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Project Title

Effects of tp73 Insertion on Cisplatin-Induced Mortality in a Mutated p53-Type Cancer Model

Abstract

Objectives/Goals

Mutant p53 proteins not only lose their tumor suppressive activities but often gain additional oncogenic functions that endow cells with growth and survival advantages. In almost half of all human cancers, the capability to induce cell death is reduced by the mutation and inactivation of p53, a tumor suppressor protein that is a central regulator of apoptosis. p73 (specifically tp73), the closely related p53 family member, can regulate many p53 target genes and therefore some of the same cellular responses as p53. p73 is seldom mutated in cancer, making it an attractive, alternative death effector to target.

Methods/Materials

As a hypothesis, I postulated that the E. coli cells that have the tp73 insertion will have a higher death rate (and thereby a lower survival rate) than the ones without, because of the p73#s suppressing interactions with the tp53. The experiment, inserting p73 and mutp53 vectors into E. coli cells into the groups mutp53+p73, mutp53, and untransformed cells allows us to determine the potential increase in efficacy of p73 insertion based on colony counting and relative cell growth, using E. coli, ampicillin, neomycin, mutp53, tp73, cisplatin, and LB Agar.

Results

The results of the experiment are that there was significantly less growth (around 34% less) in the tp73-inserted cells than those with only mutp53 insertion ($P<0.0001$). A chi-squared analysis proved that the difference between the untransformed cells and experiment group is not statistically significant (showing that the p73 essentially reduced cell growth to the level that cells without mutp53 would). The results of the experiment indicate that the p53 and p73 apoptosis-inducing pathways are at least relatively independent since the growth of untransformed cells was similar as with of p73.

Conclusions/Discussion

This means the expression of p73 can improve the efficacy of cisplatin-induced mortality, since the pathway may induce apoptosis separately from caspase triggers. This conclusion can be taken a step further to include the application of cisplatin-resistant cancers, which have mutations in caspase pathways, allowing the cells to survive chemotherapeutic treatment. With the p73 pathway as a method to induce apoptosis separately from p53 (and thus staying out of the way of mutp53), treatment for cisplatin-resistant cells can improve by expressing p73.

Summary Statement

I showed that the tp73 apoptosis-induction pathway via cisplatin was not altered by the presence of mutp53, establishing that tp73 can be used to increase cancer cell mortality in during cisplatin treatment.

Help Received

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