Translational regulation of development and maternal RNAs in *Caenorhabditis elegans*

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Post-transcriptional controls of mRNA activity are crucial for development of the nematode *Caenorhabditis elegans*. The onset of spermatogenesis in hermaphrodites is achieved by translational repression of the sex-determining gene *tra-2*; this repression depends on a direct repeat element (DRE) located in the 3′ untranslated region (3′ UTR) of the *tra-2* mRNA. In addition, the switch from spermatogenesis to oogenesis in hermaphrodites depends on a negative regulatory element in the 3′ UTR of the transcript of a second sex-determining gene, *fem-3*. Thus, post-transcriptional controls of *tra-2* and *fem-3* are essential for development of an XX animal as a hermaphrodite instead of a female. Post-transcriptional regulation by regulatory elements localized in the 3′ UTR also influences somatic development. Thus, the *tra-2* DRE also regulates *tra-2* somatic expression and the 3′ UTR of *lin-14* is involved in the post-transcriptional regulation of larval-specific somatic cell lineages. The relevance of these controls to the regulation of maternal RNAs is discussed.

**Key words:** post-transcriptional regulation / 3′ UTR / *C. elegans* / sex determination / *tra-2* / *fem-3* / *lin-14* / maternal RNAs / glp-1

Many maternal RNAs are stored in an inactive or ‘masked’ form within oocytes and are then activated during early development (ref 1 and references therein). Therefore, the activity of maternal RNAs must be tightly controlled. In recent years, it has become clear that the 3′ untranslated regions (3′ UTR) of maternal RNAs are crucial for their post-transcriptional regulation (ref 2 and references therein; see also articles by M. Wickens, N. Standart, R.P. Wharton, P.M. MacDonald, this issue). Here, we discuss evidence that 3′ UTRs mediate post-transcriptional controls in the nematode *Caenorhabditis elegans* and, further, that regulatory elements located within 3′ UTRs influence a broad spectrum of cell fate decisions during development. The powerful genetics and cellular simplicity of *C. elegans* have made this small worm particularly useful for the analysis of developmental controls. Genes that govern many aspects of development have been identified by both loss-of-function and gain-of-function mutations. Loss-of-function mutations eliminate gene function and identify genes required for specific developmental processes, such as the specification of sexual fate. By contrast, dominant gain-of-function mutations often lead to unregulated gene function and identify regulatory elements essential for controlling gene activity. In three cases, regulatory elements have been discovered that map to a 3′ UTR (refs 3, 4; E. Goodwin, T. Evans, P. Okkema, J. Kimble, in preparation).

In this review, we discuss the diverse roles played by post-transcriptional regulation in *C. elegans* development. In addition, we review genes that are expressed maternally in *C. elegans* and discuss the little that is known about the regulation of their expression. These studies demonstrate that the mechanisms regulating RNA activity in *C. elegans*, like that in other organisms, rely on elements within the 3′ UTR. Therefore, *C. elegans* may provide a system for taking a combined genetic and molecular approach to the analysis of post-transcriptional mechanisms of regulation—a strategy that will certainly prove useful for the elucidation of regulatory elements and trans-acting factors mediating this poorly understood mechanism of gene expression.

The hermaphrodite germ line and early embryogenesis

A basic knowledge of the anatomy and development of the hermaphrodite germ line is essential for understanding both the post-transcriptional controls governing the decision between spermatogenesis and oogenesis (see next section) and the role of maternal RNAs in *C. elegans* development (see later section). A diagram of the major features of the adult hermaphrodite germ line is shown in Figure 1. (For an extensive description of gonadal anatomy and development, see ref 5.) Briefly, each hermaphrodite possesses two U-shaped ovarioles that are joined...
centrally in a common uterus. At the distal ends of the ovotestes, germ cell nuclei are mitotic. More proximally, the nuclei enter meiosis, and most proximally, they undergo gametogenesis. The first germ cells to differentiate in the hermaphrodite germ line become sperm. Then, following the molt from fourth-stage larva to adult, the germline switches from spermatogenesis to oogenesis, and oocytes are produced continuously throughout adulthood. The immature germline and maturing oocytes are part of a syncytium in which all nuclei share a common cytoplasm. Therefore, maternal products must be synthesized and packaged into mature oocytes without disrupting the development of uncommitted germ cells. The particular nuclei that synthesize maternal RNAs are not known, but it seems likely that spatial and temporal controls operate within the cytoplasm shared by both immature and differentiating germ line nuclei—to prevent developmental confusion.

