Traumatic brain injury (TBI) is common and often fatal in current times. The role of poly(adenosine diphosphate-ribose) polymerase (PARP)-induced cell death (parthanatos) in TBI has not been well studied. Our past study showed that oxidative stress-induced cell death includes parthanatos by confirming the occurrence of PARP activation and nuclear translocation of apoptosis-inducing factor (AIF). As oxidative stress plays a key role in pathological progression after TBI, we believe TBI may also be alleviated by the expression of Iduna, which is the only known endogenous regulator of parthanatos. Thus, a transection model in HT-22 cells was established for present study. Downregulation of Iduna aggravated the cell damage caused by mechanical cell injury, whereas upregulation of Iduna reduced mitochondrial dysfunction induced by mechanical cell injury but exerted no effect on apoptosis associated with mitochondrial dysfunction. By contrast, Iduna prevented parthanatos by reducing PARP activation and nuclear translocation of AIF. We also investigated 2 novel p53-MDM2 pathway inhibitors, AMG 232 and Nutlin-3, which substantially reduced the protective effects of Iduna. These findings indicate that Iduna might prevent TBI by specifically inhibiting parthanatos and promoting mitochondrial function, with the p53-MDM2 pathway playing a critical role [1)].

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