香港中文大學醫學院
Faculty of Medicine
The Chinese University of Hong Kong

35th Anniversary 三十五週年

HEALTH
Li Ka Shing Institute of Health Sciences
李嘉誠健康科學研究所

Seminar:
Can We Treat Obesity and Osteoporosis With A Single Drug?

Date: *16 June 2017 (Friday)*

Time: *10:00 to 11:00 am*

Venue: *Room 407-8, 4/F, Li Ka Shing Medical Sciences Building, Prince of Wales Hospital, Shatin, New Territories*

One CME point for attendance pre-approved by the Medical Council of Hong Kong (MCHK)

Speaker: *Professor Mone Zaidi, MD, PhD, MACP, FRCP, FRCPI, FRCPath, DSc (h.c.), MD (h.c.)*

Professor of Medicine and of Structural and Chemical Biology

Icahn School of Medicine at Mount Sinai, NewYork, USA

Abstract:

The long-held belief that pituitary hormones act solely on master targets was first questioned when we documented GPCRs for TSH, FSH, ACTH, oxytocin and vasopressin on bone cells. As these hormones have primitive roles as far down as coelenterates, it is not surprising that they also have multiple functions in mammalian physiology, and hence, become potential druggable targets. Levels of FSH, an estrogen-producing hormone, rise dramatically as ability to procreate ceases at menopause. However, FSH begins to rise in the face of normal estrogen levels during the late peri-menopause, which is when the most rapid rates of bone loss occur in tandem with increasing visceral and subcutaneous adiposity. In 2006, we showed that FSH can itself stimulate the removal of bone by osteoclasts, and speculated that the late perimenopausal bone loss traditionally attributed solely to declining estrogen levels, could, at least in part, be explained by rising FSH levels[2]. These studies provided a new conceptual framework for blocking FSH to reduce rapid bone loss during this eugonadal, high-FSH phase. To provide proof of this concept, we raised a polyclonal antibody to a short peptide sequence (LVYKDPARPNTQK) within the receptor-binding domain of FSHβ. The antibody prevented the access of FSHβ to the FSH receptor (FSHR), and, by doing so, inhibited bone resorption by osteoclasts, stimulated new bone synthesis by osteoblasts, and increased bone mass in ovariectomized mice. Considering that adipocytes and osteoblasts have a common FSHR-expressing progenitor, we next questioned whether a single molecular mechanism – a high FSH level in the circulation – could explain both perimenopausal bone loss and fat accumulation. If so, we hypothesized that a FSH-blocking therapy would not only increase bone mass, but also reduce body fat. We report that our polyclonal FSH antibody causes a marked reduction in white adipose tissue accumulation in all body compartments in mice on either high-fat diet or normal chow, and in ovariectomized mice on normal chow[6]. This reduction in body fat is phenocopied in *Fshr* haploinsufficient male mice, and is accompanied with profound beiging and brown adipose tissue activation that, in turn, increases thermogenesis. Together these studies form the basis for the simultaneous treatment of two diseases of public health magnitudes – obesity and osteoporosis – with a single agent.

All are welcome. For enquiries, please contact Mr. Jonathan Lee at 3763 6005.