Once an oocyte is mature, fertilization can occur either by self-fertilization, using sperm produced by the hermaphrodite or by cross-fertilization, using sperm introduced by mating with males. Once fertilized, the zygote enters the uterus to begin early embryogenesis. The embryo develops by an invariant pattern of cell divisions to generate a first larval stage worm. The pattern of the developing embryo is established by a combination of inductive interactions between blastomeres and the segregation of cytoplasmic determinants (ref 8 and references therein). In addition, the sex of the embryo is determined by the ratio of X chromosomes to sets of autosomes, such that XX embryos become hermaphrodites and XO embryos become males.

Regulation of translation and the sperm/oocyte decision

The germline decision between spermatogenesis and oogenesis is governed by a set of regulatory genes that also control sex determination in somatic tissues (reviewed in ref 10). Briefly, four genes, fem-1, fem-2, fem-3, and fog-1, function as terminal regulators to specify spermatogenesis. Two genes, tra-2 and tra-3, negatively regulate the four terminal regulators and thereby promote oogenesis. Of particular interest for this review are two genes: tra-2 and fem-3. Genetic and molecular studies demonstrate that the activity of tra-2 RNA is repressed in hermaphrodites to allow spermatogenesis, and that the activity of fem-3 RNA is negatively regulated in hermaphrodites to allow the switch from spermatogenesis to oogenesis. For both tra-2 and fem-3, regulatory elements have been identified within the 3' untranslated regions (3'UTRs) and translational regulation has been implicated.

Translational regulation of tra-2 RNA is required for the onset of hermaphrodite spermatogenesis

The tra-2 gene is normally required for female development. In XX hermaphrodites, tra-2 is
needed for both oogenesis and female somatic fates. Loss-of-function mutations in tra-2 transform XX animals from hermaphrodites into nearly complete males. Both the expression of the tra-2 gene and the activity of its protein product are tightly regulated (refs 12-17; E. Goodwin, T. Evans, P. Okkema, J. Kimble, in preparation) suggesting that the function of tra-2 is pivotal to the decision between male and female fates. In this review, we focus on the post-transcriptional regulation of tra-2 by its 3’UTR.

To achieve the onset of hermaphrodite spermato genesis, the activity of tra-2 is normally repressed.15,16 Each of six dominant mutations, called tra-2(gf) (for gain-of-function), leads to unregulated tra-2 activity in the hermaphrodite germ line and transforms tra-2(gf) XX animals from hermaphrodites into females. Instead of producing both sperm and oocytes, tra-2(gf) XX animals make only oocytes. In addition, strong tra-2(gf) mutations feminize the germline and intestine of XO animals. In these strong tra-2(gf) XO mutants, the germ line can make oocytes and the intestine can produce yolk. Therefore, the tra-2(gf) mutations feminize both XX and XO animals and they feminize both germ line and somatic tissues.

Each tra-2(gf) mutation alters a 60 nucleotide sequence in the tra-2 3’UTR (Figure 2; E. Goodwin, T. Evans, P. Okkema, J. Kimble, in preparation). Within this 60 nucleotide sequence are two directly repeated copies of a 28 nucleotide sequence that are separated by 4 nucleotides. We call each 28 nucleotide repeat a ‘direct repeat element’, or DRE. The phenotypic strength of each allele correlates with the degree to which the two repeats are disrupted; alleles that contain one DRE still allow some repression of tra-2. Therefore, each repeat may contribute to the negative regulation of tra-2 activity.

