

## Oral Abstract

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### Modelling recalcitrant NFI bone repair in mice

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Congenital pseudarthrosis of the tibia (CPT) is a significant clinical complication associated with type I Neurofibromatosis (NFI). Bony lesions in the tibia make it prone to fracture and once a fracture occurs the tibia fails to unite. Even with modern orthopaedic techniques, sound union is difficult to achieve and permanent disability and/or amputation are common outcomes.

We have sought to model bone repair in an *Nfl*-deficient (*Nfl*<sup>+/-</sup>) mouse line using an open fracture model where the bone is broken in the distal tibia. At week 3, fracture healing was found to be significantly impaired in *Nfl*<sup>+/-</sup> mice. The majority (83%) of the wild type mouse fractures had completely bridged whereas only 36% of the *Nfl*<sup>+/-</sup> fractures had completely bridged ( $P < 0.013$ ). The histological features associated with non-united *Nfl*<sup>+/-</sup> fractures were variable, but included delayed cartilage removal, disproportionate fibrous invasion, insufficient new bone formation, and excessive resorption.

When bone morphogenetic protein-2 (BMP-2) was applied locally to the fracture site, no improvement was seen in union rates, although large amounts of ectopic bone commonly formed in the muscle compartment of the proximal tibia. We hypothesized that a cellular deficit in the distal tibia led to a deficient anabolic response. To correct for this we are developing a muscle graft model where a muscle flap is placed adjacent to the fracture site. Initial data suggests muscle grafting leads to an increased callus size in *Nfl*<sup>+/-</sup> mice.