

Effects of KPT-9274 Drug Treatment on Gene Expression in SUM159 Breast Cancer Cells

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PAK4 is a protein kinase that is typically overexpressed in human cancer, including triple negative breast cancer. Even though the mechanisms behind triple negative breast cancer are incredibly complex, PAK4 is a promising drug target due to its high protein levels in breast cancer cells and its critical role in cell survival. Therefore, we chose to treat SUM159 breast cancer cells with the drug KPT-9274, which reduces the level of PAK4 protein and triggers apoptosis in vitro. The drug has also been shown to be effective at treating triple negative breast cancer in mouse models. We tested 300 nM and 1 μ M doses of the drug on the cells and harvested protein lysates for 5 days. Also, we used data from Next Generation RNA Sequencing to identify ENO1, MAT2A, and GADD45A as cancer-related genes that were likely to be affected by the decrease in PAK4 levels due to drug treatment. The purpose of the present study is to analyze the gene expression of PAK4 and other cancer-related genes in KPT-9274 treated SUM159 cells. We hypothesized, based on the RNA sequencing, that the protein levels of MAT2A would decrease while the protein levels of ENO1 and GADD45A would increase with drug treatment. At this point, we have made important progress in trying to prove this hypothesis and we have found that KPT-9274 induced apoptosis in the drug treated cells starting around day 4. Additional experimentation is necessary to further validate our hypothesis and to analyze potential pathways for PAK4 and the other associated genes of this study. Supported by NIH R25ES020721.