Two lines of evidence indicate that the direct repeat in the tra-2 3’UTR controls the translation of tra-2 mRNA (E. Goodwin, T. Evans, P. Okkema, J. Kimble, in preparation). First, a comparison of wild-type tra-2 and mutant tra-2(gf) RNAs on northern blots does not reveal any unexpected change in the sizes of tra-2 RNAs or stage of development at which the RNAs are made; furthermore, the steady state level of tra-2(gf) RNAs is not increased. Therefore, the presence or absence of the direct repeats does not detectably alter transcription, splicing, or stability of tra-2 RNA during development. Second, tra-2(gf) mutant RNA is more heavily loaded with ribosomes than is wild-type tra-2 RNA. Most wild-type tra-2 RNA sediments with the monosome fraction on sucrose gradients, whereas a significant fraction of tra-2(gf) RNA sediments with polysomes. Therefore, the presence of the direct repeats appears to decrease the ability of tra-2 RNA to associate with ribosomes. These two experiments together indicate that the direct repeats translationally repress the activity of wild-type tra-2 RNA. However, we do not know whether the initiation of translation is controlled directly or whether tra-2 RNA is sequestered away from the translational apparatus.

The direct repeats in the tra-2 3’UTR may regulate translation of tra-2 RNA by binding a translational repressor (E. Goodwin, T. Evans, P. Okkema, J. Kimble, in preparation). A factor in crude worm extracts binds to RNA with two DREs but not to RNA with a randomized sequence of the same base composition. Maximal binding activity appears during second and third larval stages (E. Goodwin, personal communication), corresponding with the time at which tra-2 is likely to be inactivated to allow spermato genesis. Consistent with the finding that a tra-2 3’UTR with one repeat is partially regulated, the tra-2 RNA-binding factor can bind a single repeat. This result raises the interesting possibility

![Figure 2. Six tra-2 gain-of-function mutations carry molecular lesions in the tra-2 3’UTR. The wild-type tra-2 3’UTR is shown in the top diagram, and mutant alleles are below. Each copy of the 28 nucleotide sequence, or DRE, is denoted by a black arrow. Deletions are represented by parentheses and the size of the deletion (in nucleotides) is shown within the parentheses. Arrowheads marked by Tc1 represent sites of insertion of the transposable element Tc1. The tra-2(gf) alleles are listed in order of decreasing strength, with the strong alleles causing the most severe feminization.](image-url)
that the two DREs that are normally present may bind two repressors cooperatively, increasing the sensitivity of translation to changes in repressor activity. Such a mechanism, though speculative, is attractive because an efficient developmental switch between two cell fates would be greatly facilitated by cooperativity.

The trans-acting factor that binds the DREs to regulate tra-2 translation has not yet been identified genetically. The only two genes that have been proposed to negatively regulate tra-2, (i.e. her-1 and fog-2) are not good candidates for this translational repressor, because mutants in these genes do not precisely mimic the tra-2(gf) phenotype. As described above, tra-2(gf) mutations feminize the hermaphrodite and male germlines and the male intestine. In contrast, fog-2 mutations only feminize the hermaphrodite germline, and her-1 mutations only feminize the male germline and soma. Since most genes that feminize the hermaphrodite germ line as simple loss-of-function mutations have likely been identified, we speculate that a mutation in the tra-2 translational repressor will have a different phenotype. For example, if the repressor regulates multiple RNAs, mutations that eliminate its function might be lethal. Therefore, identification of this regulatory factor may require a different genetic approach (e.g. isolation of enhancers of the tra-2(gf) phenotype) or its biochemical purification.

