REPRODUCTIVE BIOLOGY

Sperm alliance

In 2002, biologists were presented with a vivid account of how sperm of the common wood mouse hook up together in 'trains'. Such trains, it was shown, form a fast vehicle in the race for the great prize — fertilization of an egg. But only one sperm can be successful in that goal. Simone Immler and colleagues have now revisited the question of what prompts the selfless behaviour of the others (*PloS One* doi: 10.1371/journal.pone.0000170; 2007).

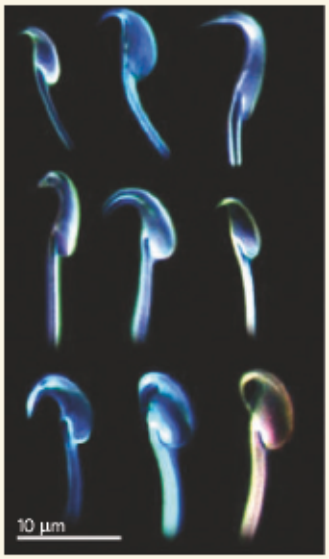
A feature of the sperm of wood mice and many of their relatives among the murine rodents is that their heads carry a hook structure, which varies in shape and size between species, as shown in the picture.

Immler *et al.* carried out a survey of the sperm of 37 species of murine rodent. They find that hook shape and curvature are more pronounced in species in which the female is more likely to mate with different males. The principle of 'together we succeed, divided we fail' makes sense in this situation. These sperm are better equipped to cooperate: so those from any one male are better able to see off the competition from another male.

The authors also looked at the behaviour of sperm in two of the species, the Norway rat and the house mouse. In both, the sperm formed groups. But in the house mouse, individual sperm outperformed the group in sheer speed. Immler *et al.* speculate that maybe speed isn't everything: perhaps in this case the group can make surer progress in the journey up the female reproductive tract.

And there remains the issue of competition among the collaborators: who gets to claim the envied job of fertilization?

Tim Lincoln



mutants, indicating that the entire ESCRT-II complex is required for *bicoid* localization[2]. Irion and St Johnston also found that the Vps36 protein, and hence ESCRT-II, co-localizes with *bicoid* mRNA at the anterior pole of the oocyte. Importantly, ESCRT-I and ESCRT-III mutants had normal localization of *bicoid* mRNA, suggesting that the function of ESCRT-II in *bicoid* localization is unrelated to its role in endosomal protein sorting.

The involvement of ESCRT-II in two seemingly unrelated processes — RNA guidance and protein sorting — may look surprising. However, the finding that a protein turns out to have an additional activity distinct from its canonical function is not unprecedented. Commonly termed 'moonlighting', this practice is exemplified by several glycolytic enzymes that have taken on jobs in gene regulation in addition to their classical involvement in energy metabolism[6]. Evolutionary pressure may have caused the selection of proteins and complexes capable of multitasking, thereby minimizing the number of genes required to make a fly or a human.

How does ESCRT-II recognize *bicoid* mRNA? Elegant experiments by Irion and St Johnston[2] showed that a unique part of Vps36 called the GLUE domain binds directly to a specific loop in the *bicoid* 3′ UTR. The GLUE domain is indeed a sticky domain as it also binds to a small protein called ubiquitin and to the lipid PtdIns(3)P, which are both associated with the function of ESCRT-II in endosomal protein sorting[7,8]. Crystallography shows that the ubiquitin-binding and lipid-binding sites of the GLUE domain are separate[8], and it will be interesting to learn whether the mRNA-binding site overlaps with one or both of these. A mutually exclusive binding to ubiquitin or lipid versus mRNA might provide a mechanism by which ESCRT-II could switch between its functions in endosomal sorting and mRNA guidance.

But how does ESCRT-II find its way to the anterior pole of the oocyte? Previous work identified a group of proteins that start the formation of anterior microtubules during the late stages of oocyte formation, and these too are required for correct localization of *bicoid* mRNA[3]. The motor protein dynein, which transports many cargoes along microtubules, is a likely candidate for moving *bicoid* mRNA to the anterior pole[3], and proteins that attach *bicoid* mRNA to dynein could thus represent the missing link between ESCRT-II and *bicoid* mRNA localization. It is interesting to note that Vps22 in mammalian ESCRT-II binds to the Rab7-interacting lysosomal protein (RILP), a protein that recruits the dynein motor complex to endosomes[9]. So maybe a RILP-like fruitfly protein participates in the ESCRT-II–RNA complex with dynein, with the latter powering transport to (or retention at) the anterior pole.

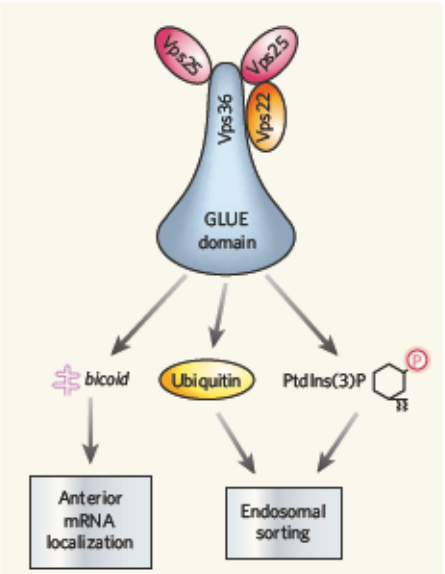


Figure 2 | The functions of ESCRT-II. The ESCRT-II complex is made up of the Vps22, Vps25 and Vps36 proteins. Irion and St Johnston[2] find that the GLUE domain of Vps36 interacts directly with *bicoid* mRNA to mediate anterior localization of the RNA in the fruitfly embryo. This domain can also bind to ubiquitin and phosphatidylinositol 3-phosphate (PtdIns(3)P) to facilitate protein sorting in the endosome.

Finally, how do these findings relate to other organisms, including humans? The fly Bicoid protein does not have a direct relative in humans, but it does belong to the homeodomain family, a group of gene regulatory factors that determine body patterning during the development of many organisms, including humans. Also, frog Vps36 can recognize the fruitfly *bicoid* mRNA[2], indicating that ESCRT-II could play a role in mRNA recognition and localization in vertebrates as well as in flies. Moreover, mammalian ESCRT-II interacts with a protein that stimulates mRNA transcription[10], suggesting that ESCRT-II might associate with selected mRNAs at an early stage of their synthesis. With this in mind, it will be interesting to investigate whether mammalian ESCRT-II can bind to specific mRNAs, and whether their localization is affected by the absence of ESCRT-II. ■

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