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MDM2/X mediates reduced apoptosis in the plateau zokor: a mechanism of high-altitude adaptation

Key words: Murine double minute 2/4 (MDM2/X); Plateau zokor; Apoptosis; Adaptation; Extreme environment

Research Summary

This study aimed to explore the molecular mechanisms of *Mdm2/x* variations in *Myospalax baileyi* (*M.b.*, plateau zokor) and *Myospalax cansus* (*M.c.*, Gansu zokor) drive adaptation to high-altitude conditions.

- There are many variation sites across MDM2 and MDMX CDS in the subterranean *M.b.* and *M.c.* (vs lab rats and humans).
- Basal MDM2/X mRNA and protein expression levels are higher in the lung, liver, and spleen from subterranean zokors.
- MDM2 and MDMX in *M.b./M.c.* mediate the lower apoptosis in a p53-dependent manner.
- The *M.b./M.c.*-MDM2 C-terminal F390/A415 variations involved in increased p53 mRNA and protein expression *via* phosphorylation modifications.

Innovation points

- Find the variations and functional convergence in MDM2/X in subterranean zokors.
- Demonstrate MDM2/MDMX regulate p53 functions to a decreased apoptosis for survival in *M.b.* and *M.c.*
- Identify loss-of-phosphorylation variations in MDM2 C-terminal invert the traditional negative regulator role of MDM2 to p53.

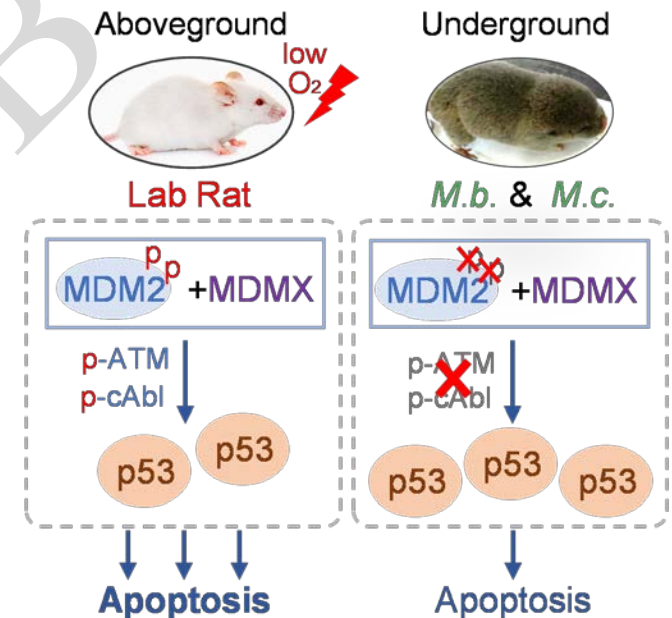


Figure 5e