**Negative regulation of fem-3 RNA by its 3’UTR promotes the hermaphrodite switch from spermatogenesis to oogenesis.**

The fem-3 gene acts maternally and zygotically to direct male development. In XO males, fem-3 is essential for specification of both spermatogenesis and male somatic fates. In XX hermaphrodites, fem-3 directs spermatogenesis. Loss-of-function mutations in fem-3 transform both XO and XX animals into females (hermaphrodite hermaphrodites). The activity of fem-3 is regulated by tra-2 and tra-3 to ensure proper sexual development; this regulation is certainly post-transcriptional and is likely to be post-translational. In this review, we focus on a distinct regulation of fem-3 that is unlikely to involve either tra-2 or tra-3—the post-transcriptional regulation of fem-3 by its 3’UTR.

To achieve the switch from spermatogenesis to oogenesis in hermaphrodites, the activity of fem-3 is normally repressed. Each of 19 temperature sensitive dominant mutations, called fem-3(gf), lead to unregulated fem-3 activity in the hermaphrodite germ line and transform fem-3(gf) XX animals from hermaphrodites into animals with a hermaphrodite soma and a male germ line, which makes only sperm. Therefore, these mutations disrupt a negative regulation of fem-3 that normally permits the sperm/oocyte switch.

Each fem-3(gf) mutation carries a molecular defect in the fem-3 3’UTR. Remarkably, 17 mutations are single-base substitutions within a 5 nucleotide sequence of the 260 nucleotide fem-3 3’UTR, and the two remaining mutations are small deletions. Each of the two deletions removes part of the 3’UTR, including the region identified by the point mutations, but leaves the fem-3 coding region and polyadenylation signal intact (Figure 3). The fem-3(gf) mutations define a region in the fem-3 3’UTR that is critical for the negative regulation of fem-3 activity. However, because isolation of the fem-3(gf) mutants required fertility, the mutations obtained may not completely eliminate function of the negative regulatory element. Therefore, other nucleotides within the fem-3 3’UTR, or elsewhere in the mRNA, may also contribute to suppression of fem-3 RNA activity.

Two lines of evidence suggest that the fem-3 3’UTR may control the translation of fem-3
mRNA. First, a comparison of wild-type fem-3 and mutant fem-3(gf) RNAs on northern blots revealed no differences in the size or abundance of the fem-3 RNAs or the developmental stage at which they appear. Therefore, the 3' UTR does not detectably alter transcription, splicing, or stability of fem-3 RNA during development. Second, fem-3(gf) mutant RNA has a longer poly(A) tail than does wild-type fem-3 RNA. An increase in polyadenylation often correlates with an increase in translation and, in some cases, an increase in polyadenylation is crucial for an increase in translation (for review see M. Wickens, this issue, pp 399-412; ref 21). However, the types of experiments done with tra-2(gf) RNAs (e.g. polysome analysis) will be needed to learn whether the fem-3(gf) RNAs are indeed translationally controlled. The fem-3(gf) mutations might alternatively interfere with RNA localization or nuclear transport.

Two observations indicate that the fem-3 3' UTR may regulate fem-3 RNA activity by binding a transacting factor. First, a factor in crude worm extracts binds to a synthetic fem-3 3' UTR RNA as short as 35 nucleotides and this binding is dependent on the sequence delineated by the fem-3(gf) mutants. Second, animals carrying a transgene with the wild-type fem-3 3' UTR fused directly to a putative fem-3 promoter make excess sperm and no oocytes; by contrast, transgenic animals that carry constructs with fem-3(gf) 3' UTRs are mostly wild-type. One interpretation of this result is that RNA corresponding to the wild-type fem-3 3' UTR, which is synthesized from the transgene, titrates a negative regulator off of the endogenous fem-3 RNA. The endogenous fem-3 RNA would thereby be activated and direct spermatogenesis inappropriately.

The best candidates for genes that may encode the trans-acting regulators of fem-3 RNA are the mog genes (ref 22; P. L. Graham, J. Kimble, in preparation). Mutations in the mog genes cause the production of excess sperm in the hermaphrodite germ line, similar to that observed in fem-3(gf) mutants. Epistasis experiments suggest that mog genes could function as negative regulators of fem-3.

