BACKGROUND: Brugia malayi, like most
human filarial parasite species, harbors an endosymbiotic bacterium of the
genus Wolbachia. Elimination of the endosymbiont leads to sterilization of the
adult female. Previous biochemical and genetic studies have established that
communication with its endobacterium is essential for survival of the worm.
METHODOLOGY/PRINCIPAL FINDINGS: We used electron microscopy to examine the
effects of antibiotic treatment on Wolbachia cell structure. We have also used
microarray and quantitative RT-PCR analyses to examine the regulation of the B.
malayi transcripts altered in response to the anti-Wolbachia treatment.
Microscopy of worms taken from animals treated with tetracycline for 14 and 21
days (14 d and 21 d) demonstrated substantial morphologic effects on the
Wolbachia endobacterium by 14 d and complete degeneration of the endobacterial
structures by 21 d. We observed upregulation of transcripts primarily encoding
proteins involved in amino acid synthesis and protein translation, and
downregulation of transcripts involved in cuticle biosynthesis after both 7 d
and 14 d of treatment. In worms exposed to tetracycline in culture, substantial
effects on endobacteria morphology were evident by day 3, and extensive death
of the endobacteria was observed by day 5. In a detailed examination of the
expression kinetics of selected signaling genes carried out on such cultured
worms, a bimodal pattern of regulation was observed. The selected genes were
upregulated during the early phase of antibiotic treatment and quickly
downregulated in the following days. These same genes were upregulated once
more at 6 days post-treatment. CONCLUSIONS/SIGNIFICANCE: Upregulation of
protein translation and amino acid synthesis may indicate a generalized stress
response induced in B. malayi due to a shortage of essential nutrients/factors
that are otherwise supplied by Wolbachia. Downregulation of transcripts
involved in cuticle biosynthesis perhaps reflects a disruption in the normal
embryogenic program. This is confirmed by the expression pattern of transcripts
that may be representative of the worms' response to Wolbachia in different
tissues; the early peak potentially reflects the effect of bacteria death on
the embryogenic program while the second peak may be a manifestation of the
adult worm response to the affected bacteria within the hypodermis. .
.