WEB WATCH

Educational efforts

- IBRO-edu: http://www.ibroedu.org

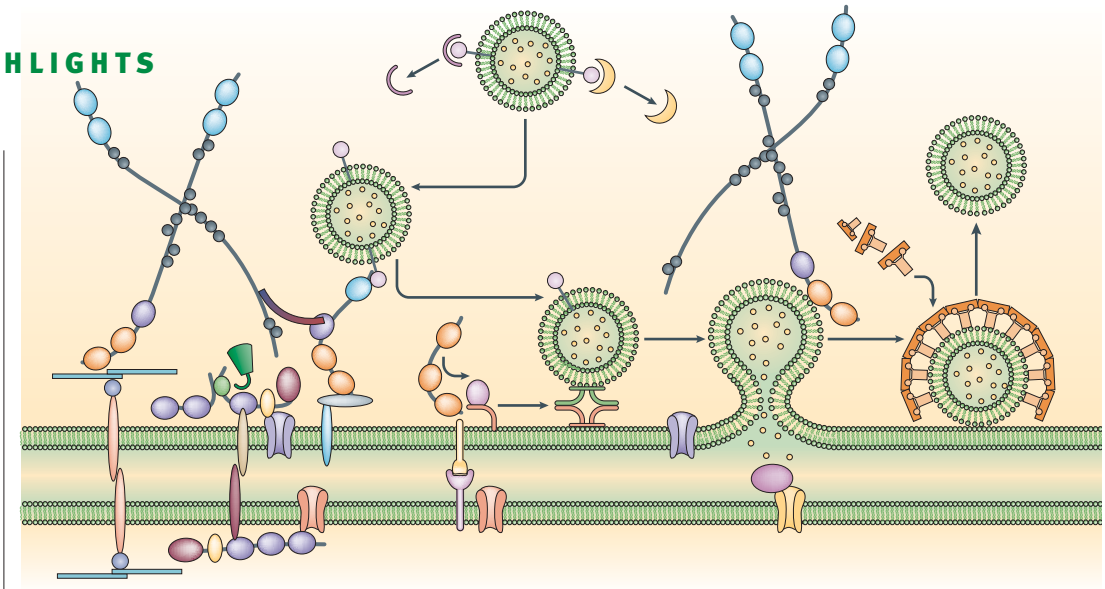
IBRO — the International Brain Research Organization — is undertaking an ambitious project on its recently relaunched website. 'IBRO-edu' is a web resource that, in the short term, aims to provide a registry of educational resources related to neuroscience that are already available on the internet. In the longer term, IBRO intends to add to the educational tools by soliciting and creating new content — presumably to fill in any gaps that are left uncovered.

The creators of the site are inviting authors of educational material that is posted on the Web to submit it for inclusion in IBRO-edu. If you have an educational website that could be included, you can register it online. The quality of the resources that are included will be ensured by the editorial committee, headed by the Editor-in-Chief of IBRO-edu, Ante Padjen (McGill University, Montréal, Canada).

The site is now up and running, with some material already included. You can search for material related to a particular topic, or you can browse through subject areas. Although coverage is rather patchy at present, there is some useful material on the site. However, it will only fulfil its potential if the creators of the vast amounts of educational material already present on the web join in by submitting details of their sites to the organizers.

IBRO's shiny new site also has plenty of other essential reading, particularly for younger neuroscientists. The 'Map and Compass' section, which bills itself as a 'survival guide for young neuroscientists', contains tips on writing a grant, preparing a poster, submitting work to journals, and more.

Rachel Jones



SYNAPTIC PHYSIOLOGY

A scaffolder at the active zone

Successful synaptic transmission involves intricate interactions of an array of proteins at the active zone. How these biochemical interactions are translated into physiological output is still largely unknown. Reporting in *Neuron*, Calakos and colleagues provide a detailed analysis of the molecular mechanism whereby an active zone protein, RIM1α, regulates neurotransmitter release.

RIM1α is localized at the presynaptic active zone and has been implicated in short- and long-term plasticity. It contains several protein-binding domains, and is regarded as a scaffold that interacts with many proteins that are involved in the late stages of neurotransmitter release. Previous studies in mice and worms indicate that RIM1α functions at a stage after the docking of synaptic vesicles at the active zone. However, several regulated steps lead up to transmitter release, including vesicle priming, binding of calcium to presynaptic sensors and fusion of vesicles with the plasma membrane, so which steps require RIM1α? Calakos *et al.* addressed this issue by carrying out a detailed analysis of presynaptic funtion in RIM1α-deficient neurons .

The authors applied the whole-cell recording technique to hippocampal autaptic cultures prepared from RIM1α$^{-/-}$ mice. They noted that RIM1α$^{-/-}$ synapses had a 50% reduction in excitatory postsynaptic charge, which could result from a decrease in synapse numbers, postsynaptic receptor response or the synaptic probability of neurotransmitter release (P_r). RIM1α$^{-/-}$ and wild-type mice had the same number of synapses, and there was no difference in the amplitude or frequency of miniature excitatory postsynaptic currents (mEPSCs), so the authors conjectured that compromised synaptic responses in RIM1α$^{-/-}$ neurons were probably a result of decreased P_r.

RIM1α binds directly to Munc13-1, an active zone protein that is essential for synaptic vesicle priming, so Calakos *et al.* asked whether priming was affected in the absence of RIM1α. The priming process influences P_r by determining the number of vesicles in the 'readily releasable pool' (RRP). The authors found that the RRP was reduced by 50% in RIM1α$^{-/-}$ synapses, and that there was no evidence for a deficiency in subsequent vesicle exocytosis.

Having established RIM1α as a priming factor, Calakos *et al.* turned to examine the effect of RIM1α deficiency on short-term plasticity. They found that when RIM1α$^{-/-}$ synapses were challenged with high-frequency stimulus trains, they could sustain responses throughout, whereas there was a 50% reduction in EPSC amplitude in wild-type cultures. Intriguingly, although there was a reduction in initial P_r in RIM1α$^{-/-}$ synapses, P_r at steady state during high-frequency activity was not altered. The authors discovered that this was due not to a difference in activity-dependent refilling of RRP, but to an increase in the vesicle release probability.

Previous studies have indicated that calcium has an important role in regulating interactions of RIM1α with other synaptic proteins. Therefore, Calakos *et al.* suspected that calcium-dependent neurotransmitter release might be abnormal in RIM1α$^{-/-}$ synapses. They found that although the overall calcium responsiveness was unchanged, the 'asynchronous' (slow) component of calcium-dependent release was markedly reduced in RIM1α-deficient synapses.

This detailed analysis shows that RIM1α is a key regulator of vesicle maturation at the active zone, from priming to calcium-dependent triggering of synaptic vesicle fusion. These results support the idea that RIM1α acts as a scaffold to localize various active-zone components and to integrate their actions. The study also provides the first direct link between a synaptic protein and the poorly understood processes that control asynchronous neurotransmitter release.

Jane Qiu

References and links

ORIGINAL RESEARCH PAPER Calakos, N. *et al.* Multiple roles for the active zone protein RIM1α in late stages of neurotransmitter release. *Neuron* **42**, 889–896 (2004)

FURTHER READING Rizo, J. & Sudhof, T. C. Snares and Munc18 in synaptic vesicle fusion. *Nature Rev. Neurosci.* **3**, 641–653 (2002)