The Ataxin-2 protein is required for microRNA function and synapse-specific long-term olfactory habituation

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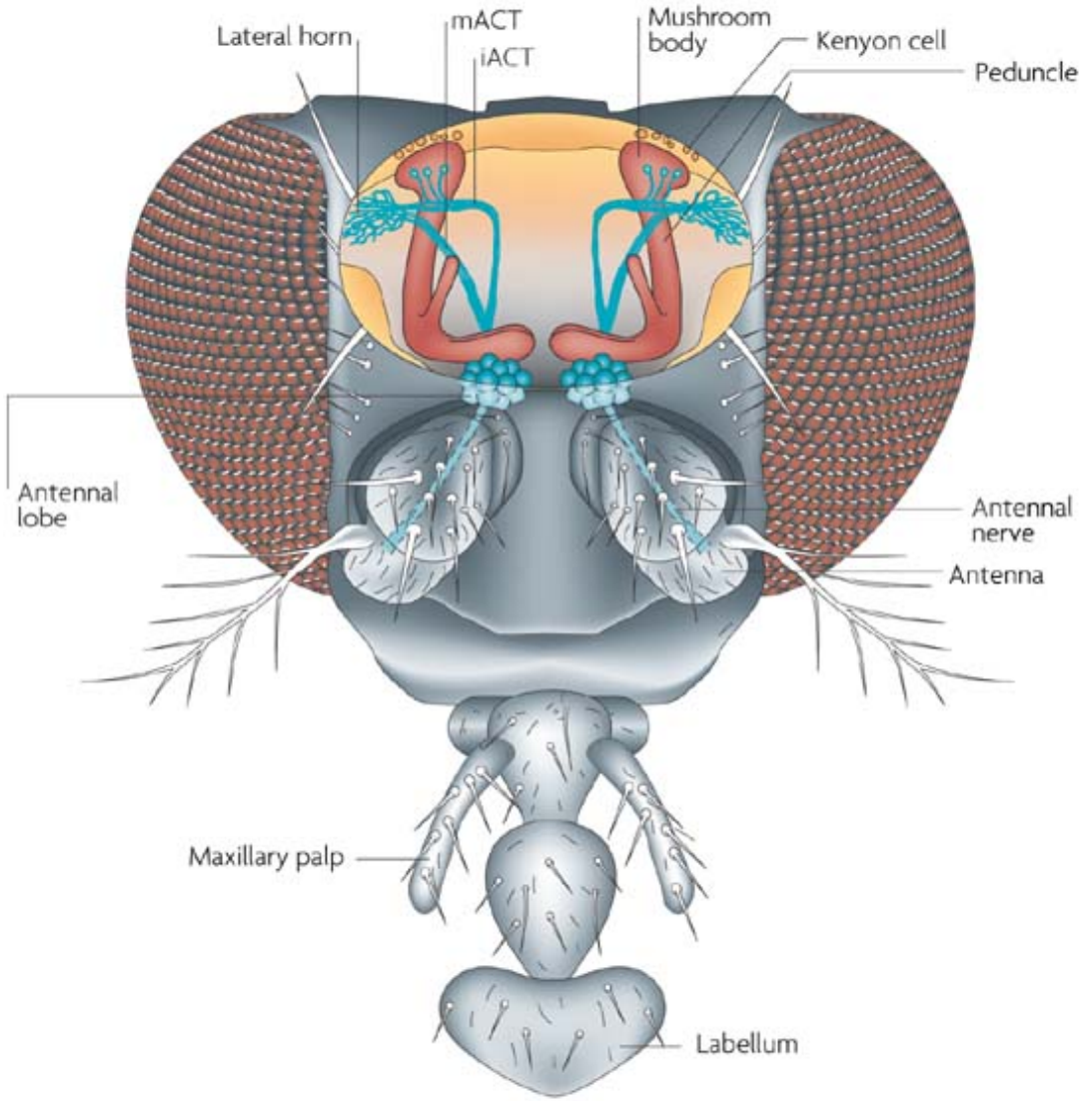

