

Foreign body-induced granulation tissue is a source of adult stem cells

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In the current study, we have cultured and propagated the cells obtained from the granulation tissue that forms around perforated polyvinyl tubes placed in the subcutaneous space of normal rats. We found that these cells (called granulation tissue-derived stem cells (GTSCs)) expressed markers of embryonic pluripotent cells (Oct-4 and Nanog) and of adult stem cells (CXCR4 and Thy1.1) as well as produced high levels of vascular endothelial growth factor (VEGF) for up to 10 passages. By fluorescence-activated cell-sorting (FACS) analysis, GTSCs were positive for stem-cell surface markers CD90, CD59, and CD44 and were negative for CD45, which suggests that they were of mesenchymal origin and not of hematopoietic lineage. When incubated in specific differentiation medium, these cells transformed into adipogenic, osteogenic, and chondrogenic lineages, which shows that they were multipotent. Furthermore, after systemic injection, these cells were found in the vicinity of an injured site created in the liver but not in normal areas of the liver, which indicates their propensity to seek and engraft to an injured area in the body. We conclude that granulation tissue induced by a large foreign body is a convenient source of adult stem cells that can be maintained in culture and can be used to repair and regenerate injured tissue. (*Translational Research* 2010;155:191-199)

Abbreviations: CD = cluster of differentiation; CXCR4 = chemokine receptor 4; DMEM = Dulbecco's modified Eagle medium; FACS = fluorescence-activated cell sorting; FBS = fetal bovine serum; FITC = fluorescein isothiocyanate; GTSC = granulation tissue-derived stem cell; IgG = immunoglobulin G; MSCGM = mesenchymal stem cell growth medium; Oct-4 = octamer-4; PBS = phosphate buffered saline; PBS-BSA = PBS containing 0.1% bovine serum albumin; PBS-T = PBS with 1% tween-20; PVC = polyvinyl chloride; SDF-1 α = stromal cell-derived factor-1 α ; SSEA-1 = stage-specific embryonic antigen 1; VEGF = vascular endothelial growth factor; WT-1 = Wilms tumor-1

When a large foreign body such as a polyvinyl tube is placed in the subcutaneous space of rats, it rapidly induces new tissue growth that encapsulates the foreign body. The new tissue, which is called the subcutaneous granulation tissue, is well organized and supplied by new blood vessels.

This type of granulation tissue was used by us previously as a convenient model to study wound healing and angiogenesis in diabetes.^{1,2} We reasoned that a newly formed tissue such as this granulation tissue must contain stem cells to create the various types of cells necessary to form an organized tissue. Indeed, we found that

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