NEWS

Molecular mechanisms: Autism gene tied to neuronal wiring

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An autism-linked protein called IL1RAPL1, or interleukin-1 receptor accessory protein-like 1, helps wire neurons together, according to two studies published in late September[1,2].

Studies have identified mutations in the gene encoding IL1RAPL1 in individuals who have autism[3] or intellectual disability[4]. The new work shows that IL1RAPL1 triggers the development of **synapses**, the junctions between neurons.

Malfunctions at the synapse are thought to play a role in autism, suggesting that ILRAPL1 mutations could underlie the social and cognitive deficits associated with the disorder.

The two new studies both find that IL1RAPL1 is localized at the tips of dendrites, the signal-receiving ends of neurons. Another protein, called protein tyrosine phosphatase delta, or PTP?, sits at the ends of axons, the signal-transmitting ends of partner neurons.

Binding between IL1RAPL1 and PTP? induces events that build a synapse between two neurons, according to one study published in the *Journal of Neuroscience*[1]. For example, proteins needed for transmitting chemical signals cluster at the axon tip and **spine-shaped protrusions** appear along the dendrite.

A second study, published online in *Human Molecular Genetics*[2], found similar effects. It also reported that a third player, Rho GTPase-activating protein 2 (RhoGAP2), interacts with IL1RAPL1 within the cell to promote spine formation.

These novel interactions add to the growing catalog of molecular pairings that help construct synapses, particularly those that promote excitatory signals between neurons. Other interactions involve autism-related proteins such as **neurexins and neuroligins**.

References:

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2: Valnegri P. *et al. Hum. Mol. Genet*. Epub ahead of print (2011) **PubMed**

3: Piton A. *et al. Hum. Mol. Genet.* **17**, 3965-3974 (2008) **PubMed**

4: Carrié A. *et al. Nat. Genet.* **23**, 25-31 (1999) **PubMed**