SEMINAR

Department of Biological Sciences

NUS National University of Singapore

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Regulation of Systemic Energy Balance and Glucose Homeostasis by Protein-Tyrosine Phosphatase 1B

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Background: Metabolic syndrome, cardiovascular disease and type 2 diabetes are complex disorders that are associated with obesity and sedentary life style. Elucidating the mechanisms underlying these diseases is vital for understanding their pathogenesis and developing therapies. Genetic and molecular studies identified tyrosine phosphorylation as a key regulator of glucose homeostasis and energy balance. Protein-tyrosine phosphatase 1B (PTP1B) is an important physiological regulator of adiposity and glucose homeostasis. Mice with whole-body PTP1B deletion exhibit increased insulin sensitivity and are protected from high fat diet-induced obesity. However, the main sites and mechanisms of PTP1B action have not been fully elucidated.

Methods: The objective of this study is to determine the metabolic role of adipose PTP1B. To address the potential role of adipose PTP1B in regulating adiposity and insulin sensitivity, we generated mice with adipose-specific PTP1B deletion using the novel Adiponectin-Cre transgenic mice. The effects of efficient and adipose-specific PTP1B deletion on adiposity and glucose homeostasis were assessed in vivo.

Results: We report that adipose-specific PTP1B deletion reduces body weight and adiposity in male and female mice on high fat diet. This is a result, at least in part, of increased energy expenditure in these mice. In addition, adipose PTP1B deletion improves systemic insulin sensitivity and glucose homeostasis. These findings correlate with enhanced tyrosyl phosphorylation of the insulin receptor and its downstream signaling pathway in knockout mice.

Conclusion: Our studies reveal that targeting PTP1B in adipose tissue may be a useful approach for treatment and prevention of obesity and insulin resistance.

Artwork by Ann Nee, DBS, NUS