

P049 *C. elegans* SIR-2.1 translocation is linked to a proapoptotic pathway parallel to *cep-1/p53* during DNA damage-induced apoptosis

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SIR-2.1 is a member of the sirtuin family of protein deacetylases that are conserved from archae to mammals and are present in virtually every species so far examined. Sirtuins are known to regulate diverse cellular processes, including transcription, ageing, metabolism, and stress responses like apoptosis and DNA repair.

We have found a novel, pro-apoptotic, sirtuin function. We show that *C. elegans sir-2.1* is essential for apoptosis specifically in response to DNA damage, while it is dispensable for other forms of apoptosis, such as developmental apoptosis, and does not overtly affect DNA repair. Genetically *sir-2.1* acts in parallel to *cep-1(p53)* and likely affects apoptosis at the level of *egl-1(BH3 only)/ced-9(Bcl-2)/ced-4(Apaf-1)*, downstream of *cep-1*. Immunostaining reveals that during apoptosis SIR-2.1 translocates from the nucleus to the cytoplasm of dying cells and transiently colocalizes with the *C. elegans* Apaf-1 homologue CED-4 at the nuclear periphery, suggesting a functional relationship. SIR-2.1 translocation is independent of *cep-1* and *ced-3(caspase)*, confirming our genetic data indicating that SIR-2.1 acts in a pathway parallel to CEP-1.