IN THE NEWS

Romantic or fly-by-night? Last month, it was reported that a single gene can determine whether voles are monogamous or prefer to play the field, and now the mating habits of fruit flies have come under the microscope. In a study reported in *Nature*, Devanand Manoli and Bruce Baker from Stanford University show that the key to successful courtship in *Drosophila melanogaster* lies in a cluster of 60 median bundle neurons in the male brain.

D. melanogaster males use an elaborate ritual to woo a female, as outlined in a handy step-by-step guide in *CBC Health & Science News* (Canada, 29 July 2004): "1. Find a female and follow her. 2. Tap female with foreleg, triggering pheromone cues. 3. Stretch out wing and vibrate it to serenade female. 4. Lick female's genitalia with proboscis. 5. Attempt copulation. 6. Copulate for 20 minutes."

When Manoli and Baker disrupted the function of the 60-cell cluster by eliminating *fruitless* gene expression, they found that "the male essentially skips the tapping step and…he tries to copulate, lick her genitalia and play her a love song simultaneously. So what normally takes a total of four minutes is reduced to just 10 seconds". According to Baker, the female flies take a dim view of this unsubtle approach: "it also took [the mutant males] longer to achieve copulation than normal males. We can well assume that, when the mutant males behave in this way, they are doing things that the female does not find attractive" (*EurekAlert*, 28 July).

Baker believes that the *D. melanogaster* courtship ritual mirrors some elements of human behaviour: "you tap them and get their attention, you play them a love song and so on. So the basic rudiments are pretty similar to what people do to get successful mating and produce an offspring" (*Reuters*, 28 July).

Heather Wood

NEURODEGENERATIVE DISORDERS

SOD1 targeting in ALS

One of the mysteries of inherited neurodegenerative diseases is how ubiquitously expressed mutant proteins can selectively target specific sets of neurons for cell death. Two studies recently published in *Neuron* now shed light on how mutations in Cu/Zn superoxide dismutase (SOD1), a normally protective protein, cause selective death of motor neurons in some cases of familial amyotrophic lateral sclerosis (ALS).

Using a series of *SOD1* mouse mutants, and tissue samples from patients with familial ALS, Liu *et al.* showed that various disease-related mutants of SOD1, but not wild-type SOD1, collected in the mitochondria of affected tissue. Specifically, mutant SOD1 preferentially associated with membrane proteins in spinal cord mitochondria, but not in the mitochondria of unaffected tissues such as muscle or liver. This build up of SOD1 in mitochondria occured at around the time of the earliest pathology and before disease onset.

The authors propose that the spinal cord mitochondrial cells are singled out probably because of an as-yet undiscovered import mechanism in these cells that causes them to recognize mutant SOD1 as a substrate for selective import. They suggest that this selective association initiates a cascade of damage, whereby SOD1 blocks the mitochondrial membranes, preventing import of necessary substances, and some even enters the mitochondria, disrupting their normal activity.

The mechanism by which SOD1 destroys spinal cord neurons once it reaches the mitochondria was the focus of the study by Pasinelli *et al.* They showed that wild-type and mutant SOD1 interact specifically with the protein B-cell leukaemia/lymphoma-2 (BCL2) — a protein that resides on the outer surface of the mitochondrial membrane and normally suppresses cell death — both *in vitro* and *in vivo* in human and mouse spinal cord. The authors went on to show that BCL2 binds to mutant SOD1-containing aggregates in mitochondria in the spinal cord but not in the liver, consistent with the findings of Liu *et al.* So, it seems that mutant SOD1 interacts with the mitochondria by binding with BCL2, which in turn leads to accelerated cell death. The mechanisms for this are unclear, but might be related to the mutant protein being positioned in a way that is toxic to the mitochondria. The authors also suggest that because SOD1-containing aggregates trap significant amounts of BCL2, this might trigger the cell-death machinery by either depleting BCL2 or rendering it non-functional, which could then make the mitochondria and its host cell less viable. It is also important to note that BCL2 is necessary for maintaining mitochondrial membrane potential, indicating another possible route for the destructive actions of SOD1 on motor neurons.

So, together, these two studies take us a step closer to understanding the mechanisms that lead to a compromise in motor neuron viability in ALS. But, as they point out, further work is needed to delineate the particular spinal cord factors that facilitate the association between SOD1 and mitochondrial membrane proteins.

Alison Rowan

References and links

ORIGINAL RESEARCH PAPERS Liu, J. *et al.* Toxicity of familial ALS-linked SOD1 mutants from selective recruitment to spinal mitochondria. *Neuron* **43**, 5–17 (2004) | Pasinelli *et al.* Amyotrophic lateral sclerosis-associated SOD1 mutant proteins bind and aggregate with Bcl-2 in spinal cord mitochondria. *Neuron*, **43**, 19–30 (2004)

FURTHER READING Cleveland, D. W. & Rothstein, J. D. From Charcot to Lou Gehrig: deciphering selective motor neuron death in ALS. *Nature Rev. Neurosci*. **2**, 806–891 (2001)

Encyclopedia of Life Sciences: http://www.els.net
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