13.6: Tumor Suppressor Genes

More than 30 genes are classified as tumor suppressors. The normal functions of these genes include repair of DNA, induction of programmed cell death (apoptosis) and prevention of abnormal cell division. In contrast to proto-oncogenes, in tumor suppressors it is loss-of-function mutations that contribute to the progression of cancer. This means that tumor suppressor mutations tend to be recessive, and thus both alleles must be mutated in order to allow abnormal growth to proceed. It is perhaps not surprising that mutations in tumor suppressor genes, are more likely than oncogenes to be inherited. An example is the tumor suppressor gene, **BRCA1**, which is involved in DNA-repair. Inherited mutations in **BRCA1** increase a woman's lifetime risk of breast cancer by up to seven times, although these heritable mutations account for only about 10% of breast cancer. Thus, sporadic rather than inherited mutations are the most common sources of both oncogenes and disabled tumor suppressor genes.

An important tumor suppressor gene is a transcription factor named **p53**. Other proteins in the cell sense DNA damage, or abnormalities in the cell cycle and activate p53 through several mechanisms including phosphorylation (attachment of phosphate to specific site on the protein) and transport into the nucleus. In its active form, p53 induces the transcription of genes with several different types of tumor suppressing functions, including DNA repair, cell cycle arrest, and apoptosis. Over 50% of human tumors contain mutations in p53. People who inherit only one function copy of p53 have a greatly increased incidence of early onset cancer. However, as with the other cancer related genes we have discussed, most mutations in p53 are sporadic, rather than inherited. Mutation of p53, through formation of pyrimidine dimers in the genes following exposure to UV light, has been causally linked to squamous cell and basal cell carcinomas (but not melanomas, highlighting the variety and complexities of mechanisms that can cause cancer).
Figure 8: p53 bound to its target site on a DNA molecule. (Wikipedia-Thomas Spettstoesser from Cho et al, Science 265PP346, 1994-CC:AS)

Contributors and Attributions

- Dr. Todd Nickle and Isabelle Barrette-Ng (Mount Royal University) The content on this page is licensed under CC SA 3.0 licensing guidelines.