A Platform to Test the Therapeutic Impact of p53 Restoration

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Cancers arise from mutations in genes regulating cell growth, with the p53 tumor suppressor gene being mutated in over 50% of cases. The p53 protein activates genes that block cell proliferation, but its mutation disrupts this function. While drugs partially reactivating mutant p53 show temporary therapeutic effects, they fail to address the genetic root of the problem. This study aimed to test the hypothesis that genetically correcting mutant p53 back to its normal, "wild type" state could block cancer cell proliferation. A platform was developed using cancer cells with inducible restoration of wild type, mutant, or corrected p53. RNA sequencing measured the expression of p53 target genes five days after restoration, revealing increased expression over time, indicating blocked proliferation. DNA sequencing and western blotting confirmed the system's ability to detect and study p53 mutation effects. These findings support the hypothesis that p53 restoration inhibits cell proliferation and demonstrate the platform's utility for engineering and studying p53 mutations. Future work will explore the therapeutic potential of correcting recurrent p53 mutations.

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