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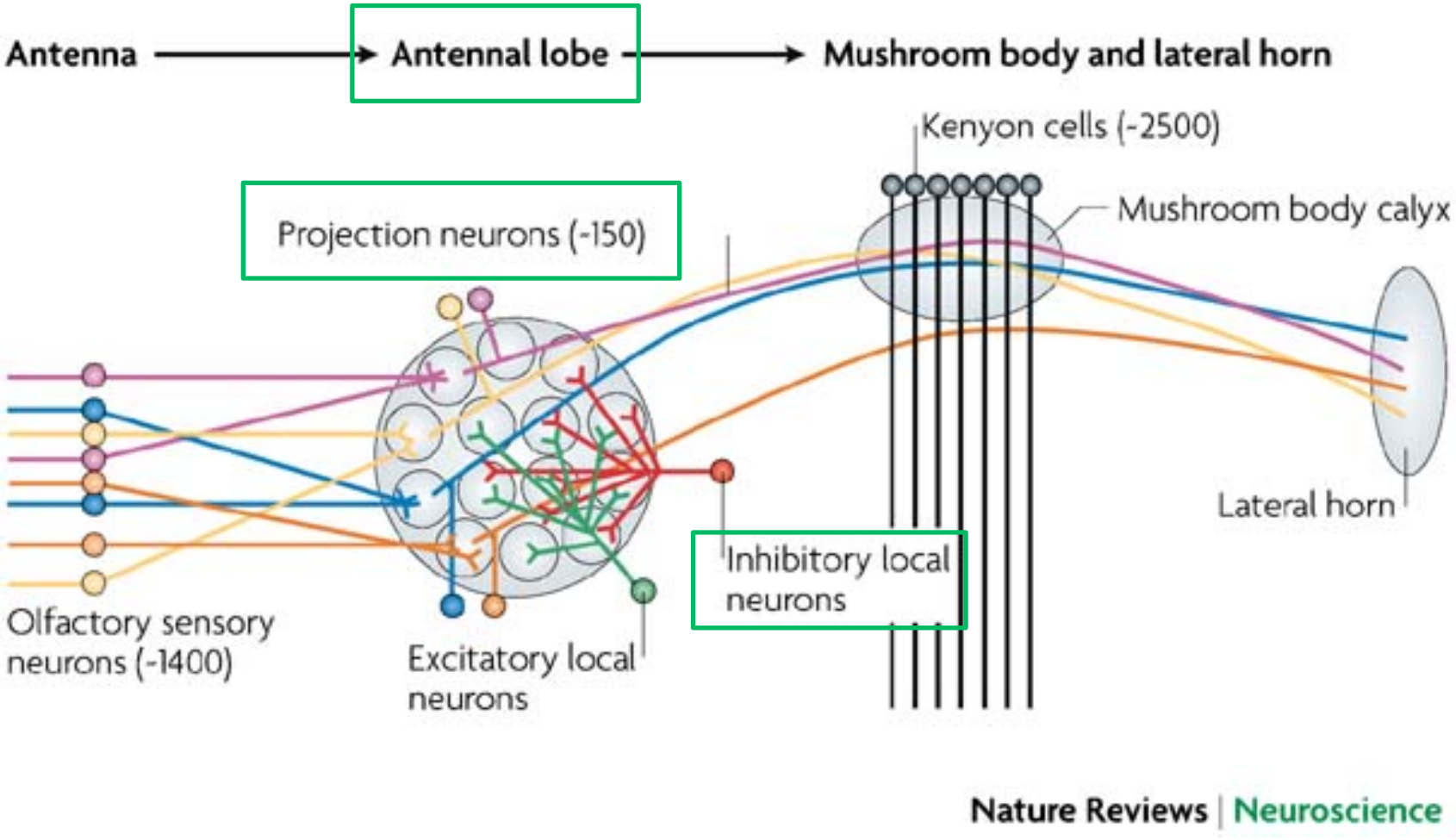

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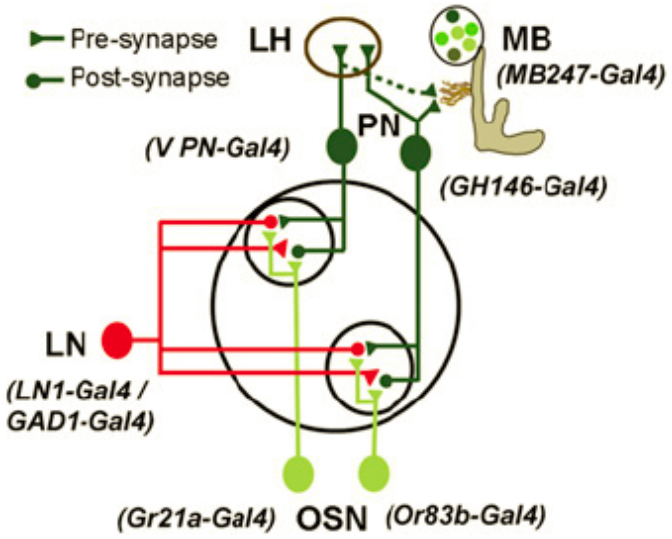
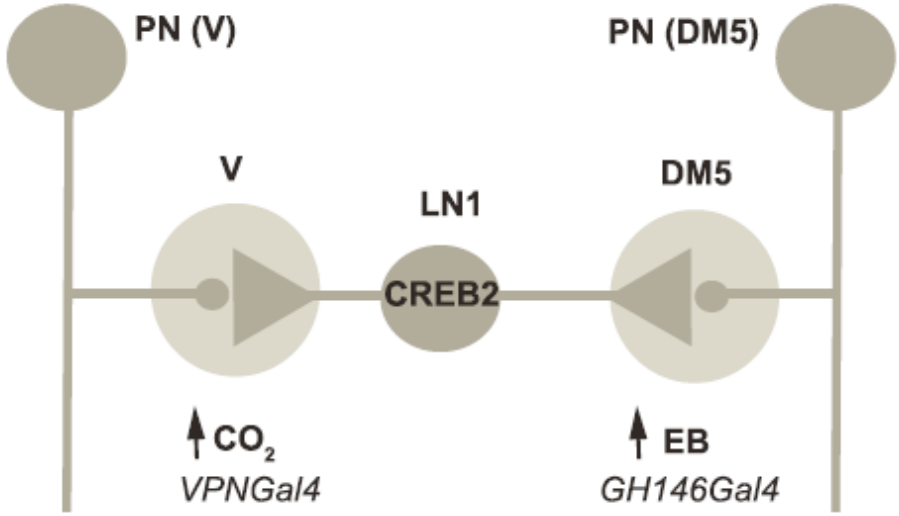
Circuitry involved in the experiments





