BIH Innovations
The Technology Transfer Office of BIH and Charité

# Technology Offer

## Anti-TNFα and anti-IFNγ for prevention or treatemen of delayed bone fracture healing

Ref. No.: CH592

### 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 IFNγ. 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 IFNγ and/or a TNFα and/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 IFNγ (*ex vivo* data) c) IFNγ and TNFα 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 anti-IFNγ or anti-TNFα antibodies
- ✓ Cost-saving treatment option – a second surgery can be avoided

### Application

Treatment and prevention of delayed bone fracture healing in risk patients

### Commercial Opportunity

Searching for a licensing or developing partner

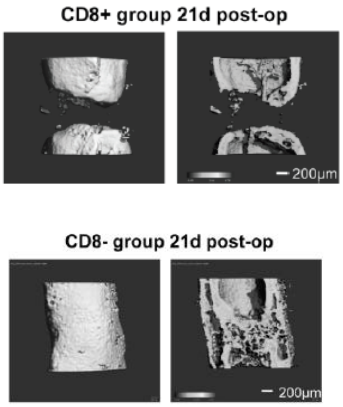


Fig. 1: CD8+ immune cell depletion improves bone fracture healing in a mouse model

### Key words

Delayed bone fracture healing, therapy, IFNγ inhibitor, TNFα inhibitor, CD8+ T-cells, TEMRA cells, antibody

### Developmental Status

*in vivo data*

### IP Status

EP patent application (02/2012)

PCT patent application (02/2013)

EP patent granted: 2019, validation in 02/2020 in DE, GB, F, IT, ES, CH

Pending applications in: US and JP

### Patent Owner

Charité – Universitätsmedizin Berlin

### Contact

Dr. Bettina Büttner
Technology Manager

Tel.: +49 30 450 570 874
Fax: +49 30 450 7570 964
Bettina.Buettner@charite.de
http://technologietransfer.charite.de
http://www.berlinhealthinnovations.com