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A low cost, high content murine model for evaluating cell-based strategies of bone regeneration: Demonstration that donor progenitor cells produce a functional repair of a long bone defect

Due to limitation of size, the advantage of mice as an experimental model for skeletal regeneration has not been fully realized. Here we demonstrate an external fixation protocol for the femur or tibia that utilizes syringe needles, dental cement and Kirschner threaded wires. It provides the option of an immediate or delayed repair of a segmental-defect of a distraction-based repair. The hardware provides long-term stability without impairing the animal's mobility does not interfere with radiographic examination and can be easily removed once the defect has healed. Acquiring full ambulation without any external support or bone deformity is our definition of a functional repair. When combined with GFP reporters and cryo-histological methods for fluorescent imaging of mineralized tissues, it is possible to interpret the outcome of an experiment within a week of animal sacrifice. Using this experimental platform, introduction of primary bone marrow derived MSCs from an animal's carrying a bone restricted Col3.6GFPcyan reporter into a the defect space of an immune-compromised (NOD. Cg-PrkdcscidIl2rgtm1Wjl/SzJ) NSG host carrying a Col3.6GFPtpz reporter results in a functional repair within 6 weeks of implantation in both the immediate or delayed (non-union) models. In both cases, the repaired segment was a product of the donor cells that had sufficient progenitor reserve to support bone remodeling to produce a cortical bone that integrated with the host bone. This research platform is readily adaptable to identify promising scaffolds, growth factors and cell sources (any species including human) for evaluation in a clinically relevant large animal model.

Biography

David W Rowe has had a career long interest in heritable diseases of bone with a specific focus on osteogenesis imperfecta (OI). The research methods used to evaluate therapies for OI have proven useful for studying models of regenerative skeletal biology. He wants to share the reporter mice, histological techniques and experimental models with other research groups and to develop commonly agreed upon success criteria for a therapeutic protocol.

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