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Spider Silk

Casting a new web

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Silk fibre based Biomaterials

Lifesaving constructs

Dr Sourabh Ghosh

During the last decade, Tissue Engineering research has made fascinating progress towards the fabrication of tissue constructs in laboratory to repair or replace lost morphology and functions in diseased or damaged organs, in an attempt to meet the demand of our increasingly aged society

In 1543 Andreas Vesalius (1514–1564) wrote a textbook of human anatomy, named 'De humani corporis fabrica libri septem' (On the fabric of the human body). That beautifully illustrated book is revered as the founding stone of modern human anatomy. Did he ever think in his wildest dream that one day human tissues can be indeed replaced by textile fibres and fabrics?

During the last decade, Tissue Engineering research has made fascinating progress towards the fabrication of tissue constructs in the laboratory to repair, or replace, lost morphology and functions in diseased or damaged organs, in an attempt to meet the demand of our increasingly aging society. Other than being highly priced textile commodity, silk fibre has emerged as a fascinating biopolymer for such challenging applications. Silk fibre can meet the growing need for highly specialized biomaterials in Tissue Engineering & Regenerative Medicine due to their biocompatibility, stability, mechanical properties, purity, ease of chemical modification and controlled degradability.

The Silk fibroin protein consists of a light chain (mol. wt ~26 kDa) and a heavy chain (mol. wt. ~390 kDa) linked by a disulfide bond. Silk fibroin is a block copolymer rich in hydrophobic beta-sheet-containing blocks, linked by small hydrophilic moieties. The crystalline regions are primarily composed of Glycine-X repeats, where X could be alanine, serine, threonine or valine. Subdomains enriched in glycine, alanine, serine and tyrosine are placed within these domains. This arrangement results in a hydrophobic protein that self-assembles to form strong and resilient materials. This understanding enables us to develop large variety of three dimensional architectures of biomaterials, in the form of fibres, hydrogel, denatured porous geometry, fibre-hydrogel composites, textile structures and patterned film. Proper selection of the biomaterial design is an important aspect to simulate target tissue morphology and mechanical properties, incorporating physical, chemical, and biological signals to ▶▶

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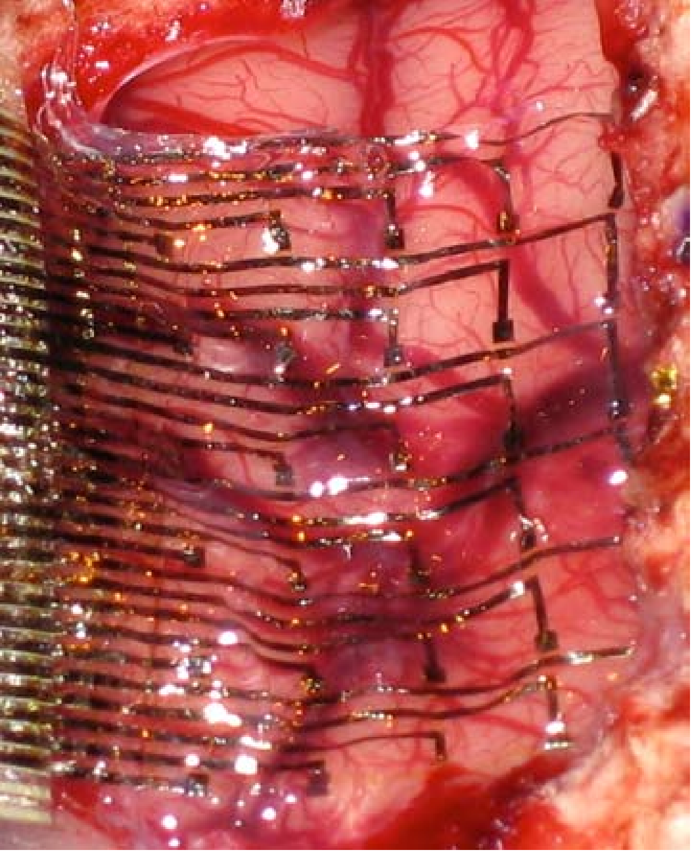

Implantable flexible optical and electronic devices made from Silk (Photo courtesy : Prof. David Kaplan)

guide cells into functional tissues via cell migration, adhesion, and differentiation.

