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Effects of cell delivery route and BMP2 gene transduction on engraftment of autologous dermal fibroblasts and bone density in a rabbit model

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Abstract

Cell-mediated gene therapy may treat bone fragility disorders; however, optimal methods for cell engraftment in target bone are needed. Dermal fibroblasts (DFb) may be an alternative cell source to mesenchymal stem cells (MSC) for orthopedic gene therapy because of their excellent plasticity, rapid cell yield, and ability to make bone when transduced with bone morphogenetic protein-2 (BMP2). Autologous MSC were administered to rabbits by two delivery routes; an intra-venous infusion and transcortical intra-medullar infusion into the femur and tibia. Both routes showed low cell engraftment and no measurable changes in bone. In the second study, autologous DFb or BMP2-expressing autologous DFb (DFb-BMP2) were administered to rabbits by two routes; a transcortical intra-medullar infusion and delayed intra-osseous injection into femoral drill defects. Both routes of DFb-BMP2 resulted in increased cell engraftment, bone volume, bone density, trabecular bone microarchitecture, bone defect filling, external callus formation, and trabecular surface area, compared to DFb, DFb-GFP, or no cells. Cell engraftment within trabecular bone and bone marrow was most efficiently achieved by intra-osseous injection of DFb-BMP2. Systemic biodistribution of the locally injected/infused DFb-BMP2 was not evident in distant organs or contralateral hindlimb. Our results suggested that DFb-BMP2 have enhanced efficiency of engraftment in target bones resulting in a measurable biologic response by the bone of improved bone mineral density and bone microarchitecture. Our results support that DFb-mediated BMP2 gene therapy warrants further study on animal models of bone fragility disorders such as osteogenesis imperfecta and osteoporosis to potentially enhance bone quality.

Biography

Bertone has completed her DVM degree from Cornell University, Ph.D from Colorado State University and postdoctoral studies from Harvard School of Medicine. She is the director of the Comparative Orthopedics Research Laboratory, the Trueman Endowed Chair, and has appointments in the OSU College of Medicine and Veterinary Medicine. She has published more than 150 original scientific papers in reputed journals and has presented research from her laboratory as senior author around the world.