Extremity Trauma Health Outcomes

Highly Targeted Delivery of Orthopaedic Biologics for Bone Regeneration

Musculoskeletal injuries comprise a significant portion of blast-related wounds and often involve complex fractures of long bones. Critical size bone defects do not heal well and in some instances, result in extremity amputation. Bone morphogenetic protein-2 (BMP-2) has been used to promote bone regeneration, but safe and targeted delivery of BMP-2 to sites of injury is a technical challenge. A team of researchers at the Geneva Foundation (Frederick, Maryland), Mayo Clinic (Rochester, Minnesota), U.S. Army Institute of Surgical Research (San Antonio, Texas), and Cleveland Clinic (Cleveland, Ohio), are collaborating to refine and evaluate a platform technology that will allow for highly targeted delivery of therapeutic proteins to any wound geometry or size (Figure 1). The researchers have successfully completed good manufacturing practice development of a targeted bone morphogenetic protein 2 variant (tBMP-2). In a good laboratory practice-compliant rodent femoral defect model, tBMP-2 was tested against Infuse®, the current gold standard recombinant human BMP-2 (rhBMP-2) product for bone repair made by Medtronic, and a vehicle control (*Medtronic Sofamor Danek USA 2013, 2016*). Biweekly radiographs were collected from each animal to evaluate bone healing and bone samples were collected for histological assessments after 4-8 weeks. Rodents that received tBMP-2 treatment for repair of the femoral defect exhibited superior bone formation within four weeks compared to the current gold standard and vehicle. Bone histology revealed the generation of mature trabecular bone as seen in late-stage bone regeneration in rodents that received treatment with tBMP2, whereas treatment with rhBMP-2 produced disorganized bone and fibrotic tissue that is indicative of early stage bone regeneration. This targeting platform technology will allow for delivery of lower doses of therapeutics and prolonged retention at injury sites, thus improving safety, efficacy, and cost of orthopedic applications.

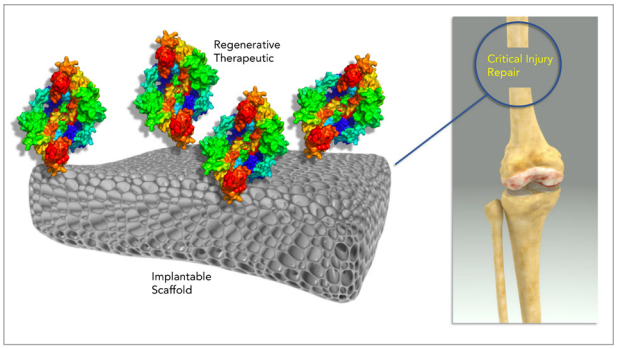

FIGURE 1: Novel targeted delivery platform enables local delivery of potent regenerative therapeutics to sites of injury without affecting surrounding tissue. (Figure used with permission from the authors)

In conclusion, novel methods to facilitate healing of nonunion bone fractures will improve the physical and functional outcomes, and potentially reduce the need for amputation, following traumatic extremity injuries in our Service members.

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REFERENCES:

Medtronic Sofamor Danek USA, I. 2013. "Summary of Safety and Effectiveness Data for Infuse Bone Graft for Open Tibial Shaft Fractures."

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