

Molecular Mechanisms of Low Dose Radiation Mediated Hormesis in *C. elegans*

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Brief exposure to a mild stress causes induction of stress gene expression leading to enhanced stress responses, improved maintenance and repair and in some cases lifespan increase. This phenomenon is termed hormesis and has been observed in several species. For example, we previously demonstrated that short periods of mild heat stress in early life increase both mean and maximum lifespan of the soil nematode *C. elegans*. Similar hormetic responses have been described for many other stressors. Here we present data showing that treatment of the nematode with low-doses of ionizing radiation (IR) significantly increases resistance to sub-sequent heat stress. Importantly, we found that the progeny of nematodes treated with IR are extremely resistant to heat stress compared to progeny of untreated controls. This novel finding is intriguing since stress resistance in the progeny generation has not been described for IR or any other stressors. Interestingly, this effect was independent of insulin signaling, a well known pathway determining stress resistance and lifespan in *C. elegans*. Likewise, the tumor suppressor p53 (*cep-1* in *C. elegans*) was not required for low-dose IR induced stress resistance in the progeny generation, similar to the relative p53-independence of radiation hormesis in human cells (Davalos et al., abstract). We are expanding our genetic analysis to include other well known DNA damage / checkpoint proteins, including the Werner and Bloom syndrome proteins (*wrn-1* and *him-6*, respectively in *C. elegans*). We have also undertaken microarray analysis of the progeny of worms exposed to IR to establish which gene expression changes are responsible for the increase in stress resistance. Since many long-lived worms are also resistant to stress, we are currently investigating whether low dose IR increases the lifespan of the nematode.