



**FIGURE 1.** Regulation of p53 by MDM2. (a) Autoregulatory feedback loop assures that both p53 and MDM2 proteins are kept at low levels in proliferating cells. p53 activates MDM2 transcription. MDM2 binds p53 and negatively modulates its activity and stability by blocking the transcriptional activation domain of p53 and targeting p53 for ubiquitin-dependent degradation in the proteasome. (b) Small-molecule antagonists of p53-MDM2 binding can release p53 from negative control and activate the p53 pathway.

*Protein-Protein Interactions: A Molecular Cloning Manual*, 2nd Ed., © 2005 by Cold Spring Harbor Laboratory Press, Chapter 46, Figure 1.