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Interaction between MDM2 and p53

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The tumour protein, p53, is one of the most conserved genes in the evolutionary process and it is a gene that is commonly mutated in many types of cancer. This gene is significant in the development of the tumour cells because when p53 is mutated, it does not just lose its function but it also gains functions that favour tumourigenesis. Some roles of p53 in the cell include cell cycle control, apoptosis, cell growth arrest and so on. Additionally, the amount of p53 in normal cells is very low; however, when there is DNA damage or other kinds of problems, levels of p53 increase. The levels of p53 are tightly regulated due to their crucial role in the cell. Moreover, one of the crucial negative regulators of p53 is the mouse double minute 2 homologue (MDM2). Further, MDM2's formation is induced by p53. p53’s transcriptional activity is inhibited by MDM2, thus triggering its degradation. Therefore, it can be said that MDM2 has negative effects on apoptosis and cell cycle arrest, due to the absence of p53. Furthermore, amplification of MDM2 is detected in many types of cancer which include colon cancer, lung cancer, etc. This amplification is mostly due to the enhanced translation ability of MDM2 RNA. In other words, it can be said that increased levels of the MDM2 are due to post-transcriptional regulation. Additionally, the malignancies in humans are protected by chemotherapy and radiotherapy, due to the overexpression of MDM2. However, restoration of p53 shows a decrease in the levels of the tumours. Therefore, the inhibition of the interaction between MDM2 and p53 is targeted in novel cancer therapy techniques. The interaction of p53 and MDM2 is regulated in diverse levels and their interaction can be disrupted by different small lipophilic molecules, such as MDM2 inhibitor-219 (MI-219) and Nutlin-3. MI-219 activates p53 and Nutlin-3 exhibits strong anti-tumour activity in mouse models of human cancer. Thus, understanding the interaction between tumour suppressor proteins and their regulators can help in identifying new therapies to battle cancer

Keywords: p53, Regulation, MDM2, Cancer, Cell Cycle, Cancer Therapy

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