Diurnal changes in autophagy and the role of the clock

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Autophagy is a cellular process whereby the cell digests its own components as a means of removing defective organelles, providing a source of amino acids or lipids in times of need, controlling inflammation and defending against invading pathogens. Reduced autophagy is implicated in a variety of conditions ranging from neurodegenerative diseases to cancer. In vivo, autophagy is increased during the sleep phase and reduced during the active phase, while the transcription of autophagy genes is rhythmic in many tissues. The control of this diurnal variability is not fully understood and the relevance of a day/night pattern in autophagy to human health and disease is unknown. Here, we investigate circadian expression of autophagy genes with the aim of further understanding the role of the circadian clock in autophagy. We show autophagy-related genes that cycle in vivo, including ulk1, atp6v1d, gabarpl1, cebp/b, atg7, p62 and atg2a, do not exhibit such cycling in entrained cells in culture with robust clocks including U2OS cells, bone-marrow derived macrophages and peritoneal macrophages. However, we also show that autophagy is altered in macrophages lacking Bmal1 and that the promoters of several autophagy genes contain E-boxes, indicating that the clock machinery may play a role in autophagy. We propose that a robust circadian clock is not sufficient to drive circadian rhythms in autophagy gene transcription in cultured cells and that Bmal1 contributes to autophagy function.

Trainee Award Eligible