Laminin builds the neuromuscular synapse

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Like a plug and a socket, a nerve and a muscle fiber mesh at the neuromuscular junction. New work by Nishimune et al published in the *Journal of Cell Biology* reveals that an extracellular matrix protein called laminin shapes both sides of the junction to ensure they fit together.

A neuromuscular junction, or synapse, in a newborn mouse is functional but simple, with a globular nerve terminal meeting a flat, oval structure on the muscle fiber. As the animal matures, the nerve terminal branches into a claw shape, and the muscle side contorts into a matching conformation. But what coordinates these changes so the two sides mirror each other? The researchers think that one molecule in the synapse sculpts both sides.

Their chief suspect was the synapse-spanning protein laminin. Made by muscle and forming part of the sheath that covers muscle, the laminin protein has different domains called alpha, beta, and gamma chains. Previous work had shown that the beta2 chain of laminin spurs differentiation of the nerve terminal. The team has now found evidence that the alpha chains of laminin influence post-synaptic patterning. For example, maturation of the muscle side slowed in mice lacking the alpha5 chain of laminin in their muscles.

The researchers discovered that cell surface receptor molecules that recognize and bind laminin, are corralled by laminin on the muscle side of the synapse. These receptors, in turn, gather other receptors that respond to signals from the nerve. Overall, the work suggests that the beta and alpha chains of laminin together influence pre-synaptic and post-

synaptic development, thus providing a way to coordinate maturation of the sending and receiving sides of the synapse.

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