

<FURTHER DEVELOPMENT 9.6>

Defining the role of SKN-1 and PAL-1 in early cell specification in *C. elegans*

Defining the role of SKN-1 and PAL-1 in early cell specification in *C. elegans*@@The SKN-1 (“skin excess”) protein is a maternally expressed transcription factor that controls the fate of the EMS blastomere, the cell that generates the posterior pharynx. After first cleavage, only the posterior blastomere—P₁—has the ability to produce pharyngeal cells when isolated. After P₁ divides, only EMS is able to generate pharyngeal muscle cells in isolation (Priess and Thomson 1987). Similarly, when the EMS cell divides, only one of its progeny, MS, has the intrinsic ability to generate pharyngeal tissue. These findings suggest that pharyngeal cell fate may be determined autonomously by maternal factors residing in the cytoplasm that are parceled out to these particular cells.

Bowerman and co-workers (1992a,b; 1993) identified maternal effect mutants that lacked pharyngeal cells and were able to isolate a mutation in the *skn-1* gene. Embryos from homozygous *skn-1*-deficient mothers lack both pharyngeal mesoderm and endoderm derivatives of EMS (FIGURE 1). Instead of making the normal intestinal and pharyngeal structures, these embryos seem to make extra hypodermal (skin) and body wall tissue where their intestine and pharynx should be. In other words, the EMS blastomere appears to be re-specified as a C blastomere. Only those cells destined to form pharynx or intestine are affected by this mutation. The SKN-1 protein is a transcription factor that initiates the activation of those genes responsible for forming the pharynx and intestine (Blackwell et al. 1994; Maduro et al. 2001).

Another transcription factor, **PAL-1**, is also required for the differentiation of the P₁ lineage. PAL-1 activity is needed for the normal development of the *somatic* (but not the germline) descendants of the P₂ blastomere, where it specifies muscle production. Embryos lacking PAL-1 have no somatic cell types derived from the C and D stem cells (Hunter and Kenyon 1996). PAL-1 is regulated by the MEX-3 protein, an RNA-binding protein that appears to inhibit the translation of *pal-1* mRNA. Wherever MEX-3 is expressed, PAL-1 is absent. Thus, in *mex-3*-

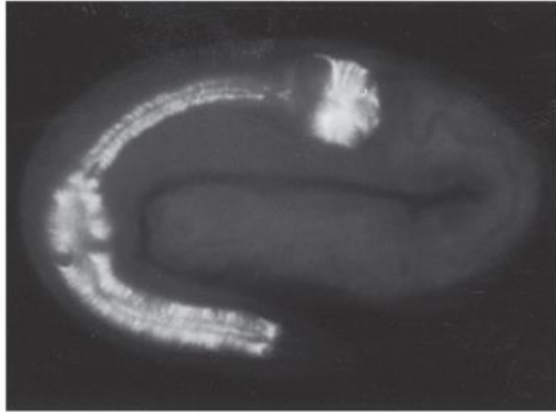
deficient mutants, PAL-1 is seen in every blastomere. SKN-1 also inhibits PAL-1 (thereby preventing it from becoming active in the EMS cell). But what keeps *pal-1* from functioning in the prospective germ cells and turning them into muscles? In the germ line, PAL-1 synthesis is prevented by the PUF-8 protein, which binds to the 3' UTR of *pal-1* mRNA and blocks its translation (Mainpal et al. 2011).

A third transcription factor, **PIE-1**, is necessary for germline cell fate. PIE-1 is placed into the P blastomeres through the action of the PAR-1 protein (**FIGURE 2**), and it appears to inhibit both SKN-1 and PAL-1 function in the P₂ and subsequent germline cells (Hunter and Kenyon 1996). Mutations of the maternal *pie-1* gene result in germline blastomeres adopting somatic fates, with the P₂ cell behaving similarly to a wild-type EMS blastomere. The localization and the genetic properties of PIE-1 suggest that it represses the establishment of somatic cell fate and preserves the totipotency of the germ cell lineage (Mello et al. 1996; Seydoux et al. 1996).

Wild-type

(A)

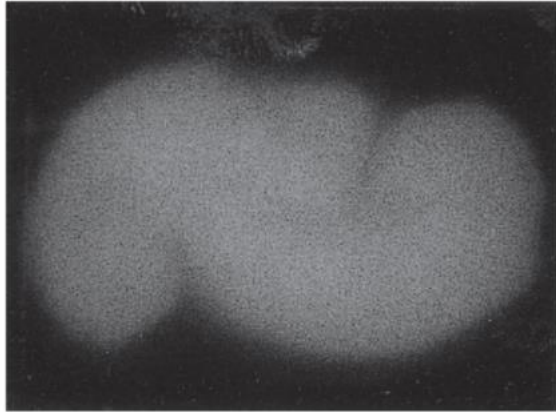
Pharynx
muscle
antigen



skn-1 mutant

(B)

