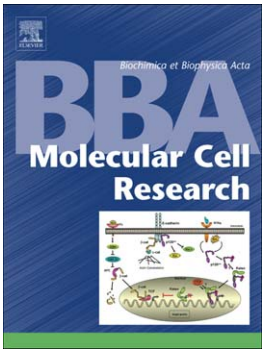

How does α-actinin-3 deficiency alter muscle function? Mechanistic insights into *ACTN3*, the 'gene for speed'

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PII: S0167-4889(16)30003-9
DOI: doi: 10.1016/j.bbamcr.2016.01.013
Reference: BBAMCR 17783

To appear in: *BBA - Molecular Cell Research*

Received date: 26 November 2015
Revised date: 15 January 2016
Accepted date: 19 January 2016

Please cite this article as: Fiona X.Z. Lee, Peter J. Houweling, Kathryn N. North, Kate G.R. Quinlan, How does α-actinin-3 deficiency alter muscle function? Mechanistic insights into *ACTN3*, the 'gene for speed', *BBA - Molecular Cell Research* (2016), doi: 10.1016/j.bbamcr.2016.01.013

How does α-actinin-3 deficiency alter muscle function? Mechanistic insights into *ACTN3*, the 'gene for speed'.

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Abstract

An estimated 1.5 billion people worldwide are deficient in the skeletal muscle protein α-actinin-3 due to homozygosity for the common *ACTN3* R577X polymorphism. α-Actinin-3 deficiency influences muscle performance in elite athletes and the general population. The sarcomeric α-actinins were originally characterised as scaffold proteins at the muscle Z-line. Through studying the *Actn3* knockout mouse and α-actinin-3 deficient humans, significant progress has been made in understanding how *ACTN3* genotype alters muscle function, leading to an appreciation of the diverse roles that α-actinins play in muscle. The α-actinins interact with a number of partner proteins, which broadly fall into three biological pathways – structural, metabolic and signalling. Differences in functioning of these pathways have been identified in α-actinin-3 deficient muscle that together contributes to altered muscle