- From Das et al., 2011

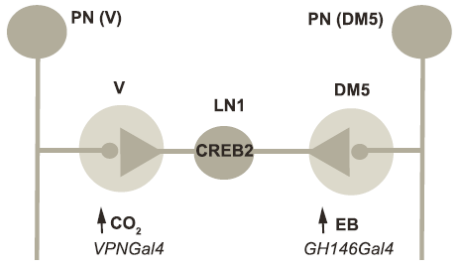
Behavioral Test

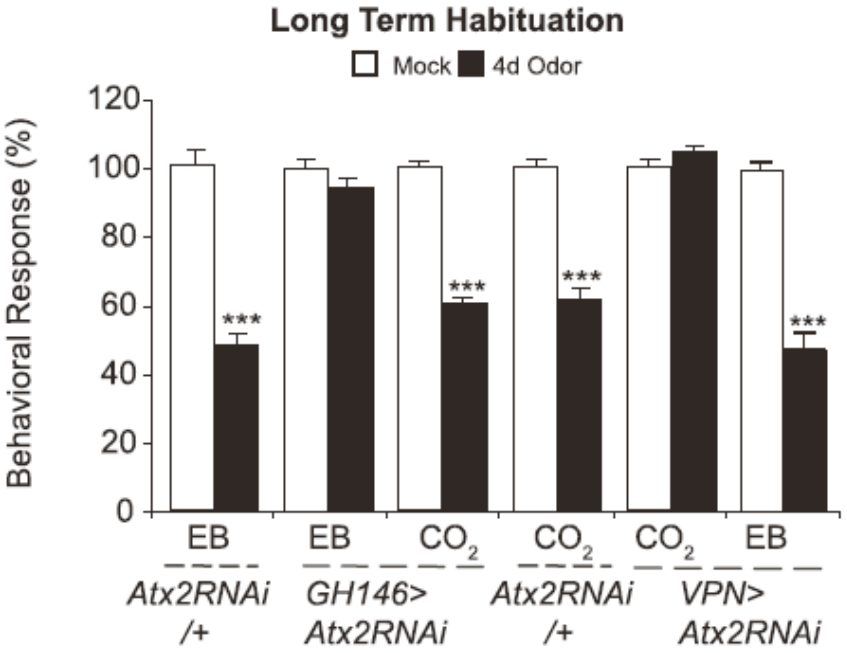
Y- Maze

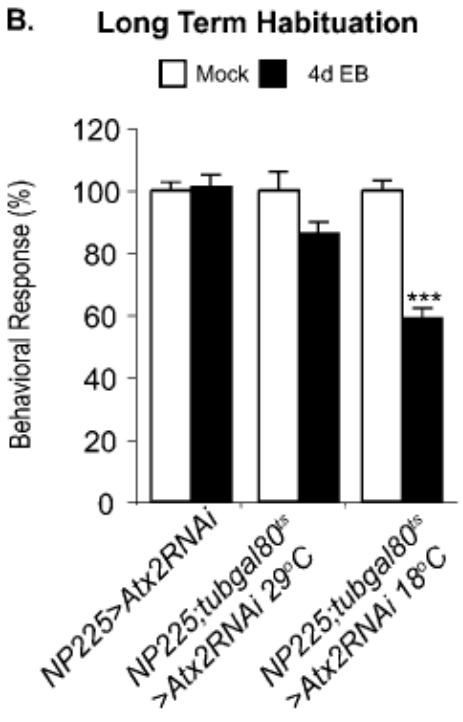
STH:
15% CO_2 or 5% EB
30 min exposure

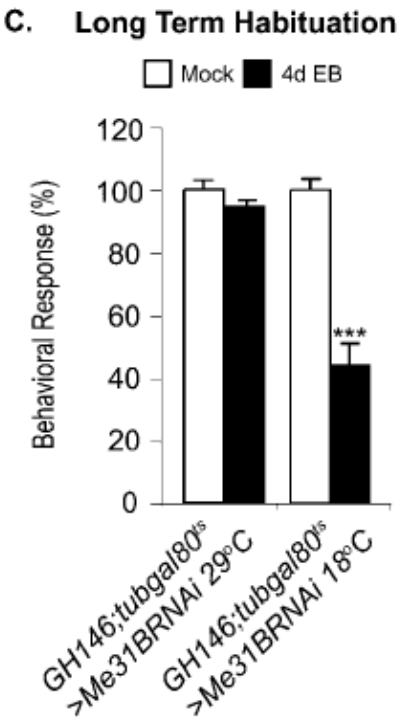
LTH:
5% CO_2 or 20% EB
4 day exposure

Atx2 is required for LTH

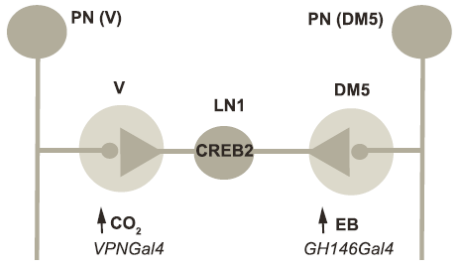


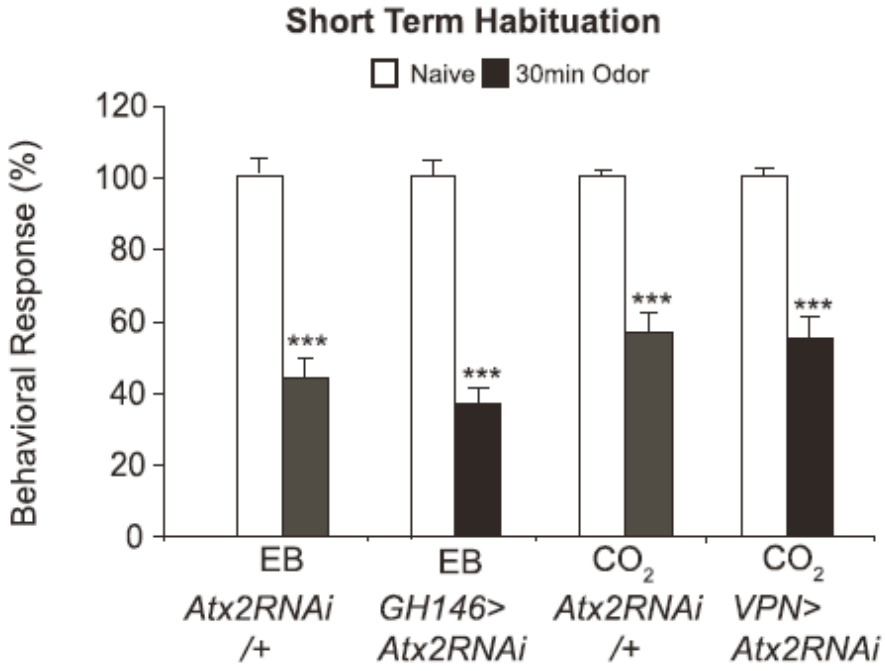




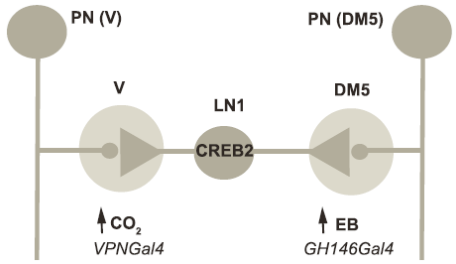


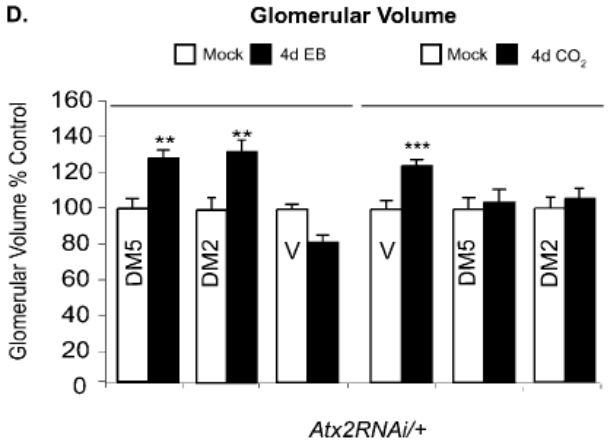
