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Role of sarcoplasmic reticulum junctional proteins in skeletal muscle strength

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Background

Skeletal muscle constitutes approximately 40% of body mass, and age-induced decrease of muscle strength impinge on daily activities and on normal social life in the elderly. Loss of muscle strength has been recognised as a debilitating and life threatening condition also in cachexia in cancer patients and in clinical conditions associated with prolonged bed rest. Skeletal muscle dihydropyridine receptors (Cav1.1) act as Ca2+ channels and voltage sensors to initiate muscle contraction by activating ryanodine receptors, the Ca2+ release channels of the sarcoplasmic reticulum. Cav1.1 activity is enhanced by a retrograde stimulatory signal delivered by the ryanodine receptor. JP45 is a membrane protein interacting with Cav1.1 and the sarcoplasmic reticulum Ca2+ storage protein calsequestrin (CASQ1).

We hypothesized that JP45 and CASQ1 form a signalling pathway which modulates Cav1.1 channel activity.

Materials and methods

We isolated flexor digitorum brevis (FDB) muscle fibres from JP45 and CASQ1 double knock-out mice (DKO) and tested whether there were differences in Ca2+ homeostasis between the different mouse lines.

Results

Our results show that Ca2+ transients evoked by tetanic stimulation in DKO fibres, result from massive Ca2+ influx due to enhanced Cav1.1 channel activity. This enhanced activity causes an increase of muscle strength both *in vitro* and *in vivo*.

Conclusions

We conclude that skeletal muscle contraction is strengthened through the modulation of Cav1.1 channel activity by JP45 and CASQ1.

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