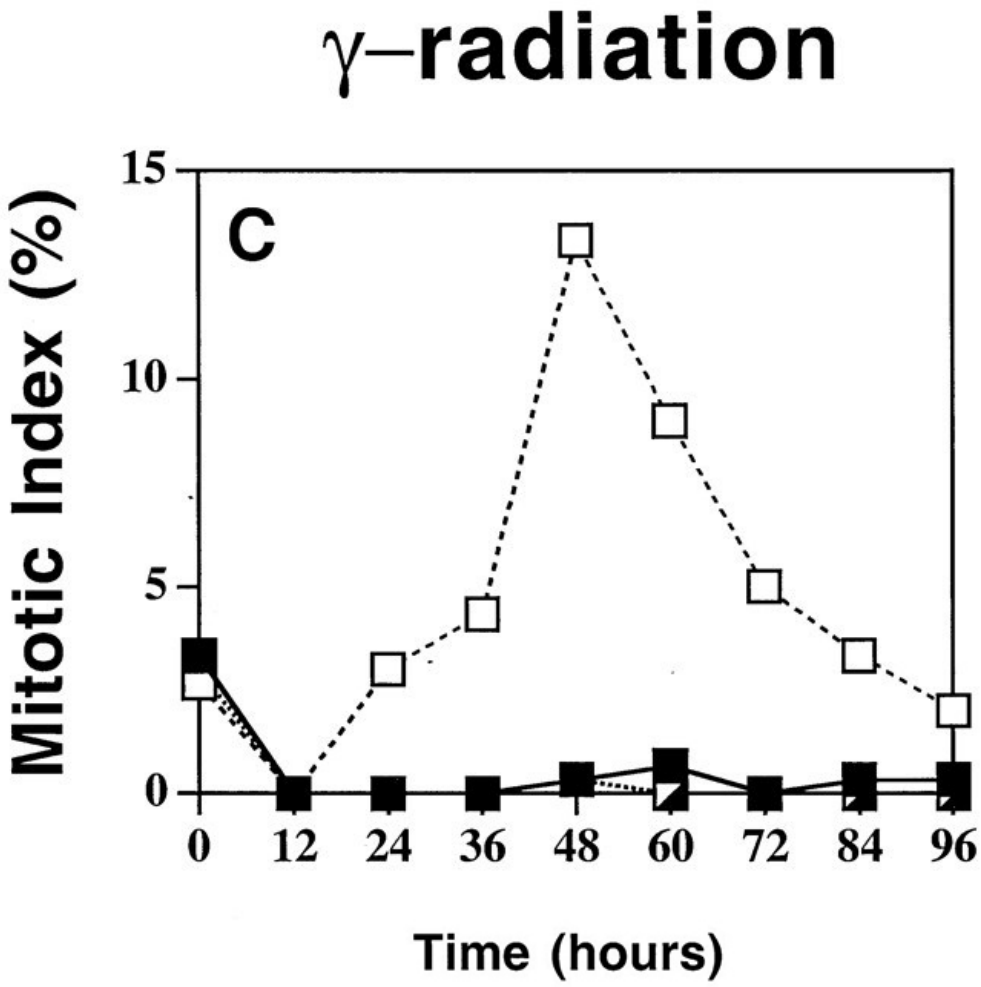

Caption: *Alleles of the* p53 *gene were selectively disrupted in a line of human cells and then monitored after exposure to DNA-damaging gamma (γ) radiation to determine what proportion of the cells entered mitosis (cell division). The shaded squares represent cells with two normal alleles of the* p53 *gene. The half-shaded squares represent cells with one normal and one disrupted allele of the* p53 *gene (note that some of the half-shaded squares are covered by the shaded squares). The unshaded squares represent cells in which both alleles of the* p53 *gene were disrupted. The mitotic index is the proportion of cells undergoing mitosis at a given time.*

BACKGROUND INFORMATION

The p53 protein, referred to as the "Guardian of the Genome," is a tumor suppressor that plays an important role in halting the division of cells (mitosis) that have sustained DNA damage. The p53 protein arrests the cell cycle at two different times: before DNA replication (between phases G_1 and S) and before cell division (between phases G_2 and M). Arresting the cell cycle at these points helps prevent the division of cells containing damaged DNA, which could become cancerous. The gene encoding p53 is often mutated in cancers. In fact, this gene is mutated more often than any of the other 20,000 human genes. A deeper understanding of the role of p53 in the cell cycle can therefore improve our understanding of cancers and perhaps lead to new forms of treatment.

In this study, researchers investigated the role of p53 in cell cycle regulation at the checkpoint between the G_2 and M phases. Most human cells contain two alleles of every gene, one allele inherited from the mother and the other from the father. Normally, an allele can be used to produce a protein, such as p53. However, researchers can use genetic engineering to "disrupt" an allele, making it unable to produce a properly functioning protein. In this case, the researchers genetically engineered a cell line to create two new cell lines, one in which a single allele of the *p53* gene was disrupted and the other in which both alleles were disrupted. Next, they exposed all three cell lines to DNA-damaging gamma radiation and observed how this exposure impacted cell division. They measured the impact by determining the proportion of cells undergoing mitosis, called the mitotic index, for each cell line every 12 hours for four days. The mitotic index was measured by fixing or preserving a sample of the cells and then staining them with a DNA-specific fluorescent stain (Hoechst). Using microscopy, cells containing condensed, evenly stained chromosomes were identified and counted. Condensed chromosomes are an indication that the cells were undergoing mitosis at the time they were fixed.