Pharynx
muscle
antigen



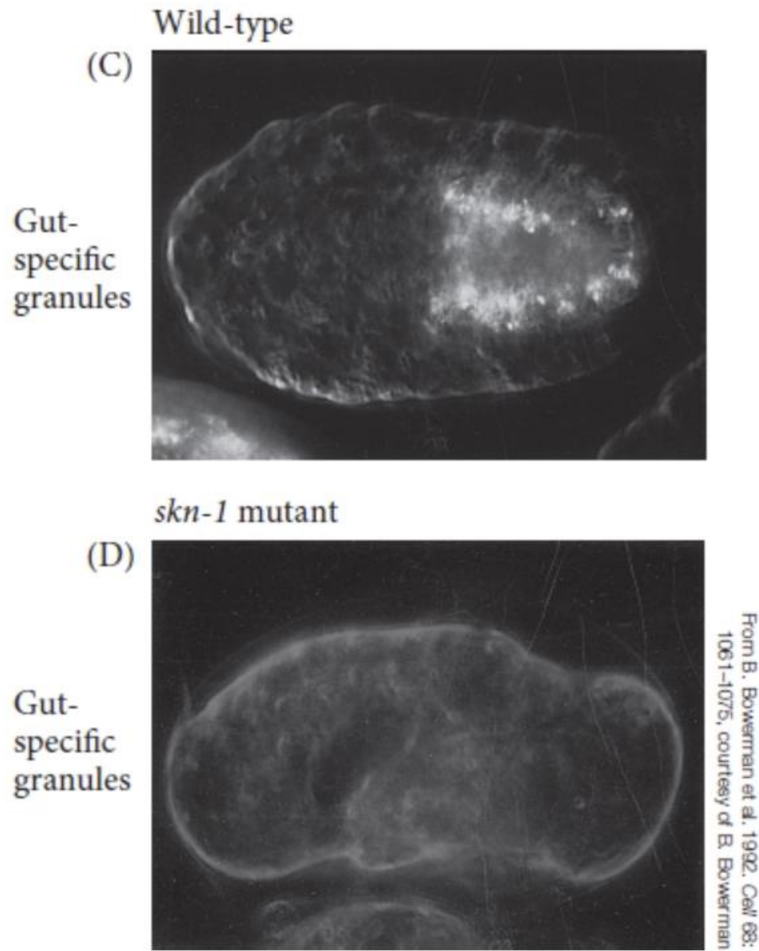


FIGURE 1@@Deficiencies of intestine and pharynx in *skn-1* mutants of *C. elegans*. Embryos derived from wild-type animals (A,C) and from animals homozygous for mutant *skn-1* (B,D) were tested for the presence of pharyngeal muscles (A,B) and gut-specific granules (C,D). A pharyngeal muscle-specific antibody labels the pharynx musculature of those embryos derived from wild-type (A) but does not bind to any structure in the embryos from *skn-1* mutants (B). Similarly, the gut granules characteristic of embryonic intestines (C) are absent from embryos derived from the *skn-1* mutants (D).

Credit

From B. Bowerman et al. 1992. *Cell* 68: 1061–1075, courtesy of B. Bowerman

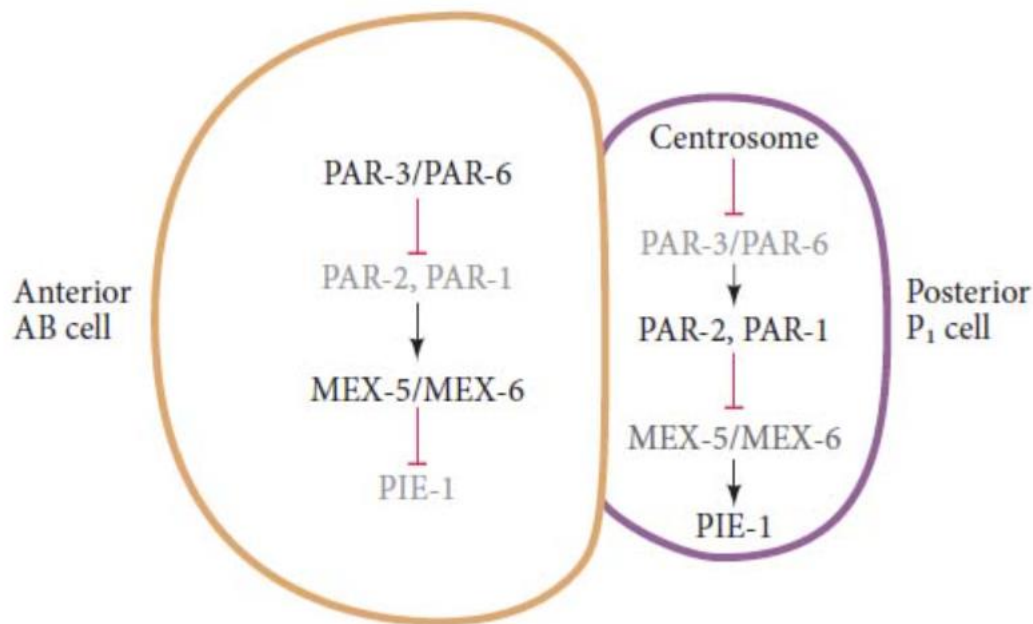


FIGURE 2@@ Segregation of PIE-1 determinant into the P₁ blastomere at the 2-cell stage. The sperm centrosome inhibits the presence of the PAR-3/PAR-6 complex in the posterior of the egg. This allows the function of PAR-2 and PAR-1, which inhibit the MEX-5 and MEX-6 proteins that would degrade PIE-1. So while PIE-1 is degraded in the resulting anterior AB cell, it is preserved in the posterior P₁ cell. (After P. Gönczy and L. S. Rose. October 15, 2005.

WormBook, ed. The *C. elegans* Research Community, *WormBook*,
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