The regulation of ZIP-10 in *C. elegans* during infection

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Objective: The nematode *Caenorhabditis elegans* is versatile model to study immune and stress responses to oxidative stress. Previously we have shown the mitis group streptococci releases hydrogen peroxide causing cytotoxic to the worm. The bZIP transcription factor ZIP-10 has been reported to participate in oxidative stress resistance and required for the survival of the worms on the mitis group. Interestingly, ZIP-10 is a target of the microRNA *mir-60*, which is activated by the splicing factor ISY-1. We hypothesize that ZIP-10 is upregulated in response to *S. gordonii*, a member of the mitis group via the splicing factor ISY-1 along with interacting partners during oxidative stress.

Methods: *zip-10*, *isy-1* knockdown and vector control treated larvae were scored for survival on *S. gordonii*. To determine the upregulation of ZIP-10, localization of ZIP-10::GFP was determined in *isy-1* knockdown worms relative to vector control treated worms. A protein network based on known interactors of ISY-1 was built using the STRING database. Knockdowns of these candidates were tested in ZIP-10::GFP strain. Thereafter, the survival of these candidates was assessed on *S. gordonii*.

Results: Survival of *zip-10* and *isy-1* knockdown worms were decreased and increased respectively in the presence of *S. gordonii*. ZIP-10::GFP levels were significantly upregulated in *isy-1* knockdown worms relative to the vector control treated worms. Protein network analysis revealed several candidate proteins that interacted with ISY-1. We observed significant upregulation of ZIP-10::GFP and increase in survival of M03F8.3, *eftu-2* and *prp-17* knockdown worms relative to the control.

Conclusion: Consistent with our hypothesis, we show that the bZIP transcription factor ZIP-10 is important for the survival of the worms on *S. gordonii*. Furthermore, we show that ISY-1, M03F8.3, EFTU-2 and PRP-17 are important modulators of ZIP-10 activity.

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