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An analysis of MOG function in germline sex determination and splicing in *C. elegans*

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The *C. elegans* hermaphrodite sequentially produces spermatids and oocytes and therefore has to override a female-specific gene expression program in order to transiently produce male gametes. This is mostly executed through post-transcriptional events, such as regulation of mRNA activity. *tra-1* pre-mRNA is alternatively spliced, giving rise to the larger *tra-1A* transcript and the smaller *tra-1B* mRNA. Interestingly, we found that *tra-1B* is produced at higher levels in *mog-2(0)* mutants, suggesting that it might be responsible for the masculinized germline phenotype. This hypothesis was verified by over-expressing TRA-1B, which remarkably led to masculinized germlines. Nevertheless, the Mog phenotype seems mostly due to a shift in the balance between the two isoforms TRA-1A and TRA-1B in favor of the isoform B, rather than from the sole over-expression of TRA-1B. Surprisingly, in at least three different mog mutants, knocking out *tra-1B* leads to a partial suppression of the Mog phenotype. We propose a molecular model where the switch to oogenesis requires the feminizing *tra-1A* transcript, which is dependent on MOG-2 for its splicing. In its absence or with reduced expression of *tra-1A*, the *tra-1B* transcript causes germline masculinization of the hermaphrodite.

The findings of the first project and the striking homology of MOG proteins to splicing factors prompted us to study splicing mechanisms in *C. elegans*. To do so, we investigated the nature and importance of the splicing Branch Point Signal (BPS) in *C. elegans*. We have determined experimentally the existence and position of over 90 Branch Points in 46 different introns. Most of the times the branching residue is an Adenosine at a median position of 18 nucleotides from the 3´ splice site. Nevertheless, sometimes the branching residue can be a Uridine, as shown in other organisms, or even Cytidine or Guanosine. As expected, the consensus of the *C. elegans* BPS is more divergent than in mammals and yeast. We nevertheless propose a 7 nucleotides motif (WWWWNAW), which preferentially harbours the splicing Branch Point in *C. elegans,* possibly allowing to predict this splicing signal in worms. Ultimately, we seek to identify precise splicing signals that are recognized by MOG-2, and possibly other MOG proteins, in order to achieve alternative splicing.

Jury:

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