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NEURAL DEVELOPMENT

A fruitless sexual switch

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In *Drosophila melanogaster*, male-specific behaviours, such as courtship, are driven by the expression of male-specific isoforms of the transcription factors encoded by *fruitless* (*fru*). However, the mechanisms by which male-specific FRU mediates these effects are unknown. Yamamoto and colleagues show that FRU interacts with two antagonistic chromatin modifiers to regulate the development of a sexually dimorphic neural circuitry.

To identify proteins that may interact with FRU to execute its masculinizing effects, the authors conducted a genetic suppressor screen. A loss-of-function mutation in *bonus* (*bon*), which encodes the transcriptional cofactor BON, suppressed the phenotypic effects of *fru* overexpression in flies. Furthermore, a *bon* loss-of-function mutation exacerbated the reduction in courtship behaviour observed in male flies carrying a loss-of function mutation in *fru*, confirming the importance of BON for the sex-specific effects of *fru* expression.

Mammalian homologues of BON silence genes through their interactions with histone modifying proteins. The authors showed that two key histone modifiers, heterochromatin protein 1α (HP1α) and histone deacetylase 1 (HDAC1), associate with FRU at a number of chromosomal sites in a BON-dependent manner. Lowering the gene dosage of either of these proteins altered courtship behaviour in flies carrying loss-of-function mutations in *fru*: loss of *Hp1a* (also known as *Su(var)205*) increased male courtship behaviour, whereas loss of *Hdac1* (also known as *Rpd3*) decreased it.

To investigate the role of these interactions in the formation of sexually dimorphic neural circuitry, the authors examined the effects of manipulating FRU, HP1α and HDAC1 levels on the mAL neuron cluster, which exhibits several sexually dimorphic features, including differences in the number of neurons and their axonal and dendritic morphology. Loss-of-function mutations in *fru* demasculinized the mAL cluster. This phenotype was exacerbated by knockdown of *Hdac1* and alleviated by knockdown of *Hp1a*.

These findings suggest that FRU recruits chromatin modifying proteins that act to either masculinize (HDAC1) or feminize (HP1α) the neural circuitry that controls sex-specific behaviours. Further work will be required to identify the genes that are subject to this regulation and determine how the balance between the antagonistic effects of these two chromatin 'switches' is achieved.

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ORIGINAL RESEARCH PAPER Ito, H. *et al.* Fruitless recruits two antagonistic chromatin factors to establish single-neuron sexual dimorphism. *Cell* **149**, 1327–1338 (2012)
FURTHER READING Jazin, E. & Cahill, L. Sex differences in molecular neuroscience: from fruit flies to humans. *Nature Rev. Neurosci.* **11**, 9–17 (2010)