

Angiotensin-II Induces Atrophic Signaling in Muscle Cells.

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Numerous chronic pathological conditions are associated with elevated circulating levels of angiotensin II (Ang II). A substantial amount of previous research has focused on the effects of elevated Ang II on the heart and vasculature. However, skeletal muscle atrophy also occurs during chronic conditions in which Ang II is elevated in circulation including cardiovascular disease, renal disease, and certain cancers. While some of the mechanisms responsible for muscle atrophy during these are well known, such as elevated glucocorticoids, it is feasible that Ang II directly results in skeletal muscle atrophy. Further, previous evidence from our lab and others indicates that microRNAs play a central role in the regulation of muscle atrophy. Specifically, miR-23a directly targets and inhibits MuRF1 and Atrogin-1 mRNA, and during certain chronic conditions miR-23a is reduced resulting in increased muscle atrophy via increased expression of these key atrophy genes. Therefore it is feasible that Ang II could directly induce atrophy in muscle cells potentially through a miR-23a mediated mechanism.

PURPOSE: To test whether Ang II directly activates atrophic signaling in skeletal muscle cells.

METHODS: Cells from an immortal cell line derived from the skeletal muscle of mice (C2C12 cells) were cultured, differentiated into full myotubes, and treated with 500 nM of Ang II for 24 hrs. Following treatment, total RNA – including microRNA – was isolated, and cDNA synthesis and subsequent qPCR were performed. **RESULTS:** Ang II treatment of muscle cells resulted in a 25% decrease in miR-23a. Since miR-23a directly targets and inhibits MuRF1 and Atrogin-1 in muscle, we then measured MuRF1 and Atrogin-1 mRNA levels. Accordingly, Ang II treatment resulted in an 18% increase in MuRF1 mRNA expression and a 16% increase in Atrogin-1 mRNA expression. **CONCLUSION:** Collectively this data indicates that Ang II induces activation of key muscle atrophy related genes in skeletal muscle cells which may be occurring due to a reduction in miR-23a.

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