ABSTRACT

The loss of tissue/organ functions as a result of injury, trauma, aging, and diseases are the primary concern in healthcare. However, the currently available clinical treatment procedures are not able to restore the functions of the tissue/organs. The author aims to develop a functional construct using a combinatorial approach involving biomaterials and primary/stem cells for restoring or replacing the damaged organ/tissue. In this endeavor, the placental derived extracellular matrix has been used throughout the study for fabricating different composite bioactive grafts for bone and skin tissue engineering. Owing to the presence of various cytokines/growth factors in the placental derived extracellular matrix, it could potentially accelerate the regeneration process of the damaged tissue.

Osteochondral defect sites experience high strain, and when scaffolds lacking strain reversibility property are used for osteochondral tissue regeneration, they would have permanent deformation. The present study describes a method for fabricating placental derived extracellular matrix sponge (PEMS) by the process of decellularization. The PEMS with its intrinsic cytokines/growth factors along with its ability to withstand alternate strain and relaxation combined with amniotic membrane-derived stem cells (HAMSCs) when implanted in the osteochondral defects demonstrated superior tissue regeneration compared to the empty defects. Composites fabricated by combining placental derived extracellular matrix, and silk fibroin exhibited enhanced mechanical properties and supported the proliferation/differentiation of HAMSCs into osteogenic lineage *in vitro.* Further, the composites facilitated enhanced bone regeneration in a critical bone defect rabbit model.

The composites fabricated from placental derived extracellular matrix, and silk fibroins were also explored for skin tissue engineering. The composites when cultivated with primary fibroblast/keratinocyte demonstrated good cytocompatibility *in vitro*. The composites did not trigger the host inflammatory/immune response when implanted subcutaneously in a rabbit

model. The composites also facilitated rapid wound closure/epithelialization of critical full-thickness defects in rat model owing to increased neovascularisation, accelerated fibroblast/keratinocytes migration, and enhanced collagen synthesis. Another class of composite nanofibers was fabricated by blending placental derived extracellular matrix with polycaprolactone. The composite nanofiber mats were proposed for wound dressing application. The composite nanofiber mats firmly adhered to the wound bed and thus provided shielding to the wound bed from the external environment. The composite nanofiber mats demonstrated enhanced angiogenesis *ex vivo* owing to the growth factors/cytokines embedded in it. Further, the composite nanofiber mats proved to be a suitable matrix for *in vitro* and *in vivo* skin tissue engineering.