Gadolinium promotes osteogenic differentiation in MC3T3-E1 cells and human adipose tissue-derived mesenchymal stem cells: a possible role of gadolinium on ectopic calcification of nephrogenic systemic fibrosis

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Keywords: Gadolinium, nephrogenic systemic fibrosis, osteoblasts, mesenchymal stem cells, calcification  
Objective: Recent studies have suggested a close association between the administration of gadolinium (Gd)-based contrast agents and the development of nephrogenic systemic fibrosis (NSF), an acquired disorder characterized by systemic fibrosis and ectopic calcification in patients with severe renal dysfunction. However, causative roles of Gd has remained unknown. The aim of this study is to investigate the effect of Gd on the development of fibrosis and calcification in cultured cells.  
Methods: MC3T3-E1 cells (pre-osteoblastic cells), human adipose tissue-derived mesenchymal stem cells (AMSCs), human osteoclasts, human preadipocytes and human dermal fibroblasts (HDFs) were cultured in each differentiation medium with or without gadolinium chloride (GdCl3). Osteogenic differentiation of MC3T3-E1 cells and AMSCs was determined by Alizarin Red staining. Adipogenic differentiation of human preadipocytes and AMSCs was determined by Oil Red O staining. Osteoclast differentiation was determined by TRAP staining. Fibrogenesis of HDFs was determined by real time PCR for the mRNA expression of type I collagen.  
Results: GdCl3 promote osteogenic differentiation and osteoclast differentiation, but not adipogenic differentiation. In addition, gadodiamide also promote osteogenic differentiation in MC3T3-E1 cells. GdCl3 did not increase the mRNA expression of type I collagen in HDFs.  
Conclusions: We have demonstrated a direct relationship between Gd and osteogenic differentiation that may be involved in the development of ectopic calcification of NSF patients.

Decorin Regulates Osteoblastic Differentiation of Mesenchymal Stem Cell  
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Keywords: Cell differentiation, Decorin, Osteoblasts  
Objective: The aim of this study was to clarify the role of decorin in osteoblastic differentiation of mesenchymal stem cell (MSC) in vivo.  
Methods: SiRNA for decorin (siDecorin)-expressing plasmid was transfected into KUSA-A1 cell (mouse MSC) and succeed to establish siDecorin-transfected cells (siDT) line. Some siDT were transplanted into abdominal cavity within diffusion chamber (DC) and another butch of siDT were transplanted in subcutaneous site with or without collagen gel for 1-8 weeks. Both transplanted cells were induced ectopic ossification and were analyzed the cellular response in osteoblastic differentiation.  
Results: KUSA-A1 (control) cell transplanted within DC strongly expressed alkaline phosphatase (ALP), also calcium (Ca) was deposited intercellular space of A1. The siDT within DC showed low level of ALP and Ca throughout the harvesting period, and possessed lipid drops in cytoplasm. Moreover the activity of glycerol 3-phosphate dehydrogenase (adipocyte specific marker) of siDT was much higher than that of A1. In subcutaneous site, the transplanted siDT without collagen gel slightly formed connective tissue structure surrounded by fatty tissue. As for this structure, the sectional area was extremely small compared with the tissue formed by A1, and levels of ALP activity and osteopontin was low. The A1 transplanted with collagen gel formed large bony tissue showing high activity of ALP and osteopontin, and high contents of Ca. While the siDT transplanted with collagen gel formed significantly small-sized tissue with low level of Ca content and osteoblastic markers.  
Conclusion: Our results indicated that decorin controls distinctly in the differentiation process of MSCs to osteoblast. Thus, decorin would regulate cell-lineage decisions and cell fate, differentiating from the MSCs to osteoblasts or adipocytes.