ten. The bent S6 model (Fig. 2) raises just about as many questions as it answers. Why, for example, is S6 bent in K_v channels? Might this smaller open pore in K_v channels serve to decrease the conductance of the channel beyond what is set at the selectivity filter, as Webster *et al.*² suggest? Might the PVP adaptation serve an important role in the unusually tight coupling²⁴ that occurs between the voltage sensors and the S6 gate in K_v channels? Clearly there is still much to learn and an X-ray structure of a K_v channel with a PVP motif would be a big step forward. For now, the message seems to be that one size, or model, may not fit all.

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And the *oskar* goes to...

What specifies that a cell will become an antenna and not a leg? For fruit flies, cell fate is determined early in the cytoplasm of the egg. Here, maternal mRNAs and proteins are localized to different regions of the egg chamber creating gradients of macromolecules throughout the cell. The redistribution of these molecules during egg development and fertilization as well as the pattern of cell cleavage is important for determining which cell acquires which fate.

For proper abdomen and germ cell development in the future embryo, *oskar* mRNA must be localized at the posterior end of the *Drosophila* egg chamber. If the mRNA is not in the correct place, the embryo is sterile and has an incorrectly formed abdomen, which can be lethal. Previous work suggested that targeting to the posterior end of the egg was dependent on the 3' untranslated region (3'UTR) of the RNA because *oskar* transcripts lacking the 3'UTR failed to localize. Furthermore, the *oskar* 3'UTR was shown to be sufficient for posterior targeting. Now, Hachet and Ephrussi (*Nature* **428**, 959–963, 2004) challenge the sufficiency of the 3'UTR for posterior targeting and show that splicing of the *oskar* mRNA is also essential for mRNA localization.

Hachet and Ephrussi generated transgenic flies expressing wild-type (*oskWT*) and intronless *oskar* (*oskΔi*) genes. They examined the egg chambers from these flies and located *oskar* mRNA using fluorescent *in situ* hybridization (red). The egg, where *oskar* mRNA will localize, is located on the right half of the oval egg chamber surrounded by a string of small cells (nuclei stained using DAPI, blue) and flanked on the left side by nurse cells (large blue nuclei). Hachet and Ephrussi show that during early egg development, the three introns (*i1*, *i2* and *i3*) in *oskar* are dispensable for both nuclear export and the early phase of *oskar*

mRNA transport. However, as egg development proceeds, the distribution of *oskar* mRNA changes. In older *oskWT* egg chambers, the mRNA is found in a discrete position at the posterior end of the egg cytoplasm. In contrast, the mRNA is diffuse and not localized in flies lacking all three introns (*oskΔi 1,2,3*). These results show that the introns are important for localization of *oskar* mRNA at the posterior of the egg.

Another unexpected finding from these studies was a role for *i1* in mRNA targeting but not for *i2* or *i3*. The mRNA localization of *oskΔi(2,3)* resembled that of wild type, whereas

that of *oskΔi(1,2)* and *oskΔi(1)* is diffuse throughout the cytoplasm. All mRNAs were correctly spliced. Hachet and Ephrussi further demonstrate that splicing of the first intron, rather than a specific requirement for the sequence of the *i1*, is essential for localization. When they replaced the sequence of *i1* with that of *i3* (*osk(i3 in i1)*) the distribution of *oskar* mRNA resembled that of *oskWT*. These data show that splicing at the first exon-exon junction of *oskar* mRNA and localization are mechanistically coupled.

The nuclear shuttling proteins Y14 and Mago nashi are also essential for *oskar* mRNA localization. These proteins are core components of the exon junction complex (EJC), which forms ~20 nucleotides upstream of the exon-exon junction. Although Hachet and Ephrussi did not analyze the composition of the EJC at the three different splice sites, they suggest that there is something fundamentally different about placing the EJC at the first exon-exon junction. The authors propose this EJC may play a pivotal role in mediating interactions between factors bound at the 5' cap, the 3'UTR and within the coding region of the *oskar* mRNA. In so doing, the EJC at the first splice site acts as a landmark for specifying an *oskar* mRNA localization complex.

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