Validation of Diet-Induced Obese Mouse Model Using Swiss Albino Mouse Strain For *In Vivo* Pharmacological Metabolic Research

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Summary

Obesity prevalence has increased constantly and reached a global epidemic proportion over recent decades[1]. Obesity and accompanied metabolic disorders such as insulin resistance, diabetes and cardiovascular complications are considered as the greatest health problems in modern society contributing to the health care burden worldwide nowadays. Obesity is a complex, chronic disorder that occurs as a result of many factors including genetic, behavioral, environmental, physiological, social and cultural factors. However, the fundamental etiology could be attributed to an energy imbalance between food consumption, basal metabolism and energy expenditure which is more and more popular with the sedentary life in modern society[2].

The animal models are extremely important tools for studying the molecular mechanisms underlying the pathogenesis of obesity and metabolic complications as well as developing therapeutic approaches in management of obesity and metabolic disorders. In addition to obese mouse models caused by genetic mutations (e.g. *ob/ob* and *db/db* mice), the mouse model of diet-induced obesity is a polygenic model and has become one of the most important tools for understanding of obesity development and in pharmacological studies[3]. C57BL/6J mouse strain is considered as the most popular diet-induced obese mouse model as this mouse strain is sensitive to high fat diet and well mimics the human metabolic derangements observed in obesity development[3]. Unfortunately, the unavailability of inventoried diet-induced obese C57BL/6J mouse strain in Vietnam limits the local scientists in the biomedical community to do research on metabolic studies with high fat diet (HFD). We herein attempted to set up and validate a diet-induced obese mouse model of low cost and easy reproducibility using Swiss albino mouse strain which is commonly available in

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Vietnam (obtained from Pasteur Institute at Ho Chi Minh city). Successfully establishing a diet-induced obese mouse model with Swiss albino mouse strain would enable further institutional pharmacological research studies in the future.

