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Fibroblasts regulate osteoblasts through gap junctional communication.

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Abstract

BACKGROUND AIMS: Fibroblasts are present in most tissues of the body, playing an active role in the regulation of homeostasis in such tissues. While fibroblast heterotypic interactions are acknowledged in the regeneration of tissues such as skin and periodontal ligament, their role in bone regeneration is far from being understood. We hypothesized that fibroblasts could influence osteoblasts, and as connexin 43 is the predominant connexin in both cell types, we speculated that those heterotypic interactions could occur through gap junctional communication (GjC).

METHODS: Direct co-cultures of human mesenchymal stromal cell (hMSC)-derived osteoblasts and human dermal fibroblasts (hDFb) were established in the presence and absence of the GjC inhibitor α-glycyrrhetinic acid. Communication between osteoblasts and hDFb via GjC was verified by transference of the gap junction-permeable dye calcein-AM. Cell proliferation was assessed by dsDNA quantification, while osteogenic differentiation was evaluated by measuring alkaline phosphatase (ALP) activity and the expression of osteogenic markers by real-time polymerase chain reaction (PCR).

RESULTS: The amount of calcein-AM transferred between the different cell types decreased when α-glycyrrhetinic acid was used. While the proliferation of the hMSC-derived osteoblasts was not affected by the presence of the hDFb, the level of osteogenic markers such as ALP activity and osteocalcin in transcripts in osteoblasts was severely diminished. This effect was partially reversed by adding α-glycyrrhetinic acid to the co-cultures.

CONCLUSIONS: The results strongly suggest that fibroblasts regulate osteoblast behavior partially through GjC. This information could be critical for predicting the outcome of strategies aimed at promoting bone regeneration as, for example, in bone tissue-engineering approaches.

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