Atx2 is required for LTH but not STH. This is great news for Atx2, but bad news for Marc.

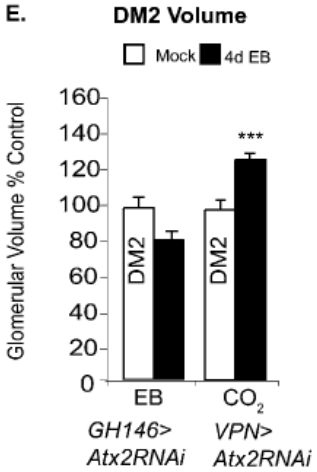


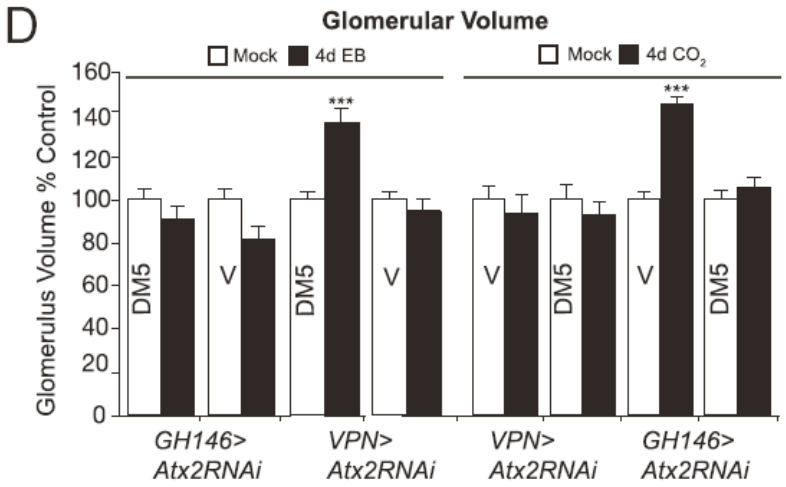


Atx2 is also required for structural plasticity associated with LTH

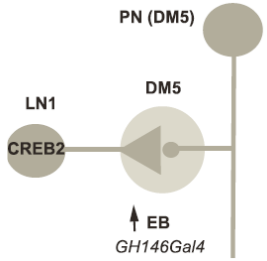


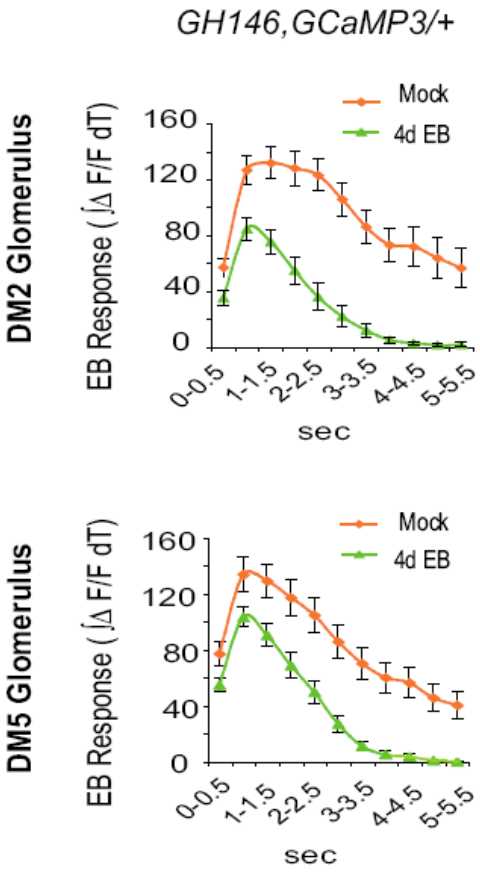


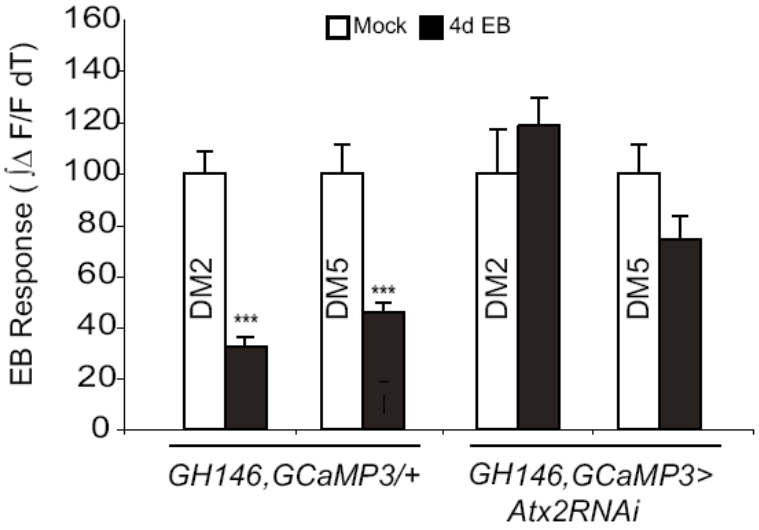




Atxn2 is required for normal function of Ca++ pathways that produce synaptic plasticity



