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Collagen XIII secures pre- and postsynaptic integrity of the neuromuscular synapse

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Abstract

© The Author 2017. Published by Oxford University Press. All rights reserved. Both transmembrane and extracellular cues, one of which is collagen XIII, regulate the formation and function of the neuromuscular synapse, and their absence results in myasthenia. We show that the phenotypical changes in collagen XIII knock-out mice are milder than symptoms in human patients, but the Col13a1 -/- mice recapitulate major muscle findings of congenital myasthenic syndrome type 19 and serve as a disease model. In the lack of collagen XIII neuromuscular synapses do not reach full size, alignment, complexity and function resulting in reduced muscle strength. Collagen XIII is particularly important for the preterminal integrity, and when absent, destabilization of the motor nerves results in muscle regeneration and in atrophy especially in the case of slow muscle fibers. Collagen XIII was found to affect synaptic integrity through binding the ColQ tail of acetylcholine esterase. Although collagen XIII is a muscle-bound transmembrane molecule, it also undergoes ectodomain shedding to become a synaptic basal lamina component. We investigated the two forms' roles by novel Col13a1 tm/tm mice in which ectodomain shedding is impaired. While postsynaptic maturation, terminal branching and neurotransmission was exaggerated in the Col13a1 tm/tm mice, the transmembrane form's presence sufficed to prevent defects in transsynaptic adhesion, Schwann cell invagination/retraction, vesicle accumulation and acetylcholine receptor clustering and acetylcholinesterase dispersion seen in the Col13a1 -/- mice, pointing to the transmembrane form as the major conductor of collagen XIII effects. Altogether, collagen XIII secures postsynaptic, synaptic and presynaptic integrity, and it is required for gaining and maintaining normal size, complexity and functional capacity of the neuromuscular synapse.

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