Dr. Li Qiang

Project Summary/Abstract
This proposal describes a five-year plan for Li Qiang to transition to an independently-funded investigator, applying rigorous scientific method to metabolic research. Dr. Qiang received PhD degree from Boston University School of Medicine in 2007 and performed postdoctoral training in Diabetes Research Center (DRC) and Department of Medicine at Columbia University since 2008. Dr. Qiang's training cemented his intent to uncover the browning mechanism of white adipose tissue (WAT) through Pparγ deacetylation, and further lead to the discovery of novel therapeutic agent to treat metabolic syndrome.

The goals of the proposed training are to provide training and mentoring to prepare Dr. Qiang for an independent research career, and additionally, to answer fundamental questions that persist in obesity research and how it goes awry in diabetic patients. Obesity leads to insulin resistance and further Type 2 diabetes. Currently available insulin sensitizer thiazolidinediones (TZDs) are at skepticism for their detrimental effects. Recently browning of WAT has been appreciated for its metabolic improvement. A mechanistic understanding of the browning function of TZD is necessary to develop new anti-diabetic drugs that are shorn of the side effects. In this application, Dr. Qiang describes preliminary data that reveal the novel role of acetylation in regulating the transcriptional selectivity of Pparγ. Dr. Qiang and one of his mentors, Domenico Accili, determined that SirT1 gain-of-function mimics TZD in browning WAT. These effects were recapitulated by the deacetylation-mimetic Pparγ-2KR mutant in vitro. Dr. Qiang proposes in this application (1) to characterize the physiological significance of Pparγ deacetylation, (2a) to determine the mechanism by which Pparγ deacetylation converts energy-storing WAT into energy-dissipating BAT-like tissue, and (2b) to study the interplay between acetylation and other post-translational modifications (PTMs) in regulating Pparγ's transcriptional selectivity and metabolic functions. The results gained from these proposed studies should yield important insights into whether reprogramming white adipose tissue into an energy-dispersal site will provide new treatment options for human obesity and diabetes, and whether it is possible to develop a new class of Pparγ ligands that displays TZD's beneficial metabolic effects but without its cardiovascular, oncogenic, and bone loss comorbidities.

Dr. Qiang's long-term career objective is to understand the mechanisms of brown remodeling WAT through PTMs of Pparγ, and further translate the seminal discoveries made at the bench into therapeutic treatments for obesity and diabetes. The scientific knowledge that required to integrate browning WAT at both molecular level and physiological level, as well as in the many complicated and technical aspects of Pparγ PTMs and SirT1 biology, can best be addressed through his choice of mentors (Drs. Domenico Accili and Wei Gu) and collaborators (Drs. Ira Goldberg and Yingming Zhao), all respected investigators who value mentoring young and aspiring faculty members. Finally, the Columbia University Medical Center environment brings together access to a diverse metabolic research groups and all the facilities and faculty developmental tools that Dr. Qiang will need in order to become an independent investigator and a productive member of the academic metabolism community.