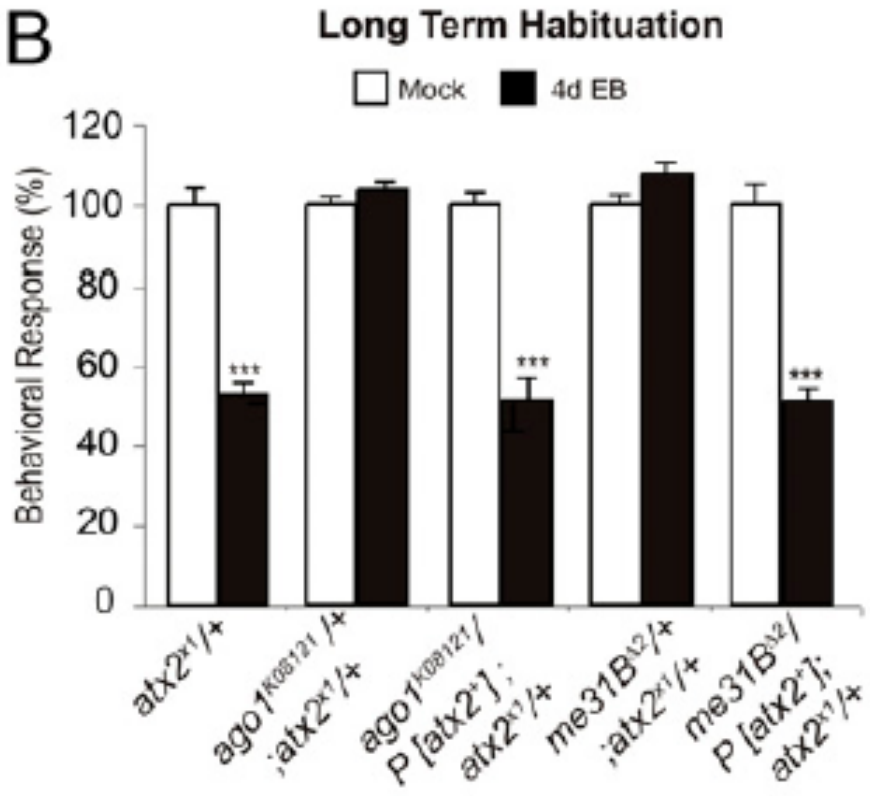


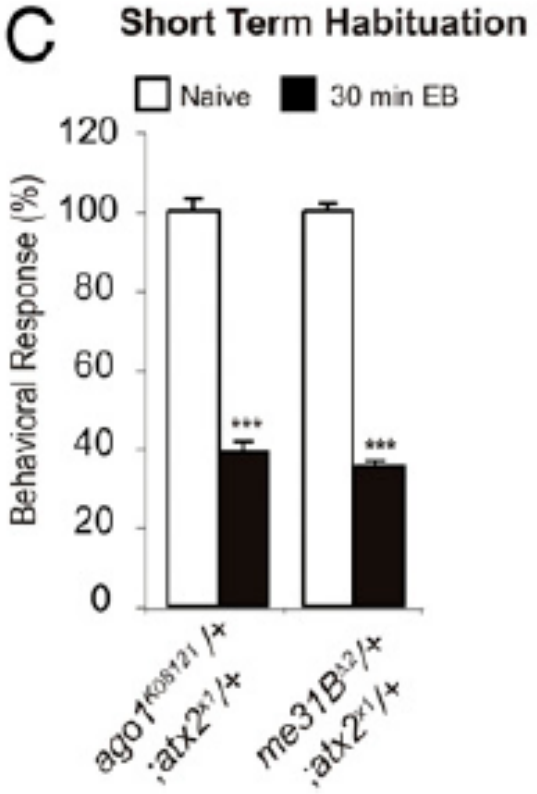


Atx2 interacts with Me31B and PABP which act with other miRNA pathway proteins, GW182 and Argonaute

