Atrogin-1 regulation in human and mouse skeletal myotubes

R.J. Stefanetti and A.P. Russell, Centre for Physical Activity and Nutrition Research, School of Exercise and Nutrition Sciences, Deakin University, 221 Burwood Highway, Burwood, VIC 3125, Australia.

Atrogin-1, an E3 ubiquitin ligase, is increased in numerous models of muscle atrophy and is seen as a potential therapeutic target to combat muscle wasting. While previous rodent studies have consistently shown that under catabolic conditions, Atrogin-1 is regulated by FoXO transcription factors, studies in atrophic human skeletal muscle do not support a dominant role of FoXO. Our aim was to identify potential transcriptional regulators of Atrogin-1 in human and mouse myotubes. Human primary and C2C12 myotubes were infected with a c-MyC, C/EBPa or PPARd adenovirus for 48 h. Atrogin-1 mRNA levels were increased by 72% and decreased by 52% with PPARd and C/EBPa over-expression, respectively. mRNA analysis in human myotubes is in progress. At the protein level there was a 74% and 46% increase in Atrogin-1 with C/EBPa over-expression in mouse and human myotubes, respectively. c-MyC and PPAR**d** over-expression increased Atrogin-1 protein by 46% and 62% in mouse myotubes respectively, while in human myotubes infection with c-MyC and PPARd decreased Atrogin-1 protein levels by 23% and 26% respectively. These preliminary results suggest that Atrogin-1 may be transcriptionally regulated by factors other than FoXO, and further highlight that Atrogin-1 regulation is species dependent. Future studies will determine direct transcriptional regulators of Atrogin-1 *via* luciferase assays.