Institute of Medical Biology
A*STAR

Seminar Announcement

- All Are Welcome -



Speaker: **Dr John J. Lemasters**

South Carolina Center of Economic Excellence GlaxoSmithKline Distinguished Endowed Chair in Advanced Cellular Technologies, Departments of Drug Discovery and Biomedical Sciences and Bio-chemistry & Molecular Biology, Medical University of South Carolina
Director, MUSC Advanced Cell Imaging Core
Director, Cell & Molecular Imaging Shared Resource, Hollings Cancer Center
Director, Center for Cell Death, Injury and Regeneration

Title : **"Real-time imaging of bioenergetic metabolism in growing hair follicles"**

Date : **26 Aug 2015 (Wednesday)**
Time : **11am – 12pm**
Venue: **Aspiration Theatrette, Matrix Level 2M, Biopolis**

Abstract of the Seminar:

Modern biotechnology tools have generated a resurgence in research on the growing hair follicle. Furthermore, it is understood that the human hair follicle utilizes considerable metabolic energy. Still, little is known about either generation of energy or the metabolic building blocks (bioenergetics) of growing, anagen hair follicles. Accordingly, the objectives of this investigation were to characterize follicular bioenergetic metabolism using real time multiphoton microscopy on isolated, viable, growing, anagen bovine hair follicles. Multiple vital dyes were applied in dual-photon microscopy to assess cellular function. Cell viability was high for germative epidermal cells and fluorescence of membrane potential-indicating fluorophores revealed polarized mitochondria inside viable cells, with the greatest polarization in epidermal cells. An abrupt transition of mitochondrial depolarization occurred moving from the base and lateral sides of growing follicles to the interior. Beyond this transition was a dark non-fluorescent zone continuous with the hair shaft. As the transition was approached, mitochondrial polarization increased and secretory granules disappeared, consistent with the transition representing degranulation of germinative epidermal cells with release of keratins. Viable but non-growing hair follicles had few polarized epidermal cell mitochondria. Reactive oxygen species (ROS) assessed by chloromethyldichlorofluorescein (DCF) fluorescence revealed some strongly labeled dermal cells, but cmDCF fluorescence was weak inside the bulb except at the apex of paraxial clefts of putative secondary keratin deposition. Epidermal cells with highly polarized mitochondria were located at the same position and formed a circumferential ring within the follicle. Three-dimensional reconstructions showed that dermal papillae entered the base of follicles from the side rather from the middle. Papillae contained fibroblasts with polarized mitochondria that produced little ROS. Overall, the results show robust mitochondrial bioenergetics metabolism in hair follicles, most markedly near sites of keratin deposition and crosslinking.

About the Speaker:

Dr. Lemasters has a long-standing interest in the role of mitochondrial metabolism in pathobiology, especially in relation to ischemia-reperfusion (IR) injury, organ preservation for transplantation, drug/ethanol-induced hepatic injury and cancer. Overall, his laboratory has published over 350 papers in peer-reviewed journals plus more than 100 book chapters. Productive, long-term collaborations with both junior and senior colleagues contributed importantly to this success.

John's major research interests relate to mitochondrial and cellular bioenergetics, including studies of the control of mitochondrial metabolism and the role of mitochondrial dysfunction in toxic, IR and cholestatic injury to hepatocytes, cardiac myocytes and organs stored for transplantation surgery. Our *in vitro* and *in vivo* studies of living cells and tissues show that mitochondrial calcium uptake, iron translocation from lysosomes to mitochondria, and oxidative stress promote the mitochondrial permeability transition (MPT). The MPT initially induces degradation of mitochondria by autophagy, a selective process we termed mitophagy. However, excess MPT induction induces both necrotic cell death from ATP depletion and apoptosis due to cytochrome c release after mitochondrial swelling. His studies show that onset of the MPT is the penultimate event leading to acetaminophen-induced hepatotoxicity, cholestatic liver injury, and IR-induced killing of hepatocytes and other cell types. The Lemasters lab also proposed and is supporting experimentally the novel hypothesis that voltage-dependent anion channels (VDAC) in the mitochondrial outer membrane act as dynamic regulators of global mitochondrial function. Specifically, VDAC closure promotes selective and more efficient mitochondrial detoxification of membrane-permeant acetaldehyde during hepatic ethanol metabolism, whereas in cancer cells VDAC closure contributes to the mitochondrial suppression and activation of aerobic glycolysis characteristic of the Warburg metabolic phenotype.

For these projects, John's laboratory extensively applies new techniques of quantitative laser scanning confocal and intravital multiphoton microscopy for physiological analysis of single cells and living tissues. The lab also extensively employs Seahorse technology to measure respiration and glycolytic flux in cultured cells. Dr. Lemasters also has extensive experience leading research teams and mentoring students, postdoctoral fellows and junior faculty.