Δ Stem Cell-Based Evidence for NSAID Safety During Fracture Healing

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Purpose: Whether nonsteroidal anti-inflammatory drugs (NSAIDs) hinder human fracture healing by direct action on osteoblast differentiation remains unknown. While animal studies suggest NSAIDs are deleterious to osteoblast differentiation in vitro and in vivo, human clinical trials have yet to demonstrate an effect of NSAIDs on fracture healing. We have prospectively purified bona fide skeletal stem cells (SSCs) from human fracture sites and hypothesized that that human SSCs (hSSCs) would not be functionally impaired by NSAID administration.

Methods: We prospectively isolated hSSCs (Podoplanin+, CD146–, CD73+, CD164+) and human osteoprogenitors (hOPs [mesenchymal stem cells]; Podoplanin–, CD146+) by fluorescence-activated cell sorting (FACS) from human fractures. Purified SSCs were cultured in the presence or absence of 3 common NSAIDs and analyzed subsequently for colony-forming units (CFU-F). After osteogenic and chondrogenic differentiation, cell avidity for Alizarin Red and Alcian Blue was quantified by spectrophotometry. Experiments were performed in triplicate on n = 4 healthy adults (age. 44-85 years).

Results: Physiologic and supraphysiologic concentrations, as well as initial pulsed and continuous NSAID administration, failed to inihibit hSSC (and hOP) differentiation into osteoblasts and chondrocytes. NSAID administration failed to affect clonogenicity of human SSCs. We demonstrate that hSSCs prospectively isolated from human fracture sites maintain functionality independent of NSAID application.

Conclusion: Our results add evidence to emerging clinical data suggesting NSAID administration for postoperative analgesia is safe for fracture healing.

Δ OTA Grant

The FDA has stated that it is the responsibility of the physician to determine the FDA clearance status of each drug or medical device he or she wishes to use in clinical practice.