SYNAPTIC PLASTICITY

# Spiny problems in MRX

Cases of nonspecific X-linked mental retardation (MRX) in humans have been attributed to mutations in 11 different genes. Three of these genes code for molecules that interact with the Rho signalling pathway, which is known to regulate the actin cytoskeleton. So, how might Rho pathway dysfunction lead to the cognitive deficits that are associated with MRX? In a new study reported in *Nature Neuroscience*, Govek and colleagues provide some answers to this question.

In one family, MRX was found to be associated with a mutation in the gene that encodes a Rho-GTPase activating protein called oligophrenin-1 (OPHN-1). Govek *et al.* showed that in the rat brain, puncta of oligophrenin-1 were present at both presynaptic and postsynaptic sites, perhaps indicating a role in synaptic development and/or function. In the postsynaptic compartment, the protein was co-localized with F-actin, which is a key component of the dendritic spine cytoskeleton.

The authors used two approaches — antisense RNA and RNA interference — to knock down *Ophn-1* gene function in hippocampal slices from rats at postnatal day 4. They found that the mean dendritic spine length was significantly reduced on neurons that had been transfected with an *Ophn-1* antisense construct or small interfering RNAs. This knock-down phenotype could be mimicked by overexpression of RhoA, but not by overexpression of the other Rho family members Rac1 and Cdc42. In addition, the Ophn-1 knock-down phenotype was rescued by inhibiting Rho-kinase, a downstream target of RhoA that was previously shown to be involved in neurite retraction.

These findings indicate that Ophn-1 normally maintains dendritic spine length by negatively regulating the RhoA/Rho-kinase signalling pathway. Govek *et al.* also showed that Ophn-1 contains a binding site for Homer, an adaptor protein that provides a link between glutamate receptor activation and cytoskeletal rearrangements. Therefore, Ophn-1 might be part of a pathway that stabilizes spines in response to synaptic activity. This points towards a model for MRX, in which the defects in spine morphogenesis and stabilization that result from loss of Ophn-1 function impair the brain's capacity for synaptic plasticity, which in turn leads to deficits in learning and memory.

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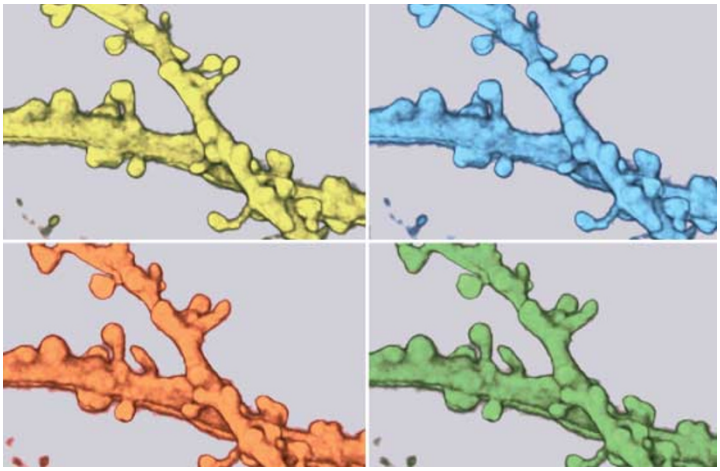
**References and links**

**ORIGINAL RESEARCH PAPER** Govek, E.-E. *et al.* The X-linked mental retardation protein oligophrenin-1 is required for dendritic spine morphogenesis. *Nature Neurosci.* **7**, 364–372 (2004)

**FURTHER READING** Yuste, R. & Bonhoeffer, T. Genesis of dendritic spines: insights from ultrastructural and imaging studies. *Nature Rev. Neurosci.* **5**, 24–34 (2004).

# IN BRIEF

GENES AND BEHAVIOUR

## Parallel *FoxP1* and *FoxP2* expression in songbird and human brain predicts functional interaction.

Teramitsu, I. *et al. J. Neurosci.* **24**, 3152–3163 (2004)

## *FoxP2* expression in avian vocal learners and non-learners.

Haesler, S. *et al. J. Neurosci.* **24**, 3164–3175 (2004)

*FOXP2* is a forkhead gene that was identified as the gene that is mutated in a family with an autosomal-dominant speech and language disorder. These two papers provide evidence that it might also be involved in learned vocalisation in birds. Teramitsu *et al.* show that *FoxP2* and the forkhead family member *FoxP1* are expressed in an overlapping pattern in the songbird, in a corticostriatal pattern that reflects that structural abnormalities seen in the human patients and that is similar to the localization of *FOXP1* and *FOXP2* in the human fetal brain. Haesler *et al.* find that *FoxP2* expression in songbirds varies seasonally, being stronger at times when vocal learning occurs in brain structures that are associated with song learning.

NEURAL DEVELOPMENT

## A role for ligand-gated ion channels in rod photoreceptor development.

Young, T. L. & Cepko, C. L. *Neuron* **41**, 867–879 (2004)

Taurine is present in the developing vertebrate CNS and has been shown to potentiate the development of rod photoreceptors. Young and Cepko now show that this effect is probably mediated by glycine α2 and $GABA_A$ (γ-aminobutyric acid, subtype A) receptors. Strychnine (a glycine receptor antagonist) and bicuculline (a GABA receptor antagonist) inhibited the ability of taurine to induce the production of rod photoreceptors, and a gain-of-function study showed that signalling through glycine α2 receptors caused cells to leave mitosis and increased the number of rods. Consistent with this, a targeted knockdown of glycine α2 receptors led to a decrease in the number of rods but an increase in other retinal cells.

SYNAPTIC PHYSIOLOGY

## The structural organization of the readily releasable pool of synaptic vesicles.

Rizzoli, S. O. & Betz, W. J. *Science* **303**, 2037–2039 (2004)

The authors labelled the readily releasable pool (RRP) — those vesicles that are recruited first during neuronal activity — with a fluorescent dye, FM1-43, that is taken up by recycling vesicles. Although it might be expected that the RRP would consist of those vesicles closest to the presynaptic membrane, Rizzoli and Betz found that the labelled vesicles were scattered throughout the nerve terminal, except for the centre of the cluster of vesicles. So, it seems that vesicle recruitment does not depend on proximity to the release sites, but instead involves a different mechanism of mobilization.