Customized Cancer Cell Weapons: Using CRISPR dCas9 Genetic Engineering to modify MCF7 Human Breast Cancer Cells into Double Agent Treatment Vectors, Year III

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The genome of cells is like an instruction book, telling cells what to do and how to do it. A behavior embedded in the genome of cancer cells known as “tumor self-seeding” (the tendency for cancer cells to transmit signals to other cancer cells around the body, while traversing multiple tumor sites) can be manipulated to engineer cancer cells into “double agents” and effective treatment vectors. Premature cell death and secondary tumor formation of engineered cells are obstacles when considering a clinical application. To this end, MCF7 human breast cancer cells were used. TRAIL was identified as an apoptotic gene effective at inducing cell death. MCF7 cells have acquired resistance to TRAIL. The native resistance to TRAIL was used to prevent premature cell death of the engineered cells. As such a modified dCas9-VPR cell line emitting TRAIL was engineered by transducing the dCas9 protein via lentiviral delivery into a group of MCF7 cells. Then, a stable line of TRAIL susceptible cells were engineered using SiRNA lipofection. Four groups were established. The dCas9 VPR cells interacted with the TRAIL susceptible cells in the Co cultured well plates at a 1:4 ratio respectively. A neutral red stain was used to monitor the engineered dCas9 VPR cells and establish a kill switch via ionized quercetin nanoparticles to prevent secondary tumor formation. Quercetin is a natural vitamin found to sensitize MCF7 cells to TRAIL’S effects. An MTT assay was utilized over numerous days to determine cell proliferation (768 trials). The Co-culture group had statistically significantly lower proliferation rates compared to the MCF7 control group (p =2.64E-6). Thus, there could be potential in using modified cancer cells as double agents in attacking tumors throughout the body.

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