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Cross-species RNAi: dermas from two Ascaris genes sterilize Caenorhabditis

The parasitic nematode Ascaris lumbricoides is the most ubiquitous human parasite, infecting ~ 1/4th of the world's population, while about 25% of Missouri swine are infected with the closely-related species A. suum. Ascaris worms lay 240,000 eggs per day! Because parasitic nematodes are rapidly developing multi-drug resistance, we reasoned that RNA interference (RNAi) might be applicable as a novel anti-parasitic agent. Since ascarid worms cannot be maintained for long in the laboratory, we have begun by testing Ascaris genes in the free-living nematode Caenorhabditis, a model organism that is amenable to laboratory culture. Several Ascaris cDNAs with stretches of identity to C. elegans of >21 nucleotides (nts) and with an overall match of >80% for ~400nts were amplified from Ascaris ovarian RNA. Thus far, after injection into C. elegans, two A. suum genes have been successful in sterilizing C. elegans. In our first tests ~90% of the offspring were either dead embryos or sterile F1 adult worms. Although both genes are highly conserved, neither has a mammalian counterpart with a match of 21 nts. To understand more about RNAi in C. elegans, we are planning to try cross-species RNAi with only a 26 nt match. We also plan to test nematode-specific genes, to expand our studies to the moreapplicable feeding methods of dsRNA delivery, and to test these candidates in isolated Ascaris worms.