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Circadian control of leptin expression and signaling maintains energy homeostasis *in vivo*

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Circadian rhythms are biological rhythms that control most aspects of mammalian physiology. These rhythms are generated by an endogenous mechanism called the circadian clock. We have demonstrated that disruption of circadian rhythm abolishes energy homeostasis and induces obesity in mice independent of all previous identified risk factors for obesity, and that the expression of the key peripheral adiposity signal leptin is primarily controlled by the molecular clock in the fat tissue but not exogenous food cues. Disruption of circadian homeostasis in mice by circadian gene mutation or jet-lag abolishes the circadian homeostasis of leptin expression and induces Leptin resistance in mice, a key pathophysiological mechanism for human obesity. Using *in vivo* ChIP approach, we demonstrated that the molecular clock directly controls the transcription of leptin in the fat tissue by rhythmically competing with other transcription factors to bind to the same promoter region on the leptin promoter. We propose that disruption of circadian control of Leptin expression and signaling is a major contributor to the diverse metabolic consequences of circadian disruption.

Biography

Loning Fu has completed her Ph.D from the University of Calgary and postdoctoral trainings in University of Toronto and Baylor College of Medicine. Her studies have led to the discovery of the role of the mammalian circadian clock in tumor suppression. Recent progress in the Fu lab have also revealed that the circadian homeostasis of Leptin expression and signaling plays a key role in energy homeostasis, and that disruption of circadian rhythm increases the risk of obesity and obesity-related cancers independent of all previously identified risk factors.

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