Customized Cancer Cell Weapons: Using CRISPR Cas9 Genetic Engineering and Human Adipose-Derived Mesenchymal Stem Cells To Overcome Platinum-Based Chemotherapy Resistance in OVCAR-3 Human Ovarian Cancer Cells, Year 4

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Ovarian Cancer is the deadliest cancer among all of the gynecological malignancies, largely due to chemoresistance. Carboplatin is a widely accepted Platinum-based chemotherapy agent used for Ovarian cancer treatment. Carboplatin can work by inducing Ferroptosis, a novel type of cell death that differs from apoptosis. Ferroptosis involves the rapid accumulation of lipid peroxides (ROS's) resulting in cell death. There are mechanisms in place to protect cells from Ferroptosis. One mechanism is through the gene-GPX4, which catalyzes the reduction of lipid peroxides. Chemoresistance in Ovarian Cancer may be related to their reliance on GPX4. Carboplatin has a cytotoxic profile when administered conventionally. Mesenchymal Stem cells have an innate homing ability to tumors. The cells can uptake and release chemotherapy in a time-dependent manner, without compromising their own cell integrity, making them ideal for safer targeted delivery. Using the CRISPR Cas9 Genetic-Engineering system, the gene GPX4 was deleted from OVCAR-3 Human Ovarian Cancer Cells that are resistant to Carboplatin. Antibiotic selection was used to kill off any Non-CRISPR transfected cells. Human Adipose-Derived Mesenchymal Stem cells were then primed with Carboplatin, and co-cultured with the CRISPR Ferroptosis susceptible OVCAR-3 cells. A group of Primed Stem cells were cultured independently, to verify cell integrity with exposure to Carboplatin. An MTT-Assay was used to determine cell proliferation (768 trials). The Co-Culture group had a statistically significant lower proliferation rate compared with the "OVCAR-3 only" control ($p < .05$). Thus, there could be potential in using Carboplatin loaded Human Mesenchymal Stem cells to target chemoresistant Ovarian Cancer.

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