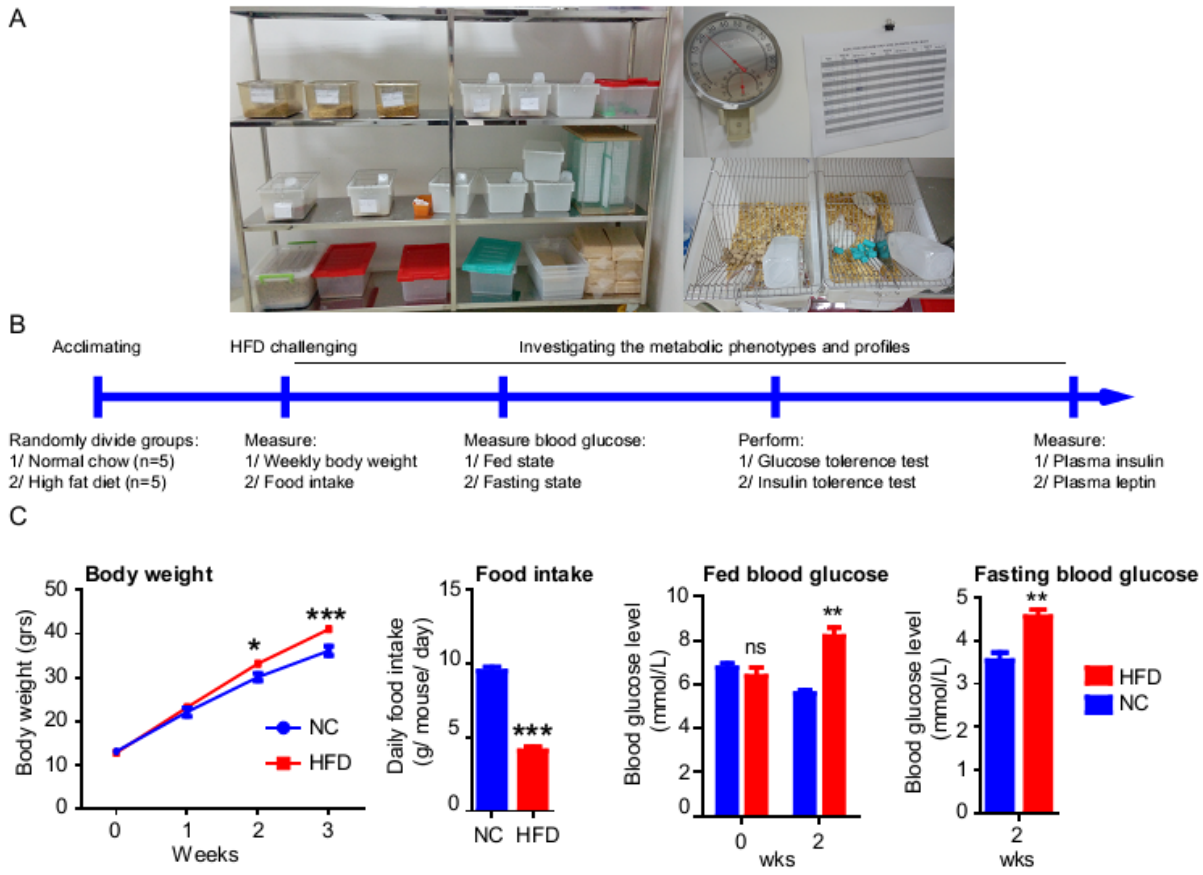

Figure 1. Establising and validating a HFD-induced mouse model using Swiss albino mouse strain.

A, Pictures of mouse model of diet-induced obesity with Swiss albino mice at TTU institutional level. Mice were kept in controlled temperature (24-26 °C) with a 12-hour-light/dark cycle (light on/off at 06:00 a.m./p.m.). All animal experiments in this study were approved by the Institutional Animal Care and Use Committee (IACUC) of the Tan Tao University School of Medicine.

B, Timeline of validating experiments.

C, Results of body weight, food intake, fed and fasting blood glucose levels after HFD challenge. Data are expressed as mean ± S.E.M. *p<0.05, **p<0.01, ***p<0.001. Two-way ANOVA or Student's t tests were used. N=5 mice/each group.

Compared to the mice fed standard diet (SD) (AniFood, Rodent Diet, 6% kcal from fat, 3.84 kcal/kg), mice fed with high fat diet (Envigo's Teklad Rodent High Fat Diet, TD.06414, with 60% kcal from fat, 5.24 kcal/kg) showed significant increase in body weight after 2 weeks of HFD (N=5, 41.06 ± 0.74 grams in HFD-fed mice *vs* N=5, 36.14 ± 1.04 grams in SD-fed mice, $p<0.001$) even though they had less food consumption (N=5, 4.1 ± 0.3 g/mouse/day in HFD-fed mice *vs* N=5, 9.5 ± 0.3 g/mouse/day in SD-fed mice, $p<0.001$). The fed blood glucose significantly increased after feeding mice with 2 weeks of HFD (N=5, 8.20 ± 0.39 mmol/l in HFD-fed mice *vs* N=5, 5.58 ± 0.15 mmol/l in SD-fed mice, $p<0.01$). The blood glucose level in fasting state of mice fed 2 weeks of HFD was significantly higher than those of SD-fed mice (N=5, 4.56 ± 0.16 mmol/l in HFD-fed mice *vs* N=5, 3.54 ± 0.19 mmol/l in SD-fed mice, $p<0.01$). Although results of full validation are updating, these preliminary results of body weight, food intake and blood glucose levels in fed and fasting states partly showed that a HFD-induced mouse model was successfully established at an institutional level.

Reference

1. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014;384:766-781.
2. Racette SB, Deusinger SS, Deusinger RH. Obesity: overview of prevalence, etiology, and treatment. Phys Ther 2003;83:276-88.
3. Wang CY, Liao JK. A mouse model of diet-induced obesity and insulin resistance. Methods Mol Biol 2012;821:421-33.

Acknowledgement

The authors would like to thank Professor Ki Woo Kim (Department of Oral Biology, Yonsei University College of Dentistry, Korea) for his advice and encouragement. This research is funded by Vietnam National Foundation for Science and Technology Development (NAFOSTED) under grant number 108.05-2017.01 (to K.V.D).