Metformin induced survival of *C. elegans* on *S. gordonii* requires MDT-15

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**Objectives:** Mitis group streptococci are an understudied group of opportunistic pathogens that reside in the oral cavity and are capable of producing hydrogen peroxide as major contributor to their pathogenesis. Using the nematode *Caenorhabditis elegans*, we have shown the oxidative stress response transcription factor SKN-1/Nrf-2 is required for the survival of the worms in response to H$_2$O$_2$. Pretreatment of worms with metformin activates SKN-1 via the p38 MAPK pathway and mediates protection from streptococcal infections. More recently we have shown the mediator subunit MDT-15 is also required for the localization of SKN-1 to the intestinal nuclei in response to metformin. Based on the data, we will elucidate the role of MDT-15 in the metformin mediated protection in response to streptococcal H$_2$O$_2$.

**Methods:** To confirm the metformin enhanced survival of the worms is mediated by *skn-1*, we compared survival of *skn-1* mutant worms on *Streptococcus gordonii* in the presence or absence of metformin. To further confirm the activation of SKN-1 is mediated by MDT-15 in response to metformin, we observed the expression of *skn-1*-dependent genes *gcs-1* and *gst-4* fused to green fluorescent protein (GFP) in *mdt-15* knockdown worms relative to vector control treated worms by epifluorescence microscopy. Finally, we determine if the enhanced survival of the worms is mediated by *mdt-15* by comparing the survival of *mdt-15* mutant worms on *S. gordonii* in the presence or absence of metformin.

**Results:** No significant difference was observed in *skn-1* mutant worms in the presence or absence of metformin. *gcs-1::GFP* and *gst-4::GFP* expression significantly decreased in *mdt-15* knockdown worms compared to the vector control treated worms. Furthermore, no significant decrease in survival of *mdt-15* mutant worms was observed in the presence or absence of metformin.

**Conclusion:** In addition to the p38 MAPK pathway, MDT-15 is required for the metformin enhanced protection of the worms.

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