Of six mog genes identified, only mog-1 is represented by numerous loss-of-function mutations. For each of the other five mog genes, only a single allele exists, suggesting that these genes may have other functions in addition to their role in the sperm/oocyte switch. Therefore, one or more of the mog genes could encode a negative regulator of several RNAs, including fem-3.

The maternal control of early embryogenesis

Many key developmental events in early C. elegans embryogenesis are governed by maternally-expressed genes. For some maternal effect genes, the specific roles of their maternal contributions are known (e.g. embryonic sex determination, partitioning of cytoplasmic factors, embryonic induction, specification of blastomere fate), whereas for others, the biological function is not understood, largely because mutants do not have a specific developmental defect (Table 1 and references therein). For each maternal effect gene, the embryonic phenotype is influenced by the mother's genotype. Consequently, most of their gene products are probably incorporated into the oocyte for subsequent use in the embryo. Given the powerful effects that many of the maternal products have on development (Table 1), the activities of these maternal products—both in the oocyte and early embryo—must be carefully controlled.

The tra-2 and fem-3 genes both appear to produce maternal RNAs. The fem-3 gene is one of the maternal effect genes (Table 1). In addition, fem-3 transcribes a maternal RNA that accumulates in the germ line with a short poly(A) tail and then obtains a longer poly(A) tail in the early embryo, a pattern of regulation that is observed in maternal RNAs from many organisms. Although tra-2 is not known to have any maternal effects, tra-2 produces a hermaphrodite germ-line-specific RNA with the same pattern of polyadenylation in oocyte and embryo described for the fem-3 RNA; therefore, this tra-2 RNA is likely to be a maternal RNA.

The regulatory elements that control fem-3 and tra-2 post-transcriptionally (see initial section) have striking parallels with regulatory elements that control maternal RNAs post-transcriptionally in other organisms. First, like many maternal RNAs, both tra-2 and fem-3 are controlled by elements in their 3' UTRs. Second, like many maternal RNAs, tra-2, and perhaps fem-3, is controlled at the level of translation. Third, like many maternal RNAs, an increase in polyadenylation is correlated with the activation of fem-3(gf) RNA. (The effect of the tra-2(gf) mutations on polyadenylation has not yet been analyzed.) An intriguing possibility is that the tra-2 and fem-3 3' UTRs may regulate the activity of their respective maternal RNAs in addition to the regulation of their activities during germ line and somatic development.

One observation may link the post-transcriptional control of fem-3 by the element identified by the
Table 1. Maternally-expressed genes that control *C. elegans* development*

