

Technology Offer

Novel therapeutic approach for preventing delayed fracture healing

Ref. No.: CH592/2011

Background

Delayed or incomplete bone fracture healing can be observed in approximately 5–10% of patients following a fracture of the long bones. Known risk factors for delayed or incomplete healing are severe fractures, old age, steroid therapy or diabetes. Recent findings suggest a key role of inflammation and T-cell response within the bone repair processes. In proximal tibia fracture patients with delayed fracture healing an enrichment of two specific CD8+ T-cell subpopulations could be detected at the site of fracture. Compared to the peripheral blood, the CD28(-)CD8(+) TEMRA cells are enriched in the fracture hematoma by a factor of 1,8-2,5 and the CD57+CD8+TEMRA cells are enriched by a factor of 1,4-3,7. Compared to other T-cells these T-cell subsets are producing increased concentrations of IFN γ . The presence of the inflammatory cytokine is supposed to play a key role in delayed fracture healing. Furthermore enriched CD28(-)CD57(+) and CD4(+)CD8(+) T-cells within the peripheral blood could be identified as specific biomarkers for delayed fracture healing.

Technology

The invention offers the possibility to prevent or treat delayed bone fracture healing by applying an inhibitor of IFN γ and/or TNF α or an inhibitor of CD8+ T-cells, such as e.g. a monoclonal antibody raised against CD8. Also other monoclonal antibodies against CD molecules expressed on activated CD8+ T-cells are possible treatment options. The novel treatment approaches result from the findings that: a) the two specific CD8+ T-cell subsets are enriched in fracture hematoma of delayed fracture healing patients, b) these CD8+ T-cells produce high concentrations of IFN γ (*ex vivo* data) c) IFN γ and TNF α inhibit concentration-dependently osteogenesis of human bone marrow mesenchymal stromal cells (BM-MCS; *in vitro* data) and d) the depletion of CD8+T-cells in a mouse model improves bone fracture healing.

Benefits

- ✓ Novel second medical use of inhibitors of IFN γ or TNF α for prevention of delayed bone fracture healing
- ✓ Cost-saving treatment option – a second surgery can be avoided

Application

Treatment and prevention of delayed bone fracture healing

Commercial Opportunity

In-licensing or industrial cooperation for further development

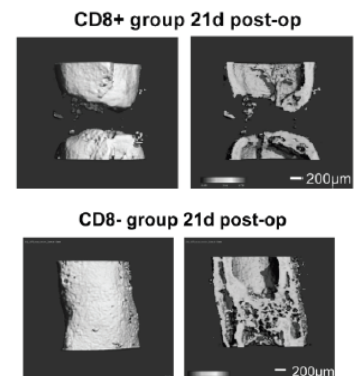


Fig. CD8+ immune cell depletion improves bone fracture healing in a mouse model

Keywords

Delayed bone fracture healing, therapy, IFN γ inhibitor, TNF α inhibitor, CD8+ T-cells

Developmental Status

in vitro and *in vivo* data

IP Status

EP patent application (02/2012)

PCT patent application (02/2013)

publication [here](#)

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