Chapter 18
Web Text Box 5

p53: all that stands between us and cancer?

TP53, the gene that encodes p53 (book pages 306-311), is perhaps the clearest example of a tumor suppressor gene. Such genes negatively regulate the cell cycle such that their absence or modification results in uncontrolled cell proliferation and the formation of tumors. In the case of p53, a transcription factor, most of the mutations that result in loss of function lie in the region of the protein that binds to DNA. TP53 is mutated in more than 50% of cases of Li-Fraumani syndrome, a genetic predisposition to multiple primary tumors. TP53 displays haploid insufficiency, that is, mutation of only one copy of the gene is sufficient to cause its inactivation. In cervical cancer, p53 is inactivated not by mutation of the gene but by binding of the protein to the E6 protein of HPV (human papilloma virus).

p53 is normally maintained at low levels by a negative regulator called Mdm2. In response to DNA damage, Mdm2 is inactivated by phosphorylation and the level of p53 rises. If the amount of damage is small then p53 induces p21 and the cell cycle is inhibited (see the main text). If, on the other hand, the damage is great then p53 induces other proteins that direct the elimination of damaged cells by apoptosis. p53 has been likened to a traffic cop who stands at a busy junction directing traffic down the appropriate cellular highway.