The tissue engineering laboratory in Hospital Universiti Kebangsaan Malaysia was set up in 1999 under the leadership of two principle researchers with support from the hospital. The laboratory focuses on the advancement and promotion of tissue engineering in Malaysia. The laboratory has developed into a center that comprises three laboratories with 15 postgraduate students, 30 co-researchers and surgeons in the span of four years. Holding three patents and awaiting four more to be granted, their work has since gained international recognition, receiving accolades such as the Geneva Innovation Gold Awards.

The first International Conference on Biomaterial and Tissue Engineering (IC-BITE) was held in Kuala Lumpur in May 2004. It was a significant event that brought together interested and active researchers in this field. The establishment of a National Tissue Engineering Society in November 2004 was yet another milestone. Tissue Engineering Society of Malaysia (TESMA) aspires to gather researchers, academicians and professionals from the commercial bodies. With a current membership of 80 members comprising representatives from major academic institutions and private companies, TESMA hopes to come up with guidelines and policies on research and clinical trials in the field of cell therapy and regenerative medicine.

In this article, an overview of the research activities of the laboratory is covered and the major achievements are highlighted.

Skin

Bilayered skin, one that composes of epidermis and dermis has been constructed (Fig. 1a). Keratinocytes and fibroblasts were grown separately and reconstructed into skin-like layer with the addition of human plasma derivative. Otosilk was used as the backing material to facilitate transportation of the fragile bioengineered skin. These bilayered skins were tested in nude mice model and the outcome was promising. After one week, the bioengineered skin fused completely with
surrounding native skin. After four weeks of implantation, the bioengineered skin matures into a smooth and elastic skin (Fig. 1b). No scarring or contraction was visible. Histological staining of the mature bioengineered skin revealed a well-defined keratin layer (Fig. 1c), which stained positively for keratin with antibodies specific against human pan-keratin. Karyotyping of the cultured cells using flow cytometry and screening for oxidative damage (8-hydroxy-2-deoxyguanosine production) has also been initiated in view of the commencement of the clinical trial early next year. Refinement to the engineered skin using various in-house developed biomaterials is currently undergoing investigation in sheep model.

Fig. 1a. Transportation of the bioengineered bilayered skin with otosilk as the backing material.

Fig. 1b. Post-implanted bioengineered skin has a smooth texture with tensile strength parallel to native skin tissue.

Fig. 1c. Histological section reveals the formation of keratin layer in post-implanted bioengineered skin (4 weeks post-implantation).
Cartilage

Three major achievements related to bioengineered cartilage formation are the formulation of a medium specific for chondrocyte proliferation and differentiation viz. UKM-MECC, the construction of bioengineered cartilage in vitro, and the establishment of the method for autologous implantation of bioengineered cartilage to treat focal cartilage defects. The technique, articular neo-cartilage implantation (ANCI), has been established for sheep model and will be ready for clinical trial next year.

Bone

In the generation of bioengineered bone, various sources of osteoprogenitor cells including bone marrow derived mesenchymal stem cells were used. The aim was to develop a bioengineered bone that is autologous, osteogenic, and moderately resorbable with good structural and mechanical properties. The team worked with a variety of ceramics as the scaffold for bioengineered bone construction. A technique has been developed to generate bioengineered bone from limited cell source and a resorbable scaffold that serves as carrier for cell and protein (cytokines). In vivo evaluation is currently being studied for posterior spinal fusion in the sheep model and treatment of segmental long bone defect in the rabbit model.

Respiratory epithelium

The construction of trachea in the laboratory attempts to restore the respiratory epithelial lining on an bioengineered cartilage in the shape of trachea. Different scaffold materials such as titanium, chitosan and human plasma derivative have been evaluated for the construction of this compound tissue. The bioengineered trachea is currently undergoing in vivo evaluation in a sheep model. A prototype air-liquid interphase bioreactor is now being developed to mimic the physiological condition for respiratory epithelial growth.

Stem Cells

In stem cell research, the team focuses on two cell lineage i.e. human bone marrow derived mesenchymal stem cells and adult stem cells or tissue specific stem cells found in various human tissues. The first challenge was to characterize and distinguish cells at various stages of differentiation during in vitro culture. This was made possible using CD marker characterization on a flow cytometer and protein profiling using 2-D gel electrophoresis and the subsequent characterization of differential proteins. This establishes a baseline for future manipulation of stem cells. Growth kinetic has been found to be a function of age hence the team is looking into the addition of various growth factors into the culture system or the cloning of telomerase gene to improve the stem cell growth properties.
Biomaterials
The laboratory has been developing biomaterials from locally available resources like chitosan from locals sea produce, natural polymers such as collagen and human plasma-based materials. The production of these biomaterials has been complemented with proper evaluation and testing including biocompatibility and mechanical properties, physicochemical characterization, and in vivo testing. Chitosan that has undergone further processing and enhancement in the laboratory has been fabricated into different sizes and shapes for a variety of application including scaffold for tissue engineering and as a wound dressing.

Fig. 2a. Scanning electron micrograph reveals the microstructure of the chitosan scaffold.
Fig. 2b. Disc shaped chitosan scaffold for tissue engineering application.

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Research Interests
- Tissue Engineering of Cartilage, Bone and Skin
- Molecular Genetics of Deafness in Malaysia