Differential Contribution of Bone Marrow-Derived Cells to Collagen Production during Wound Healing and Fibrogenesis in Mice

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Background & Aims: Recent studies have reported that bone marrow (BM)-derived cells migrating into dermal wound promote its healing by producing collagen type I. However, their contribution to the repair process has not been fully verified yet. It also remains unclear whether BM-derived cells participate in pathological dermal fibrogenesis. Here we examined the possible migration of BM-derived cells and their collagen production in experimental dermal wound healing and fibrogenesis.

Methods: Transgenic mice that harbor tissue-specific enhancer/promoter sequences of alpha2(1) collagen gene linked to enhanced green fluorescent protein (COL/EGFP) reporter gene were established. BM cells obtained from the transgenic mice were injected intravenously to the irradiated wild type animals, and the recipients underwent dermal excision or subcutaneous bleomycin injections. Skin tissues were obtained and subjected to Sirius Red staining and the expression of EGFP was analyzed by using a confocal laser-scanning microscope.

Results: Following dermal excision or subcutaneous bleomycin administration, a large number of EGFP-positive collagen-producing cells were observed in the dermis of COL/EGFP reporter mice. When wild type mice were transplanted with BM cells obtained from transgenic COL/EGFP animals and subjected to dermal wounding, no BM-derived collagen-producing cells were detected throughout the repair process. In contrast, a limited but significant number of collagen-producing cells migrated from BM following bleomycin injections.

Conclusions: These results indicate that skin resident cells are the major sources of de novo collagen deposition in both physiological and pathological conditions, while BM-derived cells participate, in part, in collagen production during dermal fibrogenesis.