<table>
<thead>
<tr>
<th>Gene</th>
<th>Embryonic function†</th>
<th>Molecular function‡</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>mei-(1,2)</td>
<td>Completion of meiosis</td>
<td>Unknown</td>
<td>31</td>
</tr>
<tr>
<td>par-(1-4)</td>
<td>Intracellular partitioning</td>
<td>Unknown</td>
<td>32-34</td>
</tr>
<tr>
<td>glp-1</td>
<td>Pharyngeal development and morphogenesis</td>
<td>Transmembrane receptor/Notch homologue</td>
<td>25,35,36</td>
</tr>
<tr>
<td>skn-1</td>
<td>Specification of blastomere fate</td>
<td>Transcription factor</td>
<td>37</td>
</tr>
<tr>
<td>mes-1</td>
<td>Generate germ cell precursors</td>
<td>Unknown</td>
<td>38</td>
</tr>
<tr>
<td>mes-(2-4)</td>
<td>Germline proliferation</td>
<td>Unknown</td>
<td>38</td>
</tr>
<tr>
<td>sid-1</td>
<td>Dosage compensation and sex determination</td>
<td>Transcription factor</td>
<td>39-41</td>
</tr>
<tr>
<td>tra-3</td>
<td>Female development</td>
<td>Unknown</td>
<td>11</td>
</tr>
<tr>
<td>fem-1</td>
<td>Male development</td>
<td>cdc10/swrif6 repeats</td>
<td>18,42,43</td>
</tr>
<tr>
<td>fem-2</td>
<td>Male development</td>
<td>Unknown</td>
<td>18,44</td>
</tr>
<tr>
<td>fem-3</td>
<td>Male development</td>
<td>Novel</td>
<td>18,45</td>
</tr>
<tr>
<td>dpy-(26-29)</td>
<td>Dosage compensation</td>
<td>Unknown</td>
<td>46</td>
</tr>
<tr>
<td>zyg-9</td>
<td>Mitotic spindle formation</td>
<td>Unknown</td>
<td>47,48</td>
</tr>
<tr>
<td>zyg-11</td>
<td>Possibly several cellular functions</td>
<td>Unknown</td>
<td>47,48</td>
</tr>
<tr>
<td>zyg*</td>
<td>Embryogenesis</td>
<td>Unknown</td>
<td>47</td>
</tr>
<tr>
<td>emb*</td>
<td>Embryogenesis</td>
<td>Unknown</td>
<td>49-51</td>
</tr>
<tr>
<td>mel*</td>
<td>Embryogenesis</td>
<td>Unknown</td>
<td>52</td>
</tr>
</tbody>
</table>

*All genes have been identified by mutation; for each gene, maternal genotype influences the progeny's phenotype.
†Gene functions are surmised from mutant phenotypes.
‡Most zyg, emb, and mel genes remain poorly characterized, see references for details.
§Molecular functions have only been deduced from DNA sequence analysis.

*fem-3(gf)* mutations and the control of maternal RNAs. As described earlier, the mutant phenotype of a group of six *mog* genes is similar to that of *fem-3(gf) mutants, suggesting that the *mog* genes may be involved in regulation of *fem-3* by its 3'UTR.

Intriguingly, all *mog* mutations are also maternally required for embryogenesis (ref 22; P. L. Graham, J. Kimble, in preparation). Thus, embryos produced by a *mog* mutant that makes oocytes (e.g. a *mog-1*; *fem-1* double mutant) are unable to survive. This embryonic lethality is strictly dependent on the maternal genotype of the *mog* mutation; a *mog-1*; *fem-1* double mutant embryo derived from a *mog-1* (+) *fem-1* mother survives. Therefore, the *mog* genes appear to be involved not only in the sperm/oocyte switch but also in a process required for embryogenesis. Such a process might be the control of maternal RNAs. Therefore, links between the elements in the 3'UTRs of *tra-2* and *fem-3*, which regulate germline sexual fates, and elements that regulate maternal RNA activity may yet be found.

The *glp-1* gene is a maternally expressed gene that appears to be regulated post-transcriptionally to generate a localized protein product within the early embryo (Table 1; S. Crittenden, E. Troemel, J. Kimble, in preparation). The *glp-1* gene encodes a membrane protein essential to a number of regulatory cell-cell interactions during development (ref 24 and references therein). Maternal *glp-1* activity is required for induction of pharyngeal development from descendants of one blastomere (AB) and for morphogenesis of the embryo. In adults, maternal *glp-1* RNA accumulates in the germline for delivery to the embryo, and decays during the 4-28 cell stage of embryogenesis. By contrast, *glp-1* protein is not detected in oocytes, but instead appears for a brief period during early embryogenesis. The *glp-1* protein first appears in the anterior two cells (ABa and ABp) of the 4-cell embryo and continues to be expressed in AB descendants through the 28-cell stage (S. Crittenden, E. Troemel, J. Kimble, in preparation). Therefore, *glp-1* RNA appears to be translationally repressed in oocytes and then activated in the early embryo. The localized appearance of *glp-1* protein may be a consequence of the selective activation of maternal *glp-1* RNA in AB descendants or its localization to those cells. Alternatively, the localized appearance of *glp-1* protein may result from post-translational regulation, perhaps through the spatial control of protein stability. Experiments are in progress to distinguish among these possibilities. One intriguing possibility is that the *glp-1* 3'UTR may control its temporal and spatial expression within the early embryo. In *Drosophila* and *Xenopus*, the regulated localization of maternal RNA is mediated.
by elements within the 3'UTRs of the localized RNAs (see P. MacDonald, this issue, pp 413-424; ref 27). Therefore, it is not unreasonable to think that a similar mechanism may control the localized expression of glp-1 in *C. elegans*.

