Institute of Medical Biology
A*STAR

# Seminar Announcement

***- All Are Welcome -***

**Speaker:** **Dr Sandrine Lablanche, PhD**
Endocrinologie-Diabétologie,
Centre Hospitalier Universitaire du Grenoble, FRANCE

**Title:** **Prevention of pancreatic β cell death during islet transplantation via inhibition of the Permeability Transition Pore opening**

**Date :** **18 July 2012 (Wednesday)**

**Time :** **4.00pm – 5.00pm**

**Venue:** **Aspiration Theatrette, Matrix Level 2M, Biopolis**

**Host :** **Dr Ray Dunn**
(Tel: 64070164, Email: ray,dunn@imb.a-star.edu.sg)

## *Abstract of the Seminar:*

Islet transplantation is a treatment to consider for selected type 1 diabetic patients. Islet exposure to hyperglycemia, hyperfructosemia and ischemia-reperfusion plays a major role in islet loss after transplantation. The permeability transition pore (PTP) is a mitochondrial channel implicated in cardiomyocyte cell death associated with ischemia-reperfusion injury and in hyperglycemia-induced cell death in endothelial cells. Here, we examine the involvement of PTP opening in the death of human pancreatic islets. We shown that the exposure of human islets to 30 mM glucose or 2.5 mM fructose induces PTP opening and leads to cell death, and further demonstrate that Metformin and Cyclosporine A (CsA) prevent this death through inhibition of PTP opening. Metformin and CsA treatment also prevent Ca2+-induced PTP opening and subsequent cell death in permeabilized and intact INS-1 cells. In a second study, we find that incubation of INS-1 cells in the absence of energy substrates in hypoxic conditions for 1 hour followed by incubation in normal conditions leads to PTP opening and to a dramatic increase in cell death. Both events were again entirely inhibited inhibited by either Metformin or CsA or when treated with the antioxidant N-acetyl-cystein (NAC), which implicates oxidative stress as a cause of PTP opening. Preventing PTP opening might therefore offer a new approach to preserve β cell viability during human islet transplantation.

## *About the Speaker:*

Dr. Lablanche recently obtained her Ph.D. in Chemistry and Life Sciences in the Laboratory of Fundamental and Applied Bioenergetics in Grenoble, FRNACE under the supervision of Professor Eric Fontaine. Her Ph.D. research focused on the mitochondrial protein complex (Permeability Transition Pore, PTP) in murine and human β cell apoptosis induced by high glucose and high fructose concentrations and by ischemia-reperfusion injury. Prior to her Ph.D., Sandrine obtained her M.D. with a specialization in Diabetology and Endocrinology. At the Grenoble University Hospital, she actively participated in clinical research on pancreatic islet transplantation since 2000 under the supervision of Professor Pierre-Yves Benhamou. Their team promoted several multi-centre clinical trials (GRAGIL consortium) that led to about a hundred islet transplants in type1 diabetic patients, which places them among the three most active groups in the world.