DukeNUS Medical School

Signature Seminar Series

Signaling through EP3 and Gαz: Divergent roles in beta-cell compensation and dysfunction in diabetes

ABOUT THE LECTURE

Prostaglandin E2 (PGE2) is an arachidonic acid metabolite whose production is increased in type 2 diabetes (T2D). Acute treatment of islets from T2D mice and humans with a Prostaglandin EP3 receptor (EP3) antagonist restores their glucose-stimulated insulin secretion (GSIS) response. In the beta-cell, EP3 is coupled to a unique inhibitory G protein, Gz. Mice lacking the catalytic alpha subunit of Gz (Gαz) are protected from high-fat-diet (HFD) induced T2D, with preserved beta-cell function and significantly increased beta-cell mass. Extra-pancreatic effects of EP3 make full-body EP3-null mice more susceptible to T2D. Yet, even beta-cell-specific EP3 -null mice become glucose intolerance upon HFD feeding, showing a significant decrement in beta-cell function not observed in Gαz-null mice. We propose differential expression of EP3 splice variants, acting through Gαz, may be required for continued beta-cell function and survival in the context of the pathophysiological conditions of insulin resistance, and that up-regulation of PGE2 production and EP3 expression may not become dysfunctional until frank T2D has occurred.

Speaker: **Dr Michelle Kimple**
Associate Professor, Endocrinology, Diabetes & Metabolism
Department of Medicine
University of Wisconsin
School of Medicine and Public Health

Host: **Prof Patrick Casey**
Senior Vice Dean, Research
Duke-NUS Medical School

Date: **Friday, 1 November 2019**

Time: **12.00 PM - 1.00 PM**
(Light refreshments will be served at 11.30 AM)

Venue: **Duke-NUS Medical School**
Amphitheatre, Level 2

Contact Person: **Ms Kathleen Chan, Duke-NUS Research Affairs Department**
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ABOUT THE SPEAKER

Michelle Kimple graduated with a PhD in Biochemistry and Biophysics from the University of North Carolina-Chapel Hill in 2003 and completed post-doctoral training in pharmacology and islet biology at Duke University in 2010. Since joining the University of Wisconsin-Madison Department of Medicine faculty, her independent research program has focused on identifying G protein signaling networks that influence pancreatic beta-cell function, with a goal of discovering new diabetes drug targets.



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