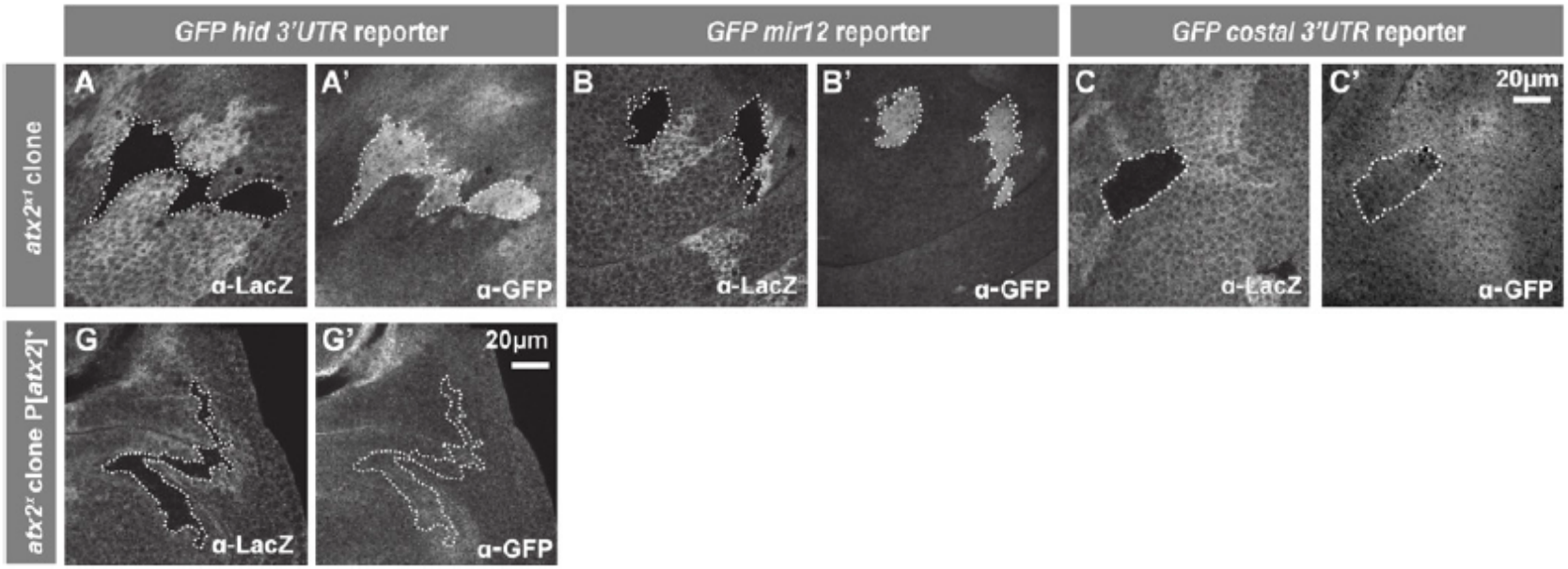
15. Nonhoff U, et al. (2007) Ataxin-2 interacts with the DEAD/H-box RNA helicase DDX6 and interferes with P-bodies and stress granules. *Mol Biol Cell* 18:1385–1396.
16. Satterfield TF, Pallanck LJ (2006) Ataxin-2 and its Drosophila homolog, ATX2, physically assemble with polyribosomes. *Hum Mol Genet* 15:2523–2532.
17. Ciosk R, DePalma M, Priess JR (2004) ATX-2, the *C. elegans* ortholog of ataxin 2, functions in translational regulation in the germline. *Development* 131:4831–4841.
19. Ralser M, et al. (2005) An integrative approach to gain insights into the cellular function of human ataxin-2. *J Mol Biol* 346:203–214.

LTH, but not STH, is disrupted in double heterozygote animals (Atx2 + Ago1 or Atx2 + Me31B). Specifically, by a defect in Atx2.

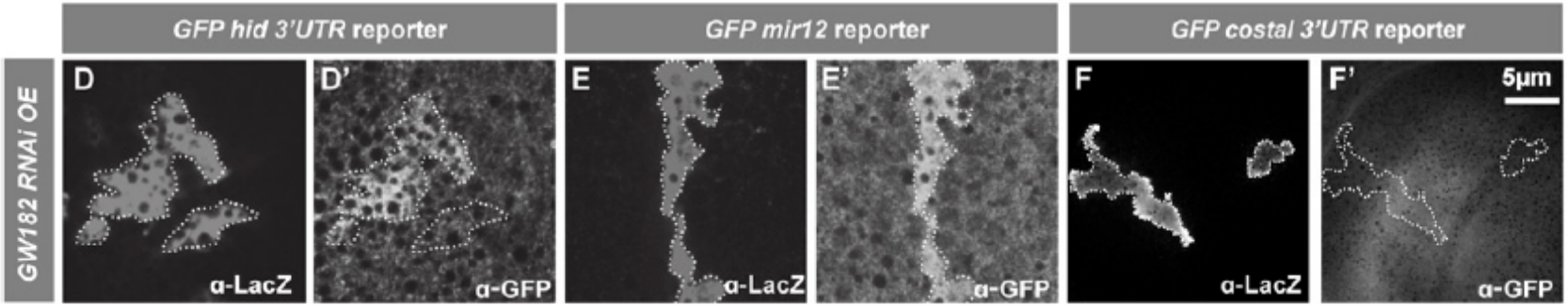




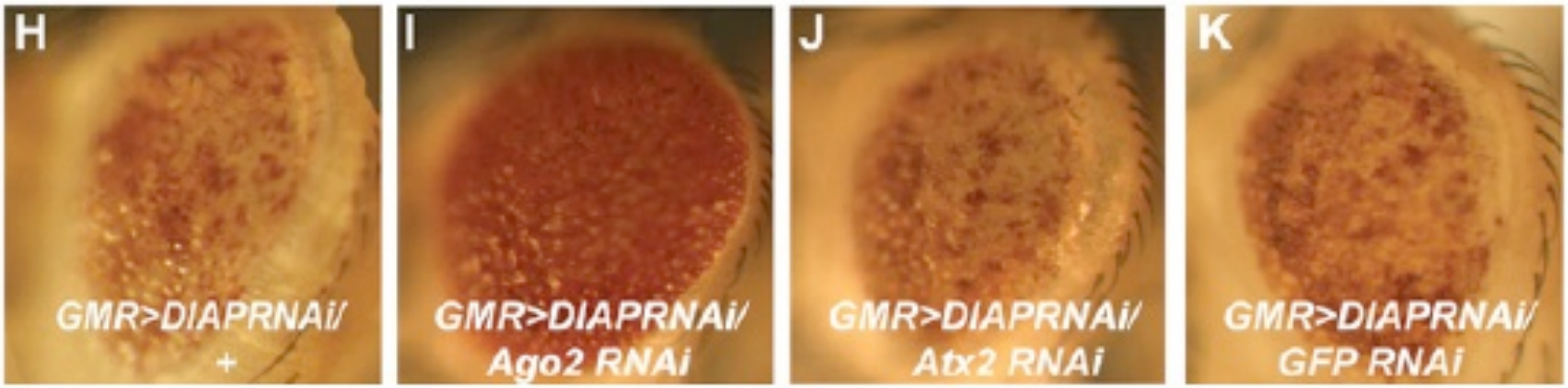
Knocking down Atx2 causes increased expression in miRNA reporters *hid* and *mir12* but not *costal*



Two possible miRNA pathways: one uses Ago1-RISC dependent upon GW182, the other uses Ago2-RISC independent of GW182 (the latter is poorly understood)



Knock-down of caspase inhibitor of apoptosis (DIAP) uses the Ago2 –dependent miRNA pathway. Ago2 RNAi rescues the phenotype; Atx2 RNAi does not. This further suggests Atx2 is only involved in the Ago1-RISC miRNA pathway.



