NANYANG TECHNOLOGICAL UNIVERSITY

# CBC SEMINAR ANNOUNCEMENT

## Professor Ramasamy Paulmurugan
## Stanford University

### Nrf2-Keap1 interaction: A double-edged sword in metabolic disorders and cancer therapy

The major failure in treatment-response to anticancer drugs is due to drug resistance in cancer cells through the activation of endogenous antioxidant detoxification mechanisms. At the same time, the cellular failure for antioxidant detoxification mechanism has been considered a major factor responsible for the destruction of β-cells in diabetes. Cells maintain their redox homeostasis by developing mechanisms that protect them from oxidative stresses. Since this mechanism is so well designed by nature to protect cells from free radicals produced during oxidative stresses in their aerobic environment, it presents a major obstacle for tumor cells responding to chemotherapy. Nrf2-Keap1 pathway regulates cellular redox homeostasis and hinders cancer therapy in the clinic. Similarly failure in Nrf2-Keap1 pathway in β-cells causes diabetes. Nrf2 is a transcription factor expressed in cells that protects cells from oxidative stresses by inducing antioxidant enzymes. We have extensively used split-reporter protein fragment-complementation assay to optically measure protein-protein interactions, protein folding, and protein dimerizations in cells and noninvasively imaging them in live animals. However, it has not been used for designing sensors to study the cellular chemoprotective antioxidant mechanism, which is an important hallmark pathway that makes drug resistance in cancer therapy, and β-cell dysfunction in diabetes. We developed split-optical reporter complementation sensors to ratiometrically evaluate the oxidative stress induced by chemotherapeutic drugs and antioxidants. The ratiometric sensors can be used to preclinically demonstrate the drug-induced antioxidant chemoprotective (cytoprotective) mechanism of cancer cells in living animals. Additionally, ratiometric sensors can be used for screening new drugs capable of effectively killing cancer cells without activating this endogenous drug resistant mechanism in cancer, and also for identifying and evaluating antioxidants which can improve β-cell function in diabetes.

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| **Date:** | **8th November 2012 (Thursday)** |
| **Time:** | **2:00pm – 3:30pm** |
| **Venue:** | **NTU SPMS CBC Building Level 2, Conference Room** |
| **Host:** | **Assoc Professor Xing Bengang** |