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Death by PARP

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PARP-1 (poly(ADP-ribose) polymerase-1) is a nuclear enzyme that is important for genome repair and DNA replication. PARP-1 also induces cell death in a number of physiological contexts. In the July 12 Science, Yu *et al.* describe a mechanism by which nuclear PARP-1 regulates a mitochondrial protein to induce apoptosis (*Science* 2002, **297:**259-263). They studied fibroblasts generated from *parp-1* knockout mice and examined the response to DNA-alkylating agents; they found that cells from the knockout mice failed to undergo apoptosis and lacked nuclear translocation of the mitochondrial flavoprotein apoptosis-inducing factor (AIF). Neutralizing anti-AIF antibodies blocked PARP-1-dependent cell death. Yu *et al.* propose a mechanism in which DNA damage induces PARP-1 activation leading to NAD+ consumption that is sensed by mitochondria and results in AIF translocation to the nucleus, nuclear condensation and death. This study thus provides a molecular link between the integrity of the nuclear genome and activation of mitochondrial killer proteins.

References

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