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## Vancomycin-bearing Synthetic Bone Graft Delivers rhBMP-2 and Promotes Healing of Critical Rat Femoral Segmental Defects

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## **Vancomycin-bearing synthetic bone graft delivers rhBMP-2 and promotes healing of critical rat femoral segmental defects**

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For graft-assisted repair of large volumetric bone loss resulting from traumatic orthopedic injuries, strategies that simultaneously promote osteointegration/graft healing and mitigate risks for infections are highly desired. Previously, we developed a poly(2-hydroxyethyl methacrylate)-nanocrystalline hydroxyapatite (pHEMA-nHA) composite as a synthetic bone graft. The composite, when loaded with a single dose of 400-ng rhBMP-2/7 and press-fit into a 5-mm rat femoral segmental defect, led to bony callus fully bridging over the defect and substantial restoration of the torsional rigidity by 12 weeks. More recently, we showed that 4.8 wt% vancomycin can be encapsulated within the composite without compromising the structural and mechanical integrity. Additionally, FDA-approved rhBMP-2 can be absorbed onto the graft and both the vancomycin and rhBMP-2 can be released in a localized and sustained manner. Here we examine the efficacy of pHEMA-nHA-vancomycin grafts pre-absorbed with rhBMP-2 in repairing 5-mm rat femoral segmental defects, and determine if vancomycin hinders the repair. pHEMA-nHA-vancomycin or pHEMA-nHA with/without 3- $\mu$ g rhBMP-2 were press-fit in 5-mm femoral defects in male rats. Histology, microcomputed tomography, and torsion testing were performed on 12-week explants to evaluate the extent and quality of repair. Partial bridging of the defect with bony callus by 12 weeks was observed with pHEMA-nHA-vancomycin without rhBMP-2 while full bridging with substantially mineralized callus and partial restoration of torsional strength was achieved with 3- $\mu$ g rhBMP-2. The presence of vancomycin did not significantly compromise graft healing. The pHEMA-nHA-vancomycin graft, with the ability to deliver safe doses of osteogenic recombinant proteins and to simultaneously release the encapsulated antibiotics in a sustained manner holds promise in improving the clinical outcome of graft-assisted repair of traumatic bone injuries.