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Making chemotherapy stronger: Targeting proteins involved in drug resistance

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Resistance to chemotherapy drugs is an issue faced in cancer treatment. Only some of the causes of drug resistance are known, and further study is needed in order to improve the efficacy of existing drugs and to develop new drugs. Previous studies have shown that the protein complex PP4C controls sensitivity to the commonly used drug cisplatin both in human cells and in the model organism Dictyostelium discoideum. Other signaling proteins have been linked to PP4C in the developmental pathways of Dictyostelium. Our goal was to determine if these proteins are involved in controlling sensitivity to cisplatin.
To standardize the results when calculating cell survival after drug treatment, a new method of analysis was developed. The effect of drug treatment is usually calculated by dividing the average value of surviving cisplatin-treated cells by the average value of surviving untreated cells to find percent survival. In the new calculation method, the growth of an individual cisplatin-treated sample is divided by the average growth of the untreated samples to determine the percent survival. An advantage to the new calculation method is that the initial number of cells in each flask does not need to be the same. Cells of Dictyostelium mutants lacking the specific signaling proteins were treated with cisplatin, and cell survival was measured. The survival of the cisplatin-treated mutants was compared to the survival of the similarly treated parent strains. Deleting these genes in Dictyostelium has a low but consistent effect on cisplatin sensitivity. The results suggest that modulation of the proteins may be useful in increasing the sensitivity of cancer cells to drug treatment and may be employed in chemotherapy.