Cosurface capacitive interdigitated stimulators of high osteoinductive and conductive performance for new personalized acting-sensing prosthetic implants

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Musculoskeletal disorders are among the uppermost causes of disability, and the incidence of replacement arthroplasties is relatively high and increasing. Given that current passive clinical implants do not reduce implant failures and revision surgeries, these are also increasing worldwide. Novel bioelectronic devices comprising biophysical stimulators ('acting') and bone monitoring systems ('sensing') are thus on demand, aiming for long-term implant survival and personalized actuation, according to the monitored osseointegration states.

Our interdisciplinary team has been developing a novel implantable electrical stimulation system promoting bone maturation and mineralization, hardly achievable with classic capacitive parallel electrodes. We here show the in vitro osteoinductive and osteoconductive effects of a cosurface capacitive stimulator, integrating micro-scaled interdigitated electrodes (100 µm) and operating at high frequency (HF, 60 kHz) to be compatible with sensor abilities.

This sensing-compatible HF electrical stimulation system significantly enhanced matrix maturation and mineralization of osteoblasts and osteodifferentiating mesenchymal stem cells (Fig. 1). HF stimulation induced osteoconductive effects on pre-osteoblasts, including increased ALP activity, collagen-I synthesis, matrix and mineral deposition. An innovative proteomic analysis on microvesicles secreted by electrically stimulated osteoblasts revealed specific pathways of osteodifferentiation and matrix mineralization favored by the electric stimulation. HF stimulation also enhanced collagen-I synthesis and hydroxyapatite deposition by osteodifferentiated stem cells.

This work provides insights on a novel cosurface capacitive system, validating a stimulation setup of high osteoinductive and osteoconductive in vitro performance. These promising cosurface stimulators may be integrated in novel bioelectronic implants, aiming for bone-implant interface monitoring and personalized therapeutics.

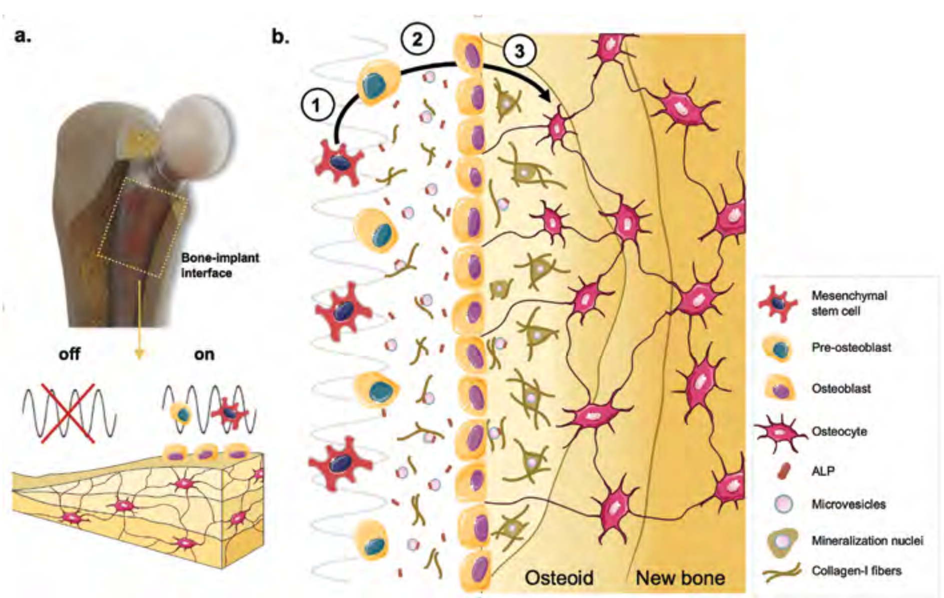

FIGURE 1
High osteoinductive and osteoconductive performance of cosurface capacitive stimulators at high frequency. Future innovative bioelectronic implants will deliver capacitive electrical stimulation of high frequency (HF, 60 kHz) around the bone-implant interface. HF stimuli promote osteodifferentiation of mesenchymal stem cells into pre-osteoblast (1) and further proliferation and maturation into osteoblasts (2). HF stimulation induces active secretion of collagen-I, alkaline phosphatase (ALP) and microvesicles with membranar ALP. These microvesicles progress as mineralization nuclei for hydroxyapatite crystals early deposition, alongside with collagen-I fibers that rearrange into a tight matrix. The mineralized matrix progressively entraps last-stage bone cells, the osteocytes (3) in the newly formed osteoid, that gradually becomes the new bone.