**Designer Chimeric Protein BV-265 Composite Matrix Demonstrates Efficacy in Nonhuman Primate Bone Repair Models at Substantially Lower Concentrations than BMP-2/Absorbable Collagen Sponge**

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**Purpose:** This study demonstrates a chimeric protein/composite matrix (BV-265/CM) is efficacious at substantially lower concentrations in nonhuman primate bone repair models than bone morphogenetic protein (BMP)-2/absorbable collagen sponge (ACS). BV-265 optimizes BMP receptor binding by combining amino acid sequences from BMP-2, BMP-6, and Activin A. The CM, containing calcium-deficient hydroxyapatite granules embedded in a fenestrated, polymer mesh reinforced, macroporous recombinant human type I collagen matrix was engineered for optimal BV-265 retention.

**Methods:** 2-cm pin-stabilized fibula defects created in adult macaques were untreated (n = 3), treated with CM (n = 3), or treated with 0.05 or 0.15 mg/cc BV-265/CM (n = 6 each). Bilateral pin-stabilized fibula wedge osteotomies created in 3 adult baboons were treated with 0.15 mg/cc BV-265/CM. Radiographs were obtained at 2-week intervals for 12 weeks. Explanted fibulae were evaluated with $\mu$CT, torsional biomechanics, and histology.

**Results:** Untreated and CM-treated defects were not bridged at 12 weeks. Defects treated with 0.05 and 0.15 mg/cc BV-265/CM were bridging at 12 weeks. Defects treated with 0.05 mg/cc BV-265/CM demonstrated more uniform bone formation compared to the rapidly formed neocortex observed bridging the 0.15 mg/cc BV-265/CM-treated defects. Callus volume was 423 ± 197 $mm^3$ and 574 ± 42 $mm^3$, respectively, in the 0.05 and 0.15 mg/cc BV-265/CM-treated defects ($P < 0.05$). Maximum torque was 0.70 ± 0.06 Nm (52% of intact fibulae) and 1.04 ± 0.1 Nm (78% of intact fibulae), respectively, for the 0.05 and 0.15 mg/cc BV-265/CM-treated defects. Torsional stiffness was 0.033 ± 0.01 Nm/deg (34% of intact fibulae) and 0.063 ± 0.01 Nm/deg (66% of intact fibulae), respectively, for the 0.05 and 0.15 mg/cc BV-265/CM-treated defects. CM-treated defects failed mechanical testing. Wedge osteotomies treated with 0.15 mg/cc BV-265/CM united by 8 weeks and continued to remodel through 12 weeks. Maximum torque was 200% greater (5.6 ± 1.3 Nm vs 2.7 ± 0.5 Nm, respectively, $P < 0.001$) and torsional stiffness was 150% greater (0.3 ± 0.01 Nm/deg vs 0.2 ± 0.1 Nm/deg, respectively, $P < 0.001$) than the values for intact fibulae.

**Conclusion:** This study demonstrates BV-265/CM can bridge macaque fibula defects and baboon fibula wedge osteotomies at 1/10 to 1/30 the BMP-2/ACS concentration reported to unite nonhuman primate fibula osteotomies.