Investigating Chemotherapy Dose-Dependent Metabolic Changes in Cancer Cells Through Computational Modeling and Experimental Validation

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A key drawback of traditional chemotherapy drugs like cisplatin is that they target both healthy and cancerous cells and are highly toxic in high or medium doses. The Warburg Effect states that cancerous cells prefer to generate energy via aerobic glycolysis over Oxidative Phosphorylation (OxPhos). Glycolysis is 100x faster than OxPhos and produces key metabolic precursors for rapid cell proliferation, a key characteristic of cancerous cells. Low doses of cisplatin have shown potential to increase cellular respiration for a short period of time before apoptosis, or programmed cell death, occurs. For this research, I developed a computational model (using the programming language R) for four cancer lines: two being cisplatin-sensitive and two being cisplatin-resistant. I implemented a dose-dependent cisplatin diffusion partial differential equation and my model proved that after the application of low-dose cisplatin in HT-29 and HeLa cancer cells, lactate production decreases and oxygen consumption increases, while ATP synthesis due to glycolysis decreases and ATP synthesis due to OxPhos increases. Through in-vitro experimentation, I validated my model's findings that the Warburg Effect is reversed by analyzing pre and post cisplatin ATP production and oxygen consumption via both CellTiter Promega Luminescent and SeaHorse XF Pro Assays. My computational model can be used by scientists and doctors in hopes of treating patients in a less invasive yet effective manner.

Awards Won:

Fourth Award of $500