Various groups around the world are working on silk fibre based tissue engineering. Prof. David Kaplan's group, from Tufts University, Boston, is a pioneer in using silk scaffolds to develop ligament, bone, cartilage tissue constructs and other innovative biomaterials. For example, Prof. Kaplan and Dr. Fiorenzo Omenetto's groups, in collaboration with Prof. John Rogers from University of Illinois Urbana-Champaign, developed implantable flexible optical and electronic devices that can wrap around tortuous tissue contours (*see figure above*). MIT's Technology Review selected silk based brain implant as one of the top 10 emerging technologies in 2010. Such silk implants could offer a plethora of biomedical applications, such as measuring electrical activity produced by the heart and brain, and for monitoring nerve and skeletal muscle activity, delivering drugs or electrical stimulations, on-line imaging, and continuous monitoring of health. This system offers great potential for studying cognition, and behavioral patterns when asleep. This system can even offer help in the treatment of people with muscular or neurological disorders, so that they can communicate or interface with computers.

Our group at IIT Delhi is working on physical and chemical modification of silk fibroin proteins to develop various types of scaffolds. For example, braided silk tapes replicating elastic behaviour of human rotator cuff muscle, or adaptation of cross-ply textile yarn winding strategies to develop fibrous scaffolds for tissue engineering of intervertebral disc

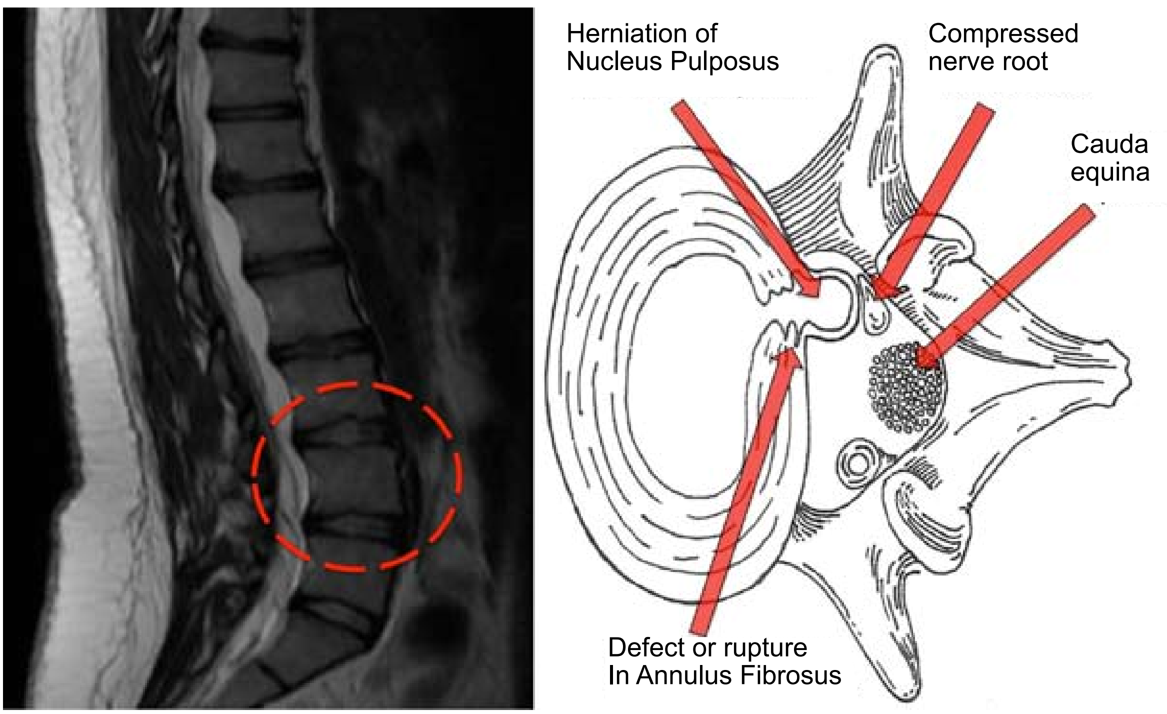

Fig. 2 : Degeneration of Annulus tissue and herniation of Nucleus pulposus cause pinching on nerves

