaling to support myofiber repair and neuromuscular junction stability (Vukojević et al., 2018; Chang et al., 2021; Sikiric et al., 2022). Despite extensive preclinical data and widespread nonclinical use among athletes and experimental medicine communities, there is a striking lack of direct evidence describing how BPC-157 influences skeletal muscle cells themselves Understanding whether its regenerative effects stem from direct action on myogenic precursor cells or from indirect systemic effects remains a key question. Therefore, this study aimed to determine the direct cellular effects of BPC-157 on proliferation, differentiation, and metabolic activity in mouse skeletal muscle cells.

METHODS:
To date, reports on effect of BPC-157 on skeletal muscle cells is limited to rat cells, and the examination of cell migration. Here we used female, muscle precursor cells or myoblast cells, and will use male murine cells to test sex-related differences in ongoing studies(as we previously detected sex-differences in regeneration potential of muscle stem cells). Muscle cells were cultured under standard growth conditions and treated with BPC-157 at concentrations of 0.1 μM and 1 μM for 48 hours. Untreated cells served as negative controls. Cell proliferation was assessed using a colorimetric metabolic assay that reflects mitochondrial activity, providing an indirect measure of viable cell number. Microscopic examination was performed to evaluate morphological features associated with proliferation and early myogenic differentiation. In addition, under cytotoxic conditions, we examined survival differences in BPC-157-treated cells. Parallel wells were inspected for signs of cytotoxicity or detachment to assess tolerability.

RESULTS:
Treatment with BPC-157 resulted in a statistically significant increase in muscle cell proliferation compared with untreated controls at both 0.1 μM and 1 μM concentrations ($p < 0.05$). The proliferative response was concentration-dependent, with the 1 μM condition producing the highest increase in metabolic activity. Cells demonstrate an increase in population proliferation via faster cell division rates and survival in treated cultures. Cells maintained normal morphology throughout treatment, and no evidence of cytotoxicity was observed. Although differentiation and myotube formation assays are ongoing, preliminary analysis shows enhanced cell fusion and in vitro myotube formation early myogenic activation.

DISCUSSION/CONCLUSION:
Our findings provide the first direct evidence that BPC-157 stimulates skeletal muscle cell proliferation in vitro. . We identified only 1 preclinical study examining the effects of BPC -157 on muscle cells in vitro, which examined its effects on migration (SH Wang et al 2019). These results support the hypothesis that the peptide exerts a cell-autonomous effect on myoblasts, in addition to its known systemic influences on angiogenesis and inflammation. The observed increase in proliferation suggests possible involvement of growth-related signaling cascades such as ERK1/2 or Akt pathways, both of which have been reported in other tissue models of BPC-157 action. Future studies will characterize expression of myogenic differentiation markers (e.g., MyoD, myogenin) and signaling intermediates to understand the underlying mechanisms.

SIGNIFICANCE/CLINICAL RELEVANCE:
BPC-157 has gained substantial popular and experimental use as a purported healing agent for musculoskeletal injuries despite the absence of FDA approval and limited human data. Demonstrating a direct stimulatory effect on skeletal muscle cells strengthens the biological plausibility of its regenerative potential and establishes a foundation for more mechanistic and translational studies. Understanding how BPC-157 influences cellular proliferation and differentiation may ultimately inform the rational design of peptide-based therapeutics for muscle repair, sarcopenia, or post-injury regeneration.