The p53 protein
Under normal conditions, p53 will not last for a long time and it degrade rapidly. The p53 suggests that a function is required only in special circumstances. The concentration of p53 rises when the cell be in danger of death or serious injury. all thesis circumstances call for desperate action, which may take either of two forms: the cell can block any further progress through the division cycle in order to take time out to repair or recover from the pathological condition, or it can accept that it must die, and do so in a way that minimises damage to the organism.

the p53 protein always acts as a transcription factor. Because p53 binds to DNA as a tetramer, a single mutant subunit within a tetrameric complex can be enough to block its function. Thus, mutations in p53 can have a dominant negative effect, causing loss of p53 function even when the cell also contains a wild-type version of the gene. For this reason, in contrast with other tumor suppressor genes such as Rb, the development of cancer does not always require that both copies of p53 be knocked out.

When there is DNA damage in the cell cycle, the p53 will be activited in a indirect mehanism. In undamaged cells, p53 is highly unstable and is present at very low concentrations. This is largely because it interacts with another protein, Mdm2, which acts as a ubiquitin ligase that targets p53 for destruction by proteasomes. Phosphorylation of p53 after DNA damage reduces its binding to Mdm2. This decreases p53 degradation, which results in a marked increase in p53 concentration in the cell. In addition, the decreased binding to Mdm2 enhances the ability of p53 to stimulate gene transcription. Then the protein p53 will stimulates transcriptionn of the gene enconding p21, a CKI protein, p21 binds to G1/S-Cdk and S-Cdk complexes and inhibits their activities, thereby helping to block entry into the cell cycle.

Similarly, in response to DNA damage that cannot be repaired, the tumor suppressor protein p53 accumulates (discussed in Chapters 17 and 20) and activates the transcription of genes that encode the BH3-only proteins Puma and Noxa. These BH3-only proteins then trigger the intrinsic pathway, thereby eliminating a potentially dangerous cell that could otherwise become cancerous.

PTEN acts as a tumor suppressor by being an antagonist of the PI3K/AKT pathway. It dephosphorylates PIP3 back to PIP2, inhibiting AKT activation. This suppression of AKT reduces cell proliferation and survival signals, preventing uncontrolled growth and tumor development. Loss of PTEN function can lead to reduced apoptosis and increased cell proliferation, contributing to cancer progression.

RAS proteins are oncogenic GTPases, acting as molecular switches in signaling pathways influencing cell proliferation, differentiation, and survival. When mutated, RAS proteins remain perpetually active, promoting unregulated growth, leading to oncogenesis. Approximately 30% of tumors harbor active RAS mutations, illustrating their critical role in cancer development.