PRINCIPE FELIPE
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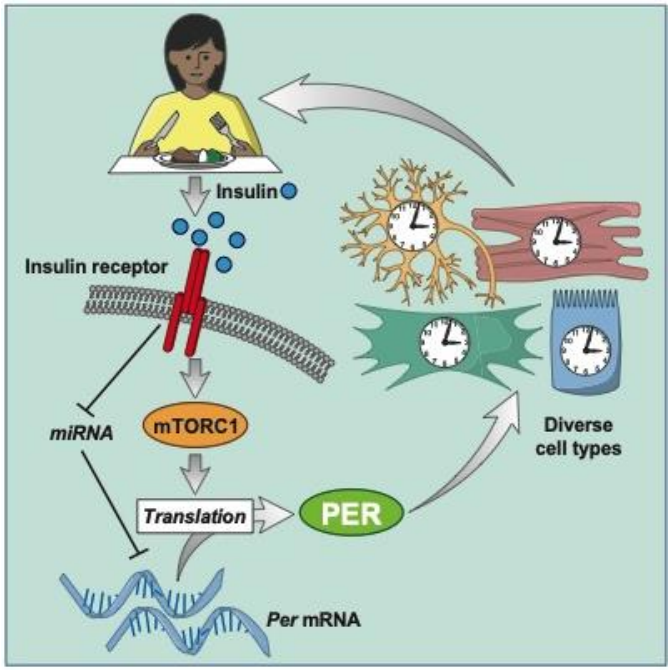
CIPF Lecture Series

Insulin/IGF-1 drives PERIOD synthesis to entrain circadian rhythms with feeding time

Speaker: **Dr. John S. O'Neill**
MRC Laboratory of Molecular Biology, Cambridge, UK
Cellular rhythms, signalling and metabolic regulation
Date: **05/04/19- 12:30 h**
Place: Salón de Actos CIPF

Abstract: In mammals, endogenous circadian clocks sense and respond to daily feeding and lighting cues, adjusting internal ~24h rhythms to resonate with, and anticipate, external cycles of day and night. The mechanism underlying circadian entrainment to feeding time is critical for understanding why mistimed feeding, as occurs during shift work, disrupts circadian physiology, a state associated with increased incidence of chronic diseases (e.g., T2 diabetes, cancer). We show that feeding-regulated hormones insulin and IGF-1 reset circadian clocks *in vivo* and *in vitro* by induction of PERIOD proteins, and that mistimed insulin signalling disrupts circadian organisation of mouse behavior and clock gene expression. Insulin/IGF-1 receptor signalling is sufficient to determine essential circadian parameters, principally via increased PERIOD protein synthesis. This requires coincident mTOR activation, increased phosphoinositide signalling and microRNA down-regulation. Besides its well-known homeostatic functions, we propose insulin/IGF-1 is the primary signal of feeding time to cellular clocks throughout the body.



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C/ Eduardo Primo Yúfera, 3 (junto Oceanográfico) · 46012 VALENCIA (Spain) · Tel: +34 96 328 96 80 - Fax: +34 96 328 97 01 / www.cipf.es / CIF G-46/923421