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Stem cell based therapies for cancer: Are we there yet?

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Stem cell based therapies are emerging as a promising strategy to tackle cancer. Multiple stem cell types have been shown to exhibit inherent tropism towards tumors. Moreover, when engineered to express therapeutic agents, these pathotropic delivery vehicles can effectively target sites of malignancy. Using our recently established invasive, recurrent and resection models of human brain tumors, glioblastomas (GBM) that mimic clinical settings, we show that that engineered human mesenchymal stem cells and neural stem cells expressing novel bi-functional proteins or loaded with oncolytic viruses target both the primary and the invasive tumor deposits and have profound anti tumor effects. These studies demonstrate the strength of employing engineered stem cells and real time imaging of multiple events in preclinical therapeutic tumor models and form the basis for developing novel cell based therapies for cancer. This presentation considers the current status of stem cell based treatments for GBMs and provides a rationale for translating the most promising preclinical studies into the clinic.

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Engineering long term multipotent hematopoietic cells from human pluripotent stem cells

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Hematopoietic stem cell (HSC) transplantation is an important curative source for malignant and non malignant blood diseases. However, HSC transplantation has limitations, including donor availability and immunologic mismatch. To resolve these issues, researchers have been mounting considerable efforts to induce HSCs from autologous sources such as induced pluripotent stem cells, hematopoietic precursors and fibroblasts. Human pluripotent stem cells (hPSCs) are intriguing platform that allow for large scale expansion culture and correction of mutations. Achieving the formation of HSCs from hPSCs would transform our ability to model and treat hematologic disease from autologous stem cells. Desired cell types have been generated from hPSCs by two approaches, one is biomimetics of developing embryos in 3D culture by supplementing signaling factors; the other is synthetic biology by exogenously expressing transcription factors (TFs). Either approach has not achieved fully functional HSCs from hPSCs so far. Thus combination of these two, biomimetic 3D culture to derive hematopoietic precursors followed by exogenous expression of TFs was taken in this study. The hPSCs was differentiated to precursors of hematopoietic cells in 3D culture; those precursors, still lacking robust hematopoietic capacity (e.g., engraftment upon transplantation) *in vivo* was induced expression of TFs specific to HSCs. Upon transplantation to immune deficient mouse models, long term and multi lineage reconstitution was observed. The future direction of this work is gene correction of hPSC derived hematopoietic cells, for example, Cas9 mediated genome editing of congenital anemia. This work will provide a significant platform to produce human HSCs for potential clinical applications as well as better understanding of hematopoiesis.

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