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Regulating p53

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MDM2 is an E3 ubiquitin ligase that regulates the activity of p53 by controlling degradation of the p53 protein, as a result of differential addition of ubiquitin. In the Advanced Online Publication of Nature Genetics, Parant *et al.* report the phenotype of mice lacking the recently cloned MDM2-related protein MDM4 (DOI:10.1038/ng714). They show that *mdm4*-null mice die at embryonic day 7.5-8.5. Analysis of the incorporation of the nucleotide analogue BrdU and TUNEL staining for apoptotic cells showed that, unlike mdm2-deficient embryos, death appears to be due to reduced cell proliferation and not induction of apoptosis. As with the *mdm2*-deficient lethality, loss of *Trp53* rescued the lethal phenotype of *mdm4*-null embryos. Thus, *in vivo* the MDM2 and MDM4 proteins are non-overlapping regulators of p53 function.

References

1. *Nature Genetics*, [http://genetics.nature.com]

2. MDMX: a novel p53-binding protein with some functional properties of MDM2

3. Rescue of early embryonic lethality in mdm2-deficient mice by deletion of p53.