**Research Statement**

Developmental and molecular biology of nematodes, Ascaris suum, Caenorhabditis elegans, and Ascaris lumbricoides.
Nematodes (round worms) are excellent models for cell-lineage studies. By the 30-cell stage, a single primordial germ cell is determined to become the entire germline of the adult. To study the molecular basis of germline determination, the free-living worm Caenorhabditis elegans is being used.

Cytoplasmic P granules, containing proteins and RNA, segregate exclusively with the germline in C. elegans. The Bennett laboratory has identified four germline RNA helicase genes, glhs, and shown them to be components of the P granules. The GLH predicted proteins are unique from other RNA helicases in containing zinc fingers, like those found in retroviruses, including HIV. Injections with double-stranded RNAs (RNA interference) reveal critical roles for GLH-1 and GLH-4 in the establishment of the germline.

We have generated deletion strains for each of the GLH proteins and also have the critical glh-1 glh-4 double mutant. A yeast two-hybrid screen identified protein binding partners of the GLHs, four of which have been pursued. One of the proteins that binds the GLHs is KGB-1, a novel MAP kinase. When KGB-1 is missing (in the deletion strain kgb-1(um3)) the levels of GLH-1 protein are excessively high and these worms are sterile. Thus, too much or too little GLH-1 protein results in loss of the germline. There are homologues of the GLH proteins in flies, mice and humans.

Our laboratory is also attempting to sterilize Ascaris nematodes using the technique of RNAi. Ascaris worms are the most abundant parasitic worm of swine (see Figure 3, which shows the worms in the small intestine of a Missouri pig ) and of humans. Thus far we have successfully used several Ascaris dsRNAs to carry out cross-species RNAi into C. elegans.

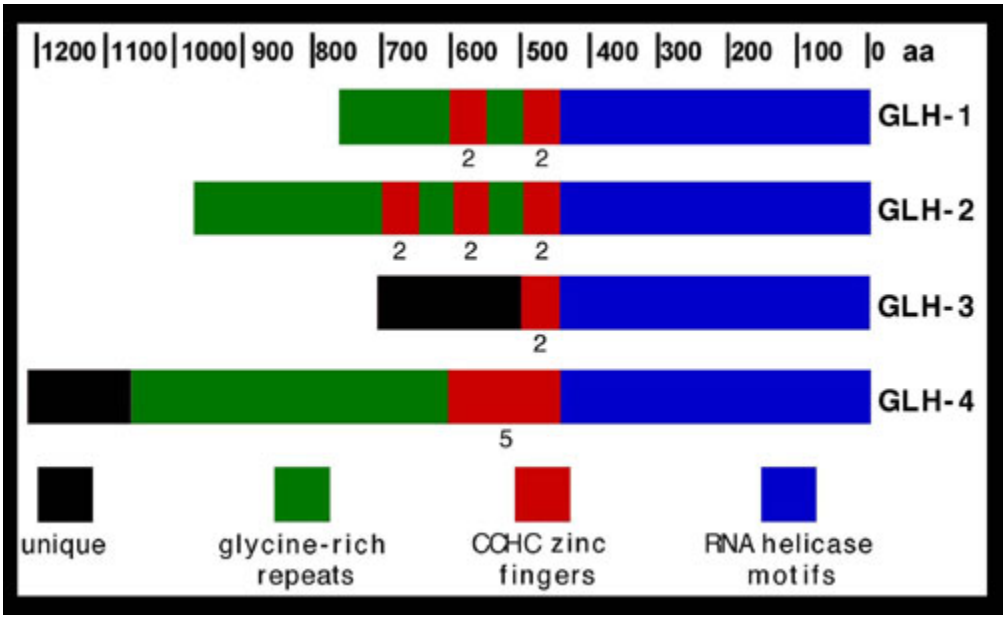

Figure 1: A comparison of the motifs of the four GLH proteins. The unique regions of GLH-3 and GLH-4 differ from one another. The numbers of zinc fingers in each group are indicated below the fingers.

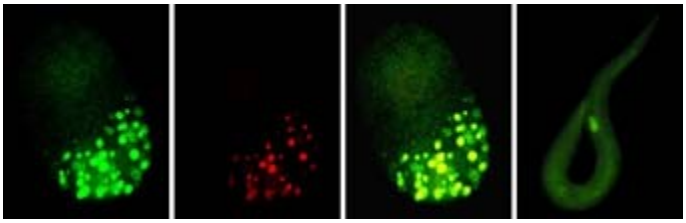

Figure 2. P granules localized even before the first cell division. Confocal image of a one-cell C. elegans embryo: aGLH-2 (green), left; aGLH-1 (red), middle; combined (yellow), right. These components co-localize to the posterior cortex of the newly fertilized P0 zygote. An L1 larvae, far right, showing GLH-1 in Z2 and Z3, the daughter cells of P4, the germline precursor. Confocal images were taken at the UMC Cytology Core.

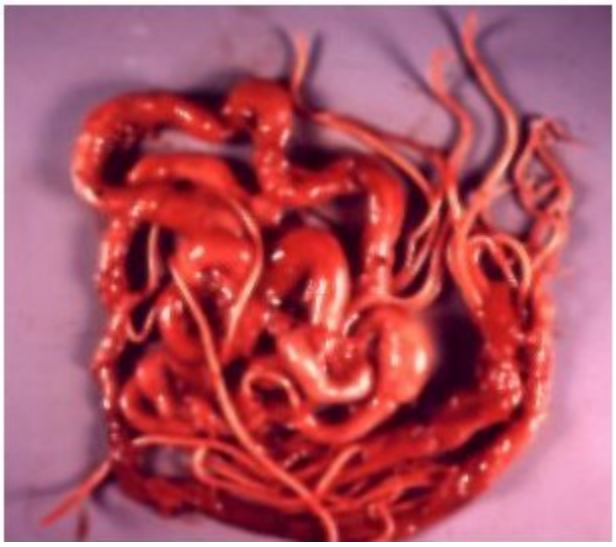

Figure 3: Parasitic Ascaris suum worms are seen in the intestine of a Missouri swine.