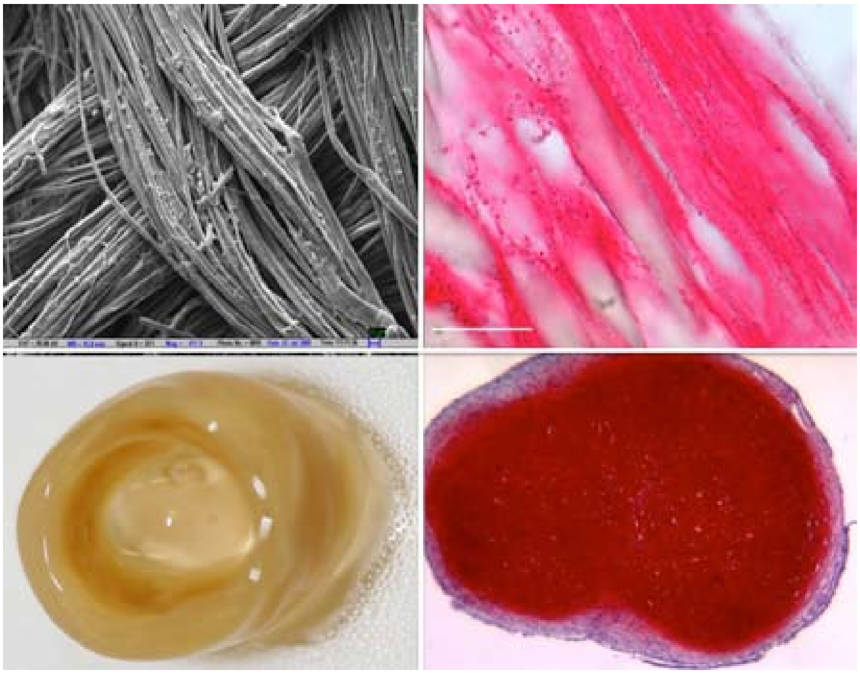

Fig. 3 : Tissue engineered Annulus Fibrosus using scaffold having criss-cross silk fibre alignment

(IVD). IVD makes the spine flexible to bend and twist in all directions. Ageing process or injury to these disks lead to dehydration of inner gel. Degeneration of Annulus tissue, disorientation of collagen fibres result in protrusion of hard Nucleus Pulposus and application of pressure on spinal nerve root and/or cauda equina (*see figure on pg. 13*), causing chronic back pain. This problem is commonly known as "slipped disc". The current approach for treating such degenerative disc problems is through reduction of inflammation and physiotherapy. Upon further degeneration, surgical removal of disk and fusion of the vertebrae is done. However, this results in reducing flexibility of the spine. Replacement of degenerated disc by a tissue engineered substitute could offer major advantages over arthroplasty or implantation of prosthetic disc, in terms of possibility of initial matching of biomechanical properties and adaptive remodeling in the long term.

Several research groups around the world are attempting to develop bioengineered IVD. But none of these studies could have been able to successfully simulate the precise anatomical orientation of collagen fibres in AF tissue in criss-cross lamellar fashion. As a result, mechanical properties of most of these engineered tissues are several orders of magnitude below the stiffness of IVD, especially under tension and compression, and as such, are expected to provide insufficient mechanical support after implantation at the challenging intervertebral joint site. We have developed a silk scaffold having custom-made fiber alignment, where silk fibres are aligned at 30 degree to the scaffold axis, and in alternate directions in successive layers. This fibrous alignment allow cells to deposit fibrous extracellular matrix proteins at a desired orientation (see figure 3) and ultimately developed optimum biomechanical functions of the IVD tissue. Furthermore, chondroitin sulfate, an important component of cartilage tissue, has been covalently attached with silk fibres to prepare chondrogenic microenvironment. Taken together, the combined effect of chemical composition and microstructural organization of scaffold gives rise to anisotropic and nonlinear mechanical behaviors replicating biomehanics of disc tissue.

Although silk fibre has been extensively used for tissue engineering, but several aspects of processing conditions still need to be optimized. For example, Prof Kaplan's group reported that the processing modalities (e.g, time of degumming) could affect overall beta-crystal content, which in turn affects mechanical properties (such as rate of degradation) and biological functionality of silk biomaterials. Processing conditions and beta-sheet content have been shown to affect the metabolism of human mesenchymal stem cells and consequently altered the rate of differentiation.

Feasibility of generating new variety of genetically modified silk chimeric protein, or tunability of silkworm silk, or spider silk, presents opportunity to develop engineered tissues for organ replacement, as well as offer a platform for systematic study for addressing fundamental questions about in-vitro tissue engineered diseased tissue model systems. The modularity and versatility of silk protein-based biomaterials make them ideal candidates for translatable biomaterials research and offer an opportunity to design a new generation of biomaterials with exciting new functionalities.■

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