**Post-transcriptional control of larval development: the *lin-14* gene**

Post-transcriptional controls are not restricted to germ line development and early embryogenesis. As mentioned in the initial section, the *tra-2(gf)* RNA is not only activated in germine tissues, but also in somatic tissue (i.e. the male intestine). The importance of post-transcriptional controls to somatic development is underscored by recent work on the regulation of the *lin-14* gene. The heterochronic gene, *lin-14*, is required for the proper temporal expression of cell lineages during larval development. Loss-of-function mutations in *lin-14* cause lineages typical of late larvae to occur prematurely in younger larvae. In contrast, *lin-14(gf)* mutations cause lineages typical of early larvae to be reiterated in older larvae. The presence of *lin-14* protein correlates with the phenotypic effects of the *lin-14* mutants. Wild-type *lin-14* protein is present during the first stages of larval development and disappears by the second larval stage, never to appear again during subsequent stages. In *lin-14(lf)* mutants, *lin-14* protein is absent throughout development, whereas, in *lin-14(gf)* mutants, the protein is present throughout development. Interestingly, the two *lin-14(gf)* mutations that have been identified map to the *lin-14* 3'UTR, and one is a deletion contained within the 3'UTR. Although the effect of the *lin-14(gf)* mutations on *lin-14* RNA level is presently uncertain, it is tempting to speculate that they disrupt the translational repression of *lin-14* RNA. The product of the *lin-4* gene may mediate the repression of *lin-14* RNA since *lin-4* mutants mirror the *lin-14(gf)* phenotype and cause prolonged expression of *lin-14* protein. Thus, a translational control mechanism may direct the temporal execution of larval cell lineages.

**Summary**

The post-transcriptional control of mRNA activity is surfacing as an important regulatory mechanism in *C. elegans* development. In hermaphrodites, the decision of a germ cell to become sperm or oocyte depends on the control of two sex-determining RNAs: *tra-2* RNA is repressed to permit spermatogenesis, and *fem-3* RNA is inactivated to allow the switch to oogenesis. Therefore, without these two post-transcriptional controls, the hermaphrodite germ line would not make sperm and then oocytes. These post-transcriptional controls are therefore essential to the development of an XX animal as a hermaphrodite rather than a female. To direct embryogenesis, oocytes accumulate maternal RNAs, which are probably controlled to provide distinct patterns of protein expression in the embryo. Some maternal RNAs, such as *glp-1*, may be inactive in oocytes and then activated at specific times and in specific embryonic cells. Furthermore, analysis of the *tra-2* and *lin-14* genes suggests that regulatory elements in 3'UTRs have significant effects on post-embryonic somatic development. These studies imply that the regulation of RNA activity has a larger influence on developmental decisions than previously appreciated.

An emerging theme of RNA control, in *C. elegans* and other organisms, is the role of regulatory elements within the 3'UTR. In organisms as diverse as worms, flies, frogs, and mice (see P. M. MacDonald, N. Standart, R. P. Wharton, M. Wickens, this issue), 3'UTRs have been implicated in the control of translation, localization, and stability of maternal mRNAs. Like gene promoters, these elements dictate when and where protein products are synthesized. Given this broad relevance, many of the underlying mechanisms are apt to be fundamental and conserved. The regulated polyadenylation of diverse types of RNAs may exemplify this conservation.

**References**

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