Nanoclay gel as a next-generation BMP carrier: Minimizing adverse events and promoting high-quality bone regeneration

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Abstract

Bone morphogenetic protein-2 (BMP-2) is a potent osteoinductive factor widely used in the United States and Europe to promote bone healing in recalcitrant fractures and spinal fusion. However, clinically used collagen sponges cause rapid burst release of BMP-2, leading to inflammation, ectopic ossification, and compromised bone quality. In this study, we demonstrate that mixing BMP-2 with a synthetic nanoclay gel (NC) enables long-term retention of BMP-2 within the gel, markedly suppresses inflammatory responses, and induces uniform cartilage formation followed by high-quality bone formation (endochondral ossification) (Fig. 1). In animal models (ectopic bone formation and spinal fusion), NC-BMP produced dense, mechanically robust bone exclusively at the intended site, without ectopic formation. These findings indicate that nanoclay gel serves as a next-generation BMP carrier that enhances both the safety and efficacy of BMP-based bone regeneration, with potential clinical benefits for patients undergoing fracture repair or spinal fusion.

Background & Results

BMP-2 is a powerful bone-forming cytokine clinically used for challenging fractures, spinal surgery in many countries. Despite its efficacy, safety concerns, particularly inflammation and unintended bone formation, have limited its approval in Japan. Collagen sponges (CS), the current standard carrier, release BMP rapidly after implantation. This burst release evokes strong inflammation, induces heterotopic ossification, and often results in poor-quality bone with fatty marrow.

To overcome these limitations, we evaluated nanoclay gel (NC) as an alternative BMP carrier. Subfascial implantation in mice revealed that NC retained BMP locally with minimal leakage, preventing the dose-dependent inflammatory response characteristic of CS. Inflammatory cells remained confined within NC, and no propagation of inflammation to surrounding tissue occurred, even at higher BMP doses (Fig.2).

Strikingly, NC induced abundant, uniformly distributed cartilage within the gel (Fig.2), which subsequently underwent endochondral ossification to form dense trabecular bone. In contrast, CS produced ectopic bone externally and fatty, fragile bone internally (Suppl. Fig.).

In a rat spinal fusion model that mimics human surgery, NC-BMP achieved solid fusion with dense bone throughout the fusion mass (Suppl. Fig.). In vitro, NC promoted chondrogenic and osteogenic differentiation while suppressing osteoclast activity, further supporting its biological advantage.

Significance of the research and Future perspective

This study shows that nanoclay gel overcomes the major drawbacks of BMP-2 therapy by enabling sustained local delivery, minimizing inflammation, and promoting high-quality bone formation through endochondral ossification. As the demand for reliable bone healing increases in aging societies, particularly in osteoporotic fractures and degenerative spinal conditions, the NC-BMP system represents a promising next-generation bone regeneration strategy. Clinical translation of this technology may enable safer and more effective bone union in cases that currently require prolonged treatment, offering substantial benefits for patients and healthcare systems.

Fig.1

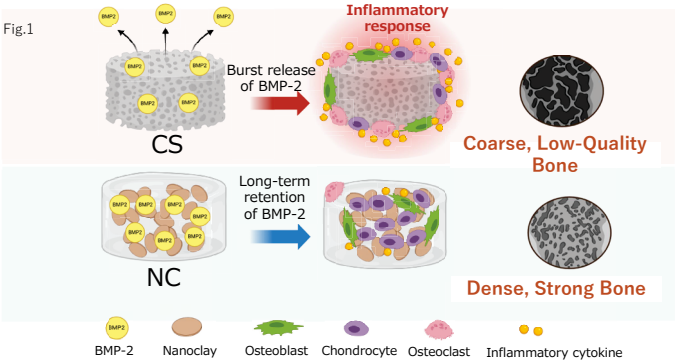
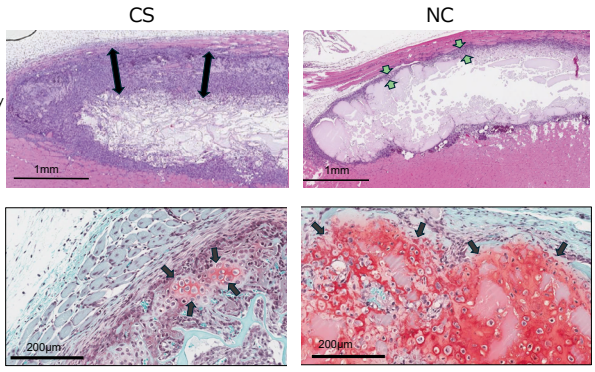
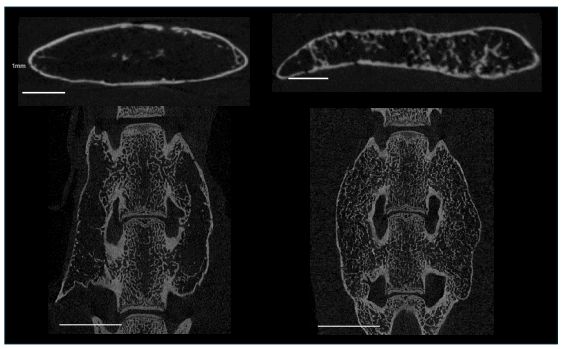


Fig.2



Suppl. Fig.



Patent

Treatise Furuichi, Takuya; Okada, Seiji; Kaito, Takashi et al. Nanoclay gels attenuate BMP2-associated inflammation and promote chondrogenesis to enhance BMP2-spinal fusion. BIOACTIVE MATERIALS. 2025, 44, 474-487. doi: 10.1016/j.bioactmat.2024.10.027

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