Superior Antitumor Fusion Proteins Genetically Engineered in Cell-Based Cancer Therapy

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Current cancer therapies face significant challenges, such as inducing adverse patient side effects, having limited access to solid tissue tumours, or failing to target metastatic tumours. A safer and more versatile approach to treating solid metastatic tumours involves genetically engineering healthy cells to home in on and deliver antitumour proteins to cancer cells. The tumour necrosis factor apoptosis-inducing ligand (TRAIL) is an antitumour protein that can specifically kill cancer cells. However, previous systemically administered soluble forms of TRAIL could not induce significant clinical effect because the TRAIL complexes degraded into inactive subunits. Recently, more stable and potent TRAIL fusion proteins have been developed. The objective of this project was to integrate TRAIL fusion proteins into a novel cell-based cancer therapy platform and evaluate their cancer cell killing activity using bioluminescence imaging (BLI). Therapeutic cell populations were produced by genetically engineering human embryonic kidney cell and mesenchymal stem cell populations to express the membrane-bound TRAIL, the scTRAIL trimer fusion, or the fc-scTRAIL hexamer fusion. Individual therapeutic cell populations were separately co-cultured with MBA-MD-231 cells from metastasized triple-negative breast cancer, PC3MLN4 cells from metastasized prostate cancer, or OVCAR8 cells from high-grade serous adenocarcinoma – previously known to resist TRAIL therapy. In vitro BLI tracking of cancer cell viability showed that the therapeutic cells producing the fc-scTRAIL fusion proteins killed all cancer cell populations more effectively than those producing other TRAIL variants. The cell-based therapy presents a powerful platform for eliminating metastatic tumour burden in cancer patients.

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