Dr. Aimin Xu
Assistant professor
Research areas: Obesity and Metabolic Syndrome
Contact address: L8-43, New Laboratory Block, 21 Sassoon Road
Tel: 852 28199754; Fax: 28162095
Email: amxu@hkucc.hku.hk

Research Interest: My primary research focus is on obesity and its related metabolic disorders, including insulin resistance, Type 2 Diabetes (T2DM), fatty liver disease and atherosclerosis. We aim to understand the molecular and cellular mechanisms that link obesity with its related disorders, with a long-term goal of developing novel diagnostics and therapeutics for these increasingly important diseases. We are currently working on several highly related projects.

1. *Structural and functional characterization of adipokines secreted from adipocytes.* Adipokines play important roles in regulating energy metabolism, insulin sensitivity and inflammation. Discordant production of adipokines is causally associated with the pathogenesis of obesity-related metabolic and cardiovascular disorders. We are currently using both *in vitro* and *in vivo* systems to characterize the functions of several key adipokines, including adiponectin, angiopoietin-like protein 4 (ANGPTL4) and adipocyte fatty acid binding proteins (A-FABP).
2. *The role of adipose tissue inflammation in the development of systemic insulin resistance, diabetes and cardiovascular disease.* Macrophage infiltration and inflammation in adipose tissue are commonly observed in obese subjects and animal models. However, whether the local inflammation in adipose tissue is the major contributor to systemic inflammation and insulin resistance remains to be clarified. We attempt to use transgenesis approaches to address this question, by selective activation and inactivation of several key transcription factors and protein kinases involved in inflammation pathways, such as NF-kappa B, Jun-kinase and hypoxia-inducible factor 1alpha et al.
3. *Discovery of novel biomarkers associated with obesity-related diseases and development of high throughput methods for clinical diagnostics.* We are interested in the use of various proteomics-based approaches to identify novel biomakers that can be used for early diagnosis, risk stratification and therapeutic monitoring of obesity-related metabolic and cardiovascular diseases.
4. *The use of adipokines as the targets to develop and rationalize Traditional Chinese Medicine (TCM) for the treatment of obesity-related disorders*. In collaboration with Shanghai Institute of Materia Medica (SIMM), we have been using several key adipokines as biomarkers to screen for natural compounds from TCM extracts with anti-obesity and anti-diabetic activities.

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C. ***Hong Kong Innovation & Technology Fund (ITS 048/03***. 2538960 HK$, Prof. K Lam as Project coordinator).

D. ***Guangdong - Hong Kong Technology Cooperation Funding Scheme (TCFS*****), (GHP/027/05,** *3,299,000 HK$*)

Selected publications

[1] A. Xu*, Y. Wang, J. Y. Xu, D. Stejskal, S. Tam, J. Zhang, N. M. Wat, W. K. Wong, and K. S. Lam, Adipocyte fatty acid binding protein is a plasma biomarker closely associated with obesity and metabolic syndrome, **Clin Chem** (2006), 52: 405-31 (*Corresponding author)

[2] A. Xu*, K. W. Chan, R. L. Hoo, Y. Wang, K. C. Tan, J. Zhang, B. Chen, M. C. Lam, C. Tse, G. J. Cooper, and K. S. Lam, Testosterone selectively reduces the high molecular weight form of adiponectin by inhibiting its secretion from adipocytes, **J Biol Chem** 280 (2005) 18073-18080 ((*Corresponding author).

[3] A. Xu, M. C. Lam, K. W. Chan, Y. Wang, J. Zhang, R. L. Hoo, J. Y. Xu, B. Chen, W. S. Chow, A. W. Tso, and K. S. Lam, Angiopoietin-like protein 4 decreases blood glucose and improves glucose tolerance but induces hyperlipidemia and hepatic steatosis in mice, **Proc Natl Acad Sci U S A** 102 (2005) 6086-6091 (*Corresponding author).

[4] Y. Wang, K. S. Lam, J. Y. Xu, G. Lu, L. Y. Xu, G. J. Cooper, and A. Xu, Adiponectin inhibits cell proliferation by interacting with several growth factors in an oligomerization dependent manner, **J Biol Chem 280** (2005) 18341-18347.

[5] A. Xu,* Y. Wang, H. Keshaw, L. Y. Xu, K. S. Lam, and G. J. Cooper, The fat-derived hormone adiponectin alleviates alcoholic and nonalcoholic fatty liver diseases in mice, **J Clin Invest** 112 (2003) 91-100 (*Corresponding author, **cover story**).