## The Potential Tripartite Connection: Alzheimer's Disease, Fracture Healing, and the Gut Microbiome

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## Abstract

Alzheimer's disease (AD), fracture healing, and the gut microbiome are interconnected aspects of health that have gained significant research interest. Recent studies suggest gut dysbiosis may play a role in AD pathogenesis, potentially through the gut-brain axis, a bidirectional communication system. Moreover, the gut microbiome's role in bone health could link dysbiosis and fracture risk. Furthermore, research reports have revealed that the brain communicates with bone, termed the bone-brain axis. Despite these insights, the effect of the gut microbiome on fracture healing in AD remains largely unexplored.

To uncover these connections, our study uses the AD mouse models, 3xTg and 5xFAD. We conducted osteotomies on these mice and analyzed fecal samples that were collected at different timepoints. Fecal samples are being examined via qPCR and 16s RNA analysis to identify and quantify bacterial phyla. These findings will be linked to both AD progression, gauged through behavior and histological analyses, and fracture healing, quantified using X-ray mRUST scoring, microCT, and histology.

We hypothesize that the progression of AD could alter the gut microbiome, potentially affecting fracture healing. This might occur through inflammation pathways triggered by specific gut bacteria. We may identify specific gut bacteria that play critical roles in both fracture healing and AD. We anticipate finding a shift towards pro-inflammatory bacterial phyla in the context of AD progression and during the fracture healing process. If this hypothesis is validated, it could unlock new therapeutic strategies aimed at targeting the gut microbiome to improve bone health, fracture healing, and AD progression in patients.