Docket #: S20-269

Biochemical activation of dysfunctional skeletal stem cells for skeletal regeneration

Stanford researchers have found that aging and disease lead to skeletal stem cell (SSC) dysfunction and hence decreased bone health. The aged SSCs have lower bone-forming potential and simultaneously give rise to high numbers of pro-inflammatory stroma which enhances bone resorption through actions on hematopoietic osteoclasts. Under these conditions, individuals are prone to diseases such as osteoporosis, sustain fractures and regenerate poorly. To remedy these aged SSCs, Stanford researchers also propose a combination therapy of a bone morphogenetic protein (BMP2), and an inhibitor of colony stimulating factor-1 (CSF1), to re-activate aged SSC's differentiation potential and simultaneously reduce crosstalk to hematopoietic cells favoring an inflammatory milieu. The combination therapy can be delivered through biodegradable hydrogels placed topical to the fracture site. This treatment expands aged SSC pools, reduces osteoclast activity, and enhances bone healing.

Stage of Development
In vivo mouse model: experimentally shown in mice, placing biodegradable hydrogels containing recombinant BMP2 and blocking antibody to CSF1 around fractured areas of bones can restore regeneration capacity of otherwise impaired phenotype.

Applications

- Bone healing after facial reconstruction
- Skeletal regeneration like fracture healing

Advantages

- Less problematic than transplantation of autologous/allogenic cells
- Suitable for high risk patients (aged, osteoporotic)
- Easy procedure: during open reduction and internal fixation (ORIF), routinely performed by orthopedic surgeons to align bone fragments, hydrogels containing the combination therapy can be placed at the fracture site

Publications

- Ambrosi, T. H., Marecic, O., et al.. (2021). Aged skeletal stem cells generate an inflammatory degenerative niche. Nature, 597(7875), 256-262.

Patents

- Published Application: WO2022232116
- Published Application: 20240181135

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