Tissue- engineered 3D osteoclast activation model

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Bone regeneration and bone resorption processes are simultaneously occurring in the bone environment. With simulations of mechanical and chemical signals, the bone metabolism maintains homeostasis or deviate to diseases. Currently, osteoblast differentiation in vitro model are well- established to screen potential treatments or materials for bone regeneration. However, not all animal response the same with the same treatment and the selection of animal model would influence the result of implantation. Even in the clinical manifestation, the successful rate of same bone grafting also vary among patients. In addition to the quality of bone, this variation may result from the diversity of individual immune responses in the bone environment. The status of osteoclast activation and recession determine the fate of bone grafts or implants and also determine bone regeneration or resorption.

The results of mechanical stimuli on osteoclast activation are equivocal among different studies. Regarding the force application such as compression, shear force, or micro-motion from the bone graft particles, the impact of mechanical stimuli could either inhibit or aggravate osteoclast activation. In addition to the type of mechanical stimuli, we noticed that matrix- derived mechanical stimuli could induce murine myoblast, C2C12, to promote osteoblast differentiation synergistically and cancer cells were able to switch their competent and quiescence state with alteration of matrix. We hypothesized that the matrix- induced mechanical signal could lead pro-osteoclasts to perform proliferative or non- proliferative state and this on-going status may synergistically influence pro- osteoclasts with additional mechanical loading or chemical stimuli to decide activate or inactivate.

In the Col-Tgel 3D model, we observed the progression of Raw264.7 cell proliferation, migration, and activation without chemical signals under a specific Col-Tgel condition. The activated Raw264.7 cell displayed tartrate- resistant acid phosphatase activity with staining and p-nitrophenyl phosphate substrate conversion. For those conditions were not optimal for osteoclast activation, Raw264.7 cells tend to migrate out of gel and release protease to modify extracellular matrix (ECM). The treatment of lipopolysaccharide or BMP2 can alter the Raw264.7 cell state of activation. These phenomena implied that cells dynamically interact with ECM simultaneously with and without external signals. This model demonstrated that extracellular matrix played as inertial driven force to impact the cell to response external signals.