Stimuli-responsive biomaterials for pathological tissue regeneration

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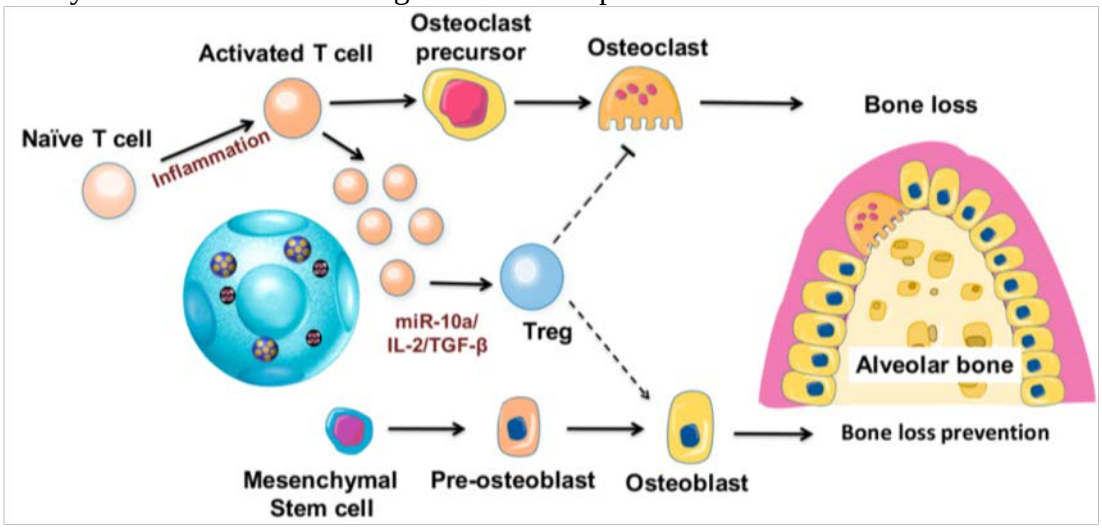
Periodontal diseases, a chronic osteolytic inflammatory diseases, are highly prevalent in up to 90% of the worldwide population caused by bacteria in plaque, which would present sustained inflammation challenge leads to irreversible bone loss. Conventional tissue engineering only focused on the tissue regeneration using growth factors, and therefore produce weak therapeutic effect due to the uncontrolled inflammatory responses. Regulatory T cells (Tregs) play important roles both in microenvironment modulation for tissue regeneration and in immune response for inflammatory inhibition, which open a door to control inflammation meanwhile perform osteo-inductive effect to promote the restoration of bone defects in periodontal disease. However, there are currently few options available other than introducing more Tregs or immunosuppressive drugs to locally enrich Tregs. Herein, poly(L-lactic acid) (PLLA) nanofibrous spongy microspheres (NFSMS), PLLA/polyethylene glycol (PEG) co-functionalized mesoporous silica nanoparticles (MSN), and poly(lactic acid-co-glycolic acid) microspheres (PLGA MS) are integrated into one multibiologic delivery vehicle for in situ Treg manipulation, where the MSNs and PLGA MS were utilized to distinctly release IL-2/TGF-β and miR-10a to locally recruit T cells and stimulate their differentiation into Tregs, while PLLA NF-SMS serve as an injectable scaffold for the adhesion and proliferation of these Tregs. In a mouse model of periodontitis, the injectable and biomolecule-delivering PLLA NF-SMS lead to Treg enrichment, expansion, and Treg-mediated immune therapy against bone loss. This system can potentially be utilized in a wide variety of other immune and regenerative therapies.



Scheme 1. Schematic illustration of the therapeutic process based on stimuli-responsive biomaterials