Three models for regulation of miRNA by Atx2

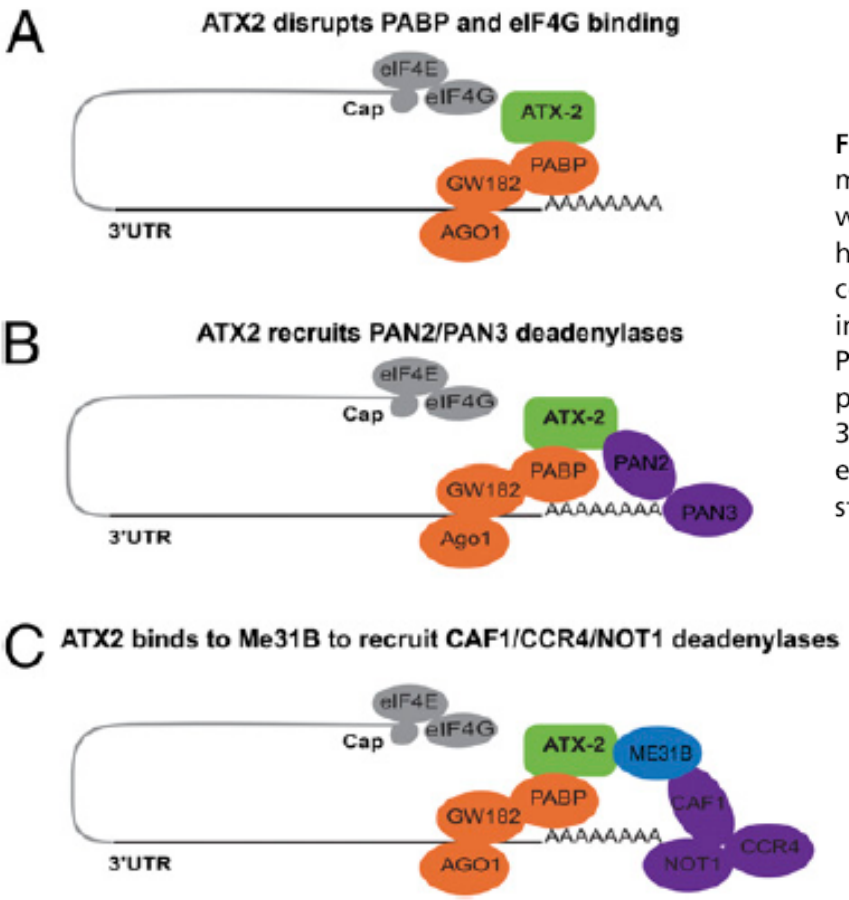
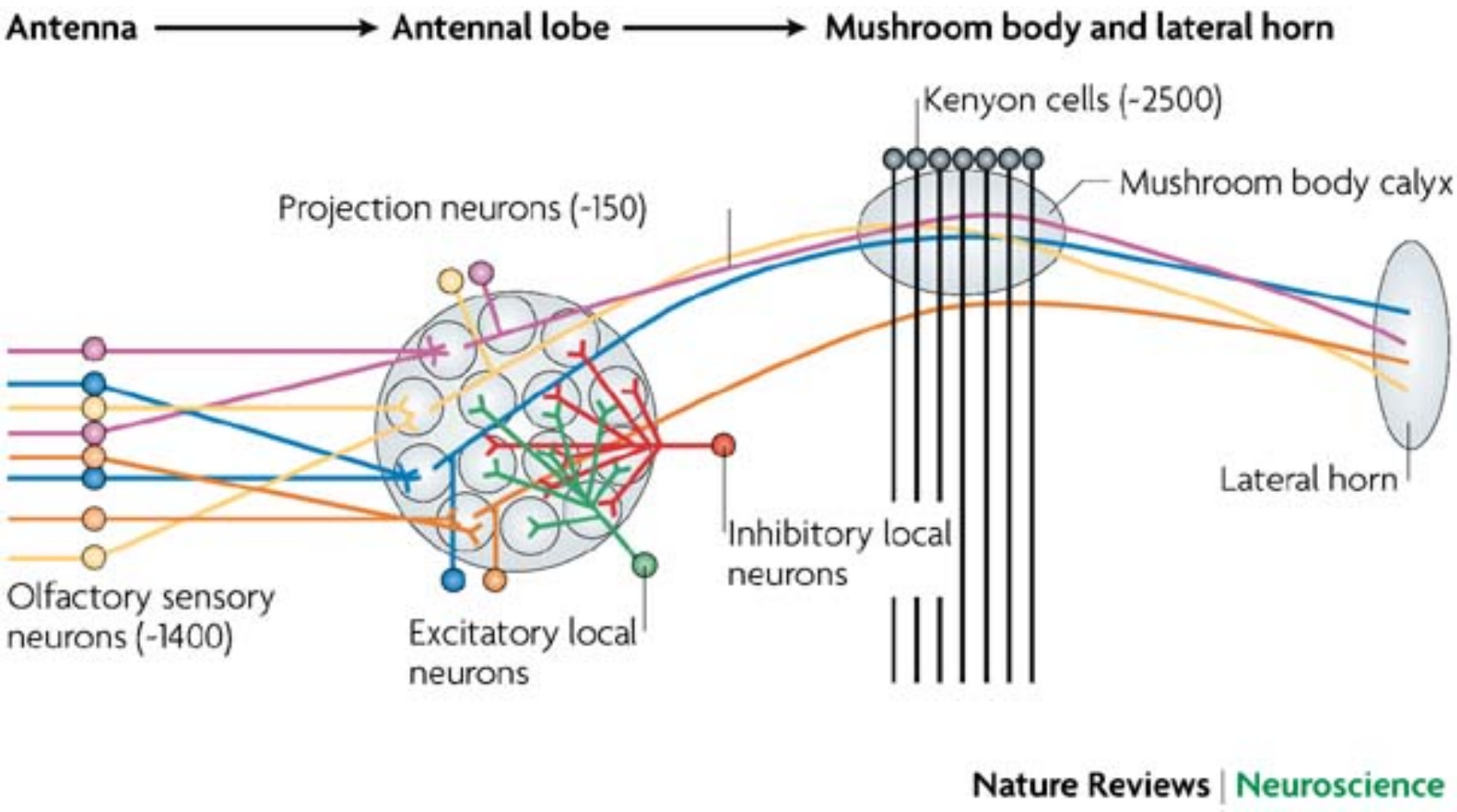


