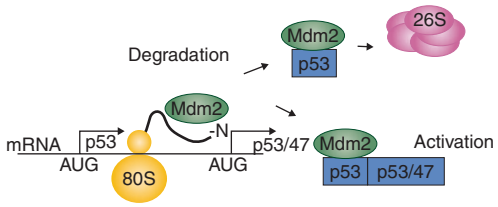
Mini p53

The tumour suppressor gene *p53* was named after the apparent molecular mass of its protein product. This nomenclature is not ideal as can lead to confusion between proteins that have the same masses. It is even more confusing in the light of the report by Robin Fåhraeus and colleagues on page 462 of this issue that there are two alternative products of the p53 gene, which have relative masses of 53K and 47K, respectively. The authors found that the *p53* gene contains two in-frame alternative start codons. Initiation of translation at the internal start codon leads to the synthesis of truncated form of p53, designated p53/47, which lacks the Mdm2-binding site and most of the amino-terminal transactivation domain of full-length p53. Expression of p53/47 does not depend on expression of full-length p53.

Mdm2 is known to regulate p53 levels by targeting p53 for degradation. Fåhraeus' team found that, because p53/47 fails to interact with Mdm2, p53 tetramers containing p53/47 are more stable in the presence of Mdm2. The authors also found that Mdm2 regulates p53 levels not only by regulating its degradation, but also by inducing its translation, and that these activities result from two separate functions of Mdm2. Previous studies have shown that Mdm2 interacts with ribosomes and with RNA, observations that provide clues about possible mechanisms for how Mdm2 regulates p53 translation (see Figure).

Although Mdm2 also regulates the translation of p53/47, it does not induce its degradation, so Mdm2 expression alters the ratio of p53 to p53/47 (see Figure).



Model proposed by R. Fåhraeus

The Fåhraeus lab also found that the profile of genes activated by p53/47 is different from that of the genes activated by p53, presumably because the transactivation domains of the two proteins are different. Indeed, increasing levels of p53/47 relative to p53 leads to reduced expression of p21 but higher expression of Bax, which are two targets of p53 involved in cell-cycle arrest and apoptosis, respectively. So the switch in the relative levels of p53 and p53/47 brought about by Mdm2 could have biological consequences. But the authors did not see any difference in apoptosis, under the conditions they tested, when they expressed wild-type p53 or a mutant that does not allow expression of p53/47, so the physiological role of p53/47 and of Mdm2's function in regulating p53 and p53/47 levels remain to be established.

VALERIE FERRIER