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# Dynamic changes in the skeletal muscle proteome during denervation-induced atrophy

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Loss of neuronal stimulation enhances protein breakdown and reduces protein synthesis, causing rapid muscle mass loss. To elucidate the pathophysiological adaptations that occur in atrophying muscles, we used stable isotope labelling and mass spectrometry to accurately quantify protein expression changes during denervation-induced atrophy after sciatic nerve section in skeletal muscle. Additionally, mice were fed a SILAC diet containing $^{13}C_6$ lysine for four, seven, or eleven days to calculate relative levels of protein synthesis in denervated and control muscles. Ubiquitin remnant peptides (K-ε-GG) were profiled by immunoaffinity enrichment to identify potential substrates of the ubiquitin proteasomal pathway. Besides a protein expression profiling we used a pulse-SILAC labelling approach to identify differential Lys6 incorporation rates between control and denervated muscle. Enrichment of diglycine remnants identified 2100 endogenous ubiquitination sites and revealed a metabolic and myofibrillar protein diglycine signature, including myosin heavy chains (MyHC), myomesins and titin, during denervation. Comparative analysis of these proteomic datasets with known atrogenes using a random forest approach identified 92 proteins subject to atrogene-like regulation that have not previously been directly associated with denervation-induced atrophy. Comparison of protein synthesis and proteomic data indicated upregulation of specific proteins in response to denervation is mainly achieved by protein stabilization. This study provides the first integrated analysis of protein expression, synthesis and ubiquitin signatures during muscular atrophy in a living animal.

## Biography

Marcus Krüger studies Chemistry and received his PhD in Natural Sciences from the Univeristy of Halle-Wittenberg, working on basic-helix-loop-helix transcription factors in mouse. He did his Postdoctoral work at the Syddansk University in Odense working on quantitative mass spectrometry and stable isotope labeling of living animals. Since moving to the MPI for Heart and Lung Research in 2008, he became a Service Group Leader and in 2014 he was recruited as a Principle Investigator to the Institute for Genetics in Cologne. His current research interests includes quantitative mass spectrometryand the enrichment of posttranslational modifications in both health and disease related conditons.

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