Abstract

Biomaterial based tissue models serve as well defined tools for basic and applied research. FDA-approved silk fibroin from mulberry silkworm *Bombyx mori* is been studied extensively as a natural biomaterial for tissue engineering and regenerative medicine. Fibroin from Indian origin non-mulberry silkworm, *Antheraea mylitta*, possesses nearly all the properties of mulberry silk fibroin, with additional features such as higher mechanical strength and excellent cell adhesion properties. The present work is an endeavor towards engineering 3D *in vitro* tissue models of normal and malignant tissue by integrating the principles of biomaterials and tissue engineering. It is observed that silk fibroin from silkworm *A. mylitta* serves as a compatible platform to study scaffold-cell and cell-cell interactions. 3D silk based bovine cartilage constructs are biochemically similar to native cartilage with comparable content of Type II collagen and glycosaminoglycan. In addition, significant relationships were observed between effects of cell seeding on compressive biomechanical properties and matrix accumulation. For the development of malignant tissue model, 2D and 3D *A. mylitta, B. mori* silk matrices, Matrigel, and tissue culture plates are compared as biomaterials for *in vitro* tumor modeling. The attachment and morphology of cancer cells on *A. mylitta* silk matrices was found to be better than on *B. mori* matrices and comparable to Matrigel and tissue culture plates. *A. mylitta* fibroin not only provides better cell adhesion, but also improved cell viability and proliferation. Growth kinetics and glucose metabolism of 3D cultures were found to be similar to that of cancer cells *in vivo*. The engineered tumor constructs showed avascular tumor-like morphology. Higher and combinatorial treatments of drugs were required to achieve a comparable reduction in cell viability and invasive potential in 3D than standard 2D cultures. The functional dynamics underlying the tumor cell-microenvironment metastatic interactions still remain poorly understood, highlighting the need for metastasis models. Human breast cancer, human osteoblast-like and mesenchymal stem cells are cocultured to develop a breast cancer metastasis model. Coculture constructs show significantly increased drug resistance, invasiveness, angiogenicity, migration of cancer cells and tumor mediated osteolysis. This interaction varies with spatial organization and presence of osteogenic factors. The results indicate that *A. mylitta* fibroin scaffold can provide an easily manipulated microenvironment system to investigate tissue formation, differentiation, as well as evaluation of drugs.

Key words: Non-mulberry, silk, fibroin, biomaterials, scaffold, tissue modeling, 3D cell culture