Engineering teratoma-derived fibroblasts to enhance osteogenesis

TDFs induce greater osteogenic differentiation than human osteoblast-like cells A) Osteogenesis-related morphological changes of different cell types, B) ALP levels and C) calcium assays were significantly higher for TDFs, confirming greater osteogenic ability compared with diverse osteoblast-like cells. Credit: Scientific Reports, doi: 10.1038/s41598-018-32946-6

Additional concerns of the emergence of cancer cell-like features in the TDF population after in vivo stimulation of bone regeneration were addressed with previous reports showing that the re-injection of TDFs did not re-establish teratomas in mice with severe combined immunodeficiency (SCID). In the study, the engineered cell line showed enhanced alkaline phosphatase activity (ALP), elevated calcium content and mRNA expression of osteogenic genes in vitro, followed by
remarkably improved bone volume formation in animal models in vivo. The research revealed a safe and highly efficient technique for therapeutic application of bone regeneration.

The authors initially observed the morphology of TDFs and MSCs, followed by ALP activity, rates of proliferation and rates of differentiation. The MSCs indicated greater capacity to differentiate into osteoblasts compared with TDFs, while proliferative assays showed a significant increase in the rate of TDF growth. Trilineage differentiation typically observed with MSCs was similarly confirmed with TDFs using histological staining to distinguish osteogenesis, adipogenesis and chondrogenesis.

In addition, when compared with diverse human osteoblast-like cells, TDFs demonstrated greater capacity for osteogenic differentiation. The authors further investigated the functional cell line with bright field imaging, ALP activity and calcium deposition assays in growth media (GM) and osteogenic induction media (OIM).

The study cleverly exploited the gold standard of pluripotent stem cell analysis to generate teratoma-derived fibroblasts (TDFs) that differentiated into bone tissue. Such TDFs can be engineered from the patient’s own cells to form patient-specific osteoblasts for transplantation. The authors ultimately intend to generate safe and functional cell lines for therapy in bone research. Immortalized osteoblast cell lines can be used to test new drugs in preclinical models for orthopedic applications. The authors incorporated HSV-tk as a suicide gene to eliminate unexpected cancerous proliferation of the engineered cell line, which, when triggered by GCV treatment, led to programmed cell death. The cell line has great potential as an unlimited cell source that genetically matches the patient to differentiate and regenerate bone for immunologically safe clinical translation.

Explore further:
Cell biology: The role of the alkaline phosphatase (Alpl) gene in preventing premature bone ageing

More information:

Hoseok Song et al. Modeling Disease in Human ESCs Using an Efficient BAC-Based Homologous Recombination System, Cell Stem Cell (2010). DOI: 10.1016/j.stem.2009.11.016