Muscle weakness: New mutation identified

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New research, published in *The Journal of Physiology*, has identified a novel mutation associated with muscle weakness and distal limb deformities. The study demonstrates that muscle weakness experienced by persons with a regulatory protein tropomyosin mutation is directly related to a mechanism by which the mutant tropomyosin modulates contractile speed and force-generation capacity.

Dr. Julien Ochala and co-workers at the Department of Clinical Neurophysiology, University of Uppsala, in collaboration with scientists at the Department of Pathology, University of Göteborg, explored the mechanisms underlying the muscle weakness experienced by a woman and her daughter with a β-tropomyosin mutation, i.e., muscle weakness in the absence of macro or microscopic signs of muscle wasting.

The results from single fibre contractile measurements and in vitro motility analyses demonstrated a mechanism where tropomyosin modulates myosin-actin kinetics. A slower motor protein myosin attachment rate to and a faster detachment rate from actin, caused by the mutation, results in a reduced number of myosin molecules in the strong actin binding state and muscle weakness. The results also implicate a potential role of the regulatory protein tropomyosin in modulating contractile speed and force-generation under physiological conditions.

It is suggested that the findings at the gene, protein and muscle cell levels in this specific neuromuscular disorder will have a significant impact on our understanding of the disease pathogenesis and provide important information for future therapeutic strategies. Walter R. Frontera, an

independent expert, says: "Dr. Ochala and collaborators have published elegant proof of the clinical consequences of mutations in the regulatory proteins of skeletal muscles. Their data provide strong support for the dissociation between qualitative alterations in muscle contractility and quantitative evidence of muscle atrophy".

Source: Blackwell Publishing Ltd.