Centre for Molecular Medicine
A*STAR

Singapore Skin Club

- All Welcome -

Date – **6pm, Thursday 1st February 2007**

Speaker – **Professor Michele De Luca**
Department of Biomedical Sciences, University of Modena and Reggio Emilia, Modena, Italy

Scientific Director, Veneto Eye Bank Foundation, Epithelial Stem Cell Research Center, Venice, Italy

Title – ***Human epithelial stem cells in regenerative medicine***

Venue – Aspiration, Matrix L2M, Biopolis

Host – Prof Birgit Lane (tel: 6586 9847; email birgit@cmm.a-star.edu.sg)

Abstract: Knowledge of human epithelial stem cells is now being used to refine therapeutic cell grafting strategies in human patients, in the eye and the epidermis. Adult stem cells have a high capacity for self-renewal and can produce progeny capable of terminal differentiation; they generate an intermediate population of committed progenitors, transit amplifying (TA) cells, that terminally differentiate after a limited number of cell divisions. In the cornea of the human eye, stem cells are situated in the limbus and limbal-derived TA cells form the corneal epithelium. The role of p63 alpha and C/EPB delta transcription factors in regulating limbal stem cell proliferation and renewal will be addressed. Cultivated limbal stem cells generate sheets of corneal epithelium suitable for clinical application. We report clinical results obtained in a homogeneous group of over 200 patients presenting with corneal opacification and visual loss due to chemical burns and consequent limbal stem cell deficiency. The corneal epithelium and the visual acuity of these patients have been restored by grafts of autologous cultured limbal stem cells. Secondly, we report that gene therapy is now being used to treat junctional epidermolysis bullosa (JEB), a devastating and often fatal skin adhesion disorder caused by mutations in laminin 5 genes of the basement membrane. Epidermal stem cells from an adult patient with LAM5-beta3-deficient JEB were transduced with a retroviral vector expressing the beta3 cDNA and used to prepare genetically corrected cultured epidermal grafts. Nine grafts were transplanted onto surgically prepared regions of the patient's legs. Engraftment was complete after 8 days. Synthesis and proper assembly of normal levels of functional LAM5 was observed, together with the development of a firmly adherent epidermis that remained stable for the duration of the follow-up (15 months) without blisters, infections, inflammation or immune response. Proviral integration site analysis indicated that the regenerated epidermis is maintained by a defined repertoire of transduced stem cells. These data show that *ex vivo* gene therapy of JEB is feasible and leads to full functional correction of the disease.

Biography: Michele De Luca is a Full Professor of Biochemistry at the University of Modena and Reggio Emilia, Modena, Italy, and Scientific Director of the Veneto Eye Bank Foundation, Venice, Italy. Previously he has been the Director of the Laboratory of Tissue Engineering at the Istituto Dermopatico dell'Immacolata, Rome; Deputy Head, Laboratory of Cell Differentiation, National Cancer Institute, Genova; Visiting Scientist at the Department of Cell Biology, Harvard Medical School, Boston, USA; Fogarty Fellow at the National Institutes of Health (NIH), Bethesda, USA. He graduated M.D. in 1980, and obtained a Specialty in Endocrinology in 1984. He is member of numerous scientific societies and member of several national and international committees. He is author of over 100 scientific publications in major international journals. Michele De Luca was born in Savona, Italy, in May, 17, 1956.