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Nucleotide-sugar biosynthesis and glycosylation are involved in vulval morphogenesis

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Eight *sqv* (squashed vulva) genes (*sqv-1* to *8*) have a mutant vulval morphogenetic phenotype that is defined by reduced separation between the anterior and posterior halves of the vulva in the L4 (1). SQV-3 and SQV-8 are glycosyltransferase-like proteins, and SQV-7 is similar to a putative nucleotide-sugar transporter (2). We have previously reported the cloning of *sqv-1* and *sqv-4* (3). Both SQV-1 and SQV-4 are similar to enzymes involved in nucleotide-sugar metabolism. These molecular identities suggest that glycosylation is important in shaping the vulva during development.

We have now determined biochemically that SQV-4 is a UDP-glucose dehydrogenase. Recombinant SQV-4 expressed in *E. coli* can reduce NAD in the presence of UDP-glucose, suggesting that UPD-glucose is being converted to UDP-glucuronate. Like known UDP-glucose dehydrogenases, SQV-4 appears to act specifically on UDP-glucose, as it fails to reduce NAD using any of the many other nucleotide-sugars tested. Mutant recombinant SQV-4 derived from either of the two genetically identified mutant alleles does not show detectable activity.

Preliminary antibody staining using a rabbit polyclonal antibody directed against a GST::SQV-4 indicates that SQV-4 is localized to the vulval cells and several other tissues, including seam cells. This result agrees with the expression of SQV-4::GFP fusion protein and supports a model in which SQV-4 acts in the vulval cells during vulval development.

We also are trying to determine the functions of the other four cloned *sqv* genes using biochemical assays and heterologous complementation. Lastly, we are mapping and cloning the three remaining *sqv* genes.

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1. Herman, T. et al. (1999). PNAS **96**: 968-973.

2. Herman, T. and Horvitz, H.R. (1999). PNAS **96**: 974-979.

3. Hwang, H. and Horvitz, H.R. (1998) East Coast C. elegans meeting, p. 103.