Fig. 5. Three models for Atx2 regulation of miRNA function. It is likely that miRNAs and RISC factors such as Me31B help recruit Atx2 to an mRNA's 3′ UTR, where Atx2 interacts with PABP. The recruitment of Atx2 also may be enhanced by additional sequence-specific mRNA-binding proteins or by RISC cofactors not considered in these models. (*A*) Atx2 binding to PABP inhibits interactions between the mRNA 5′ Cap and 3′ polyA tail mediated by eIF4G–PABP interactions necessary for efficient translation. (*B*) Atx2 recruits the poly(A) nuclease 2/3 (PAN2/PAN3) deadenylase complex that destabilizes the 3′ UTR. (*C*) Alternatively, Atx2 via Me31B recruits the CCR4/CAF1/NOT1 deadenylase complex, which may enhance mRNA recruitment to P-bodies for storage or degradation.

- Can we make any associations with Atx2 and its potential role in the mammalian olfactory system?



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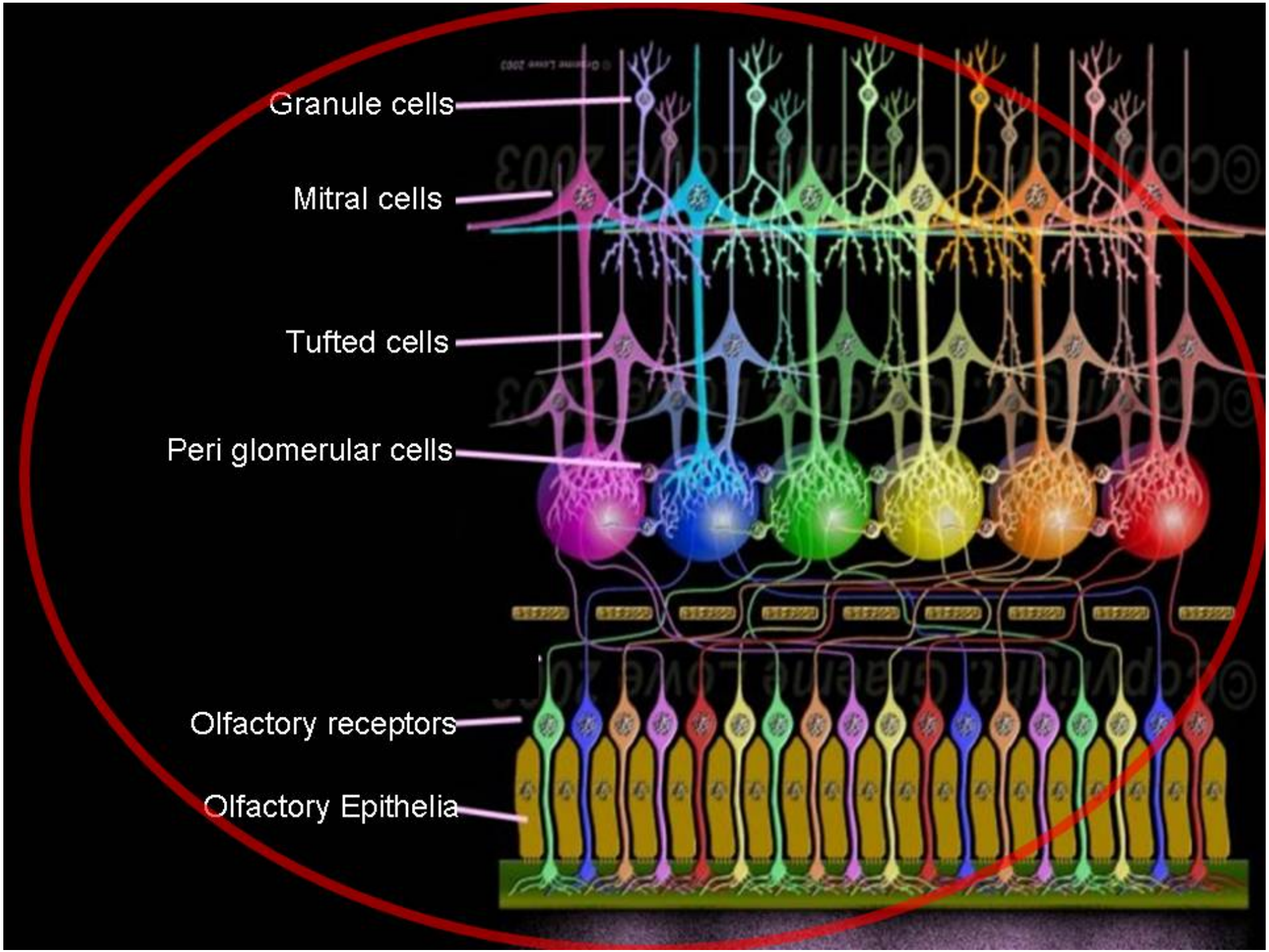
Granule cells
Mitral cells
Tufted cells
Peri glomerular cells
Olfactory receptors
Olfactory Epithelia

Possible connections

- Projection neurons (insects) and mitral cells(mammals) are homologous.
- Both are second order neurons that synapse onto first order olfactory sensory neurons in the glomeruli and project into the brain.
- Both contain Atx2.