# BOSCH INSTITUTE

## Bosch Distinguished Seminar Series

## Heat Shock Protein 72:
## A Panacea for Disease Prevention?

**Speaker:**
Professor Mark Febbraio

**Title:**
Heat Shock Protein 72:
A Panacea for Disease Prevention?
**Date:**
Thursday 31 October, 2013
**Time:**
1.00pm - 2.00pm
**Venue:**
Education Lecture Theatre 351, Education Building
Manning Road, University of Sydney

***Professor Mark Febbraio*:**

Professor Mark Febbraio is a Senior Principal Research Fellow of the NHMRC, is the head of the Cellular and Molecular Metabolism Laboratory and Program Leader of Cell Signalling & Metabolism at the Baker IDI Heart & Diabetes Institute. He is also the Chief Scientific Officer and on the Board of Directors of N-Gene Research Laboratories Inc., a USA based Biotechnology company. His research is focussed on understanding cellular and molecular mechanisms associated obesity and type 2 diabetes. He has authored over 180 peer reviewed papers in leading journals such as *Nature, Nature Medicine, Cell, Cell Metabolism, The Journal of Clinical Investigation, PNAS and Diabetes.* His work is extremely well cited (over 9500 citations, H factor 61). He has won prizes at international, national and institutional levels including the A K McIntyre Prize for significant contributions to Australian Physiological Science (1999), the Colin I Johnson Lectureship by the High Blood Pressure Research Council of Australia (2006) the ESA/ADS Joint Plenary Lecture (2009) and the Sandford Skinner Oration (2011). He is on the Editorial Board of Diabetes, The American Journal of Physiology Endocrinology & Metabolism, Exercise Immunology Reviews and Journal of Applied Physiology. He is a member of seven National or International Professional bodies. He has served on The Council of The Australian Diabetes Society and is a past Honorary Treasurer of this Society (2006-2008). He has served on National Health and Medical Research Grant Review Panels for several years in the areas of Physiology, Cell Biology and Diabetes/Obesity. Professor Febbraio is also dedicated to health and fitness and continues to complete in running races and multi-sport events.

**Summary:** It is well known that when proteins aggregate, illnesses such as Alzheimer's disease, Huntington's disease, and amyotrophic lateral sclerosis can arise (1), and activation of chaperone proteins can suppress diseases associated with protein misfolding (2). However, the role of chaperone proteins in the treatment of metabolic diseases such as type 2 diabetes (T2D) has been relatively understudied. For the past decade, we (3-5) and others (6) have been examining the role of molecular chaperone proteins in the treatment of metabolic disease. Specifically, we have been

studying the role of the inducible form of the 70kDa family of heat shock proteins, namely heat shock protein 72 (HSP72). We have identified an essential role of HSP72 in preventing obesity-induced insulin resistance, using both loss of function and gain of function genetic mouse models and, via the use of small molecule activators of HSP72 currently in human clinical trials for T2D. Moreover, we have demonstrated that activation of HSP72 can preserve muscle function, slow disease progression and increase life span in muscular dystrophy (7). Finally, in unpublished work, we have shown that a small molecule activator of HSP72 improves heart rhythm and function in a mouse model of atrial fibrillation. In this lecture, I will discuss common pathways in these seemingly unrelated diseases that may be regulated by the activation of HSP72.


1. Hartl, F.U., et al. Molecular chaperones in protein folding and proteostasis. *Nature* 475, 324-332 (2011).
2. Hoshino, T., et al. Suppression of Alzheimer's disease-related phenotypes by expression of heat shock protein 70 in mice. *J Neurosci.* 31:5225-5234 (2011).
3. Chung, J., et al. HSP72 protects against obesity-induced insulin resistance. *Proc Natl Acad Sci U S A* 105, 1739-1744 (2008).
4. Bruce, C.R., et al. Intramuscular heat shock protein 72 and heme oxygenase-1 mRNA are reduced in patients with type 2 diabetes: evidence that insulin resistance is associated with a disturbed antioxidant defense mechanism. *Diabetes* 52, 2338-2345 (2003).
5. Crul T., et al. Hydroximic acid derivatives: Pleiotropic HSP co-inducers restoring homeostasis and robustness. *Curr Pharm Des* 19: 309-346 (2013).
6. Ozcan, U., et al. Chemical chaperones reduce ER stress and restore glucose homeostasis in a mouse model of type 2 diabetes. *Science* 313, 1137-1140 (2006).
7. Gehrig, S., et al. HSP72 preserves muscle function and slows progression of severe muscular dystrophy. *Nature* 484: 384-398 (2012).