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# Channels News & Views

## It takes two to tango

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The vertebrate inner ear has time and again surprised neurobiologists by adding new wrinkles to known mechanisms of cellular signaling. Among those surprises, was the discovery that nicotinic acetylcholine receptors (related to those that excite muscle) inhibit cochlear hair cells when acetylcholine (ACh) is released from efferent neurons. Inhibition occurs because calcium entering through the ionotropic receptor binds to nearby calcium-dependent SK2 potassium channels that hyperpolarize and shunt the hair cell membrane. Now Scholl and co-authors provide evidence for molecular interactions that support this functional coupling.[1] They show that SK2 channels and the α9α10 subunits of the hair cell acetylcholine receptor (AChR) co-immuno-precipitate after expression in Xenopus oocytes, demonstrating a physical association between these essential elements of the post-synaptic complex. From cochlear lysates they also show that SK2 immuno-precipitates with α-actinin-1, an actin cross-linking protein. Furthermore, SK2 and α-actinin-1 label the same region of hair cells, postsynaptic to the efferent terminal contact.

These observations gain additional significance from the unusual ultrastructure of efferent synapses on hair cells.[2,3] These are cisternal synapses like the cholinergic inputs to cranial motor neurons,[4] in which a near-membrane reticulum aligns with the presynaptic contact. The exact role of the postsynaptic cistern remains unclear, but its precise alignment with the plasma membrane5 requires extensive molecular attachments. Scholl et al. found that the levels of 2 splice variants of the SK2 channel varied during development, and were differentially sensitive to calcium-calmodulin that regulates intermolecular binding of the channel. Thus, alternative splicing of the SK2 message is a potential mechanism for activity-dependent stabilization of cholinergic efferent synapses on hair cells.

These observations help solidify emerging notions that SK2 channels not only mediate hair cell inhibition, but also serve as arbiters of synapse formation and stabilization. The postsynaptic cholinergic complex becomes functional with the acquisition of SK2 channels during development,[6] while hair cells of SK2-null mice lose efferent innervation and do not respond to ACh.[5,7,8]

It remains a mystery why hair cells have adopted this complicated form of synaptic inhibition. But thanks to the work of Scholl et al., we are gaining a better appreciation of the role that SK2 channels play as cornerstones of that complexity.

**References**

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