

LEARNING AND MEMORY

ORB2 marks the spot

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The synaptic tagging hypothesis posits that recently activated synapses are marked with a 'tag' that facilitates the capture of proteins required for the maintenance of long-term potentiation and the formation of long-term memory. The nature of the postulated tags has been elusive, but now Keleman *et al.* show that the cytoplasmic-polyadenylation-element-binding (CPEB) protein

ORB2 has the predicted characteristics of a putative synaptic tag in *Drosophila melanogaster*.

The authors generated mutant flies in which the glutamine-rich region of ORB2 was deleted. The flies were used to test learning and memory in a courtship conditioning paradigm: when exposed to females that have recently mated, male flies learn to suppress subsequent courtship behaviour towards such 'unreceptive' females but not towards receptive virgins.

Keleman *et al.* demonstrated that mutant males had normal courtship behaviour and short-term memory for unreceptive females. However, unlike wild-type flies, they showed no long-term suppression of courtship behaviour. Further analysis revealed that the mutant flies' memory was intact up to 6 hours after training but was lost by 9 hours.

Although in wild-type flies ORB2 is expressed throughout the nervous system, courtship behaviour in the mutant flies could be rescued by reintroducing *orb2* to neurons

expressing the male isoform of *fruitless* (*fru*) — specifically, the γ neurons in mushroom bodies, which are required for olfactory memory. Moreover, it was shown that *orb2* function in these neurons is acutely required during or shortly after training.

These findings indicate that ORB2 expression in neurons that are associated with olfactory memory is required for long-term, but not short-term, olfactory memory. Unlike other CPEB proteins, ORB2 has not yet been shown to regulate local mRNA translation, which would be a fundamental function for the putative synaptic tag. Nevertheless, this study suggests that ORB2 might mark recently activated synapses and help to consolidate memories by modulating local protein synthesis.

Leonie Welberg

ORIGINAL RESEARCH PAPER Keleman, K. *et al.*
Function of the *Drosophila* CPEB protein Orb2 in
long-term courtship memory. *Nature Neurosci.*
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