The bZIP transcription factor, ZIP-2 is activated by *Streptococcus gordonii*

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Objective: The mitis group streptococci that resides within the oral cavity have shown to be opportunistic pathogens. These microorganisms produce hydrogen peroxide (H_2O_2) as a major virulence factor that contributes to the pathogenicity. The immune responses induced to this group of opportunistic pathogens have not been extensively studied. Previously, we have shown the BZIP transcription factor, ZIP-2 activates in an immune response in the nematode *Caenorhabditis elegans* against the mitis group streptococci. *C. elegans* is an excellent model to elucidate innate immune responses that are conserved in higher organisms. In this study we characterized the role of ZIP-2 and the induced response to a representative of the mitis group, *Streptococcus gordonii*.

Methods: To determine if *zip-2* is required for the survival of worms on *S. gordonii*, we performed killing assays using wild-type (WT) and *zip-2* mutant worms in the presence or absence of catalase. To establish if ZIP-2 is activated in response to *S. gordonii*, we imaged the localization of ZIP-2 fused to green fluorescent protein (GFP) in the intestinal cells of worms exposed to *S. gordonii* in presence or absence of catalase and on non-pathogenic *E. coli.* In addition, we imaged worms expressing *zip-2*-dependent gene *irg-1* fused to GFP in the presence of *S. gordonii* and *E. coli*.

Results: A significant decrease in the survival of the *zip-2* mutant worms was observed relative to the WT worms. No deaths were observed in the presence of catalase suggesting H_2O_2 mediates killing of the worms. Activation of ZIP-2 was observed in the intestinal cells of the worm in response to *S. gordonii* and was mediated by H_2O_2. Lastly, we observed the expression of *irg-1*::GFP in worms exposed to *S. gordonii* compared to *E. coli*.

Conclusions: Taken together, ZIP-2 is important to the survival of *C. elegans* when exposed to *S. gordonii*.

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