ABSTRACT

Selection of novel biomaterial blends for developing unique bio-inspired scaffold for soft tissue engineering practices and in providing patches for scarless wound repair and cancer research is demanding. Adoption of soft lithography and lyophilization to fabricate desired bio-matrix with honey-silk fibroin blend may extend smart synergism of biophysical and biochemical cues for cell-cell/matrix interaction in varied wound beds. Present study develops nanopatterned, micropillared and 3D porous honey/silk-fibroin matrices using soft lithography and lyophilization, and physico-chemically characterizes matrices for surface architecture, mechanical strength, and biodegradability. Nanopatterned matrices examined for cell-matrix interaction, and on micropillar substrates ultrastructural, molecular and nanomechanical behavior of normal and pre-cancer associated primary oral fibroblast and cancer epithelial cells were studied. Matrices further tested for mesenchymal stem cell's biocompatibility and impact on cutaneous wound healing in normal and diabetic murine models. Again 3D porous scaffold tested as a dermal substitute *in vivo*. Nano-patterned matrices with 2% honey showed better fibroblast-matrix interaction which was further amplified in micropillared ambience. Micro-pillared matrix with aspect ratio (~8μm) and elastic modulus (~70Mpa) favored proliferation of normal fibroblast and epithelial cells but inhibited primary pre-cancer fibroblasts and cancer epithelial cells as evident by morphology, gene expressions, apoptosis, cytoskeleton rearrangement and nanomechanical features. Matrices also favored stem cells growth and augmented *healing* of normal and diabetic wounds, supported through ultrastructural and nanomechanical profiling of tissue collagen. 3D scaffolds accelerated infiltration of cells *in vitro* and *in vivo*, which led to faster re-epithelialization and matrix remodeling as evidenced by expressions of p63, ck10, MMP9 and collagen expressions. This dissertation thus successfully developed honey-silk fibroin matrices having potential to favor normal cells including stem cells and scarless wound healing with inhibitory impact on pre-cancer and cancer cells. Hence, it paved the path in developing smarter bio-matrix with tunable textural, mechanical and compositional attributes for regenerative medicine and cancer tissue engineering application.

Keywords: Soft tissue engineering, honey- silk fibroin blends, soft-lithography, biophysical and biochemical cues, cancer inhibition and wound healing, cell-matrix interaction, dermal substitute.