



PRINCIPE FELIPE
CENTRO DE INVESTIGACION

CIPF Seminar

Characterization of RNA splicing factors involved in metabolic regulation in the liver

Speaker: **Santiago Vernia, PhD**

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Date: **21/06/19- 12:30h**

Place: Salón de Actos CIPF

Pre-mRNA alternative Splicing (AS) has been implicated in a growing number of human diseases such as cancer and neurodegeneration. However, the contribution of AS to metabolic regulation in health and disease is poorly understood. We have combined RNAseq and high-throughput proteomics analyses to identify splicing factors involved in metabolic homeostasis. We have found that a group of splicing factors including Hnrnp3, undergo metabolic modulation in the liver. Our results show that Hnrnp3 expression is induced by insulin, suggesting that this splicing factor might play a role in the transcriptional response during feeding/fasting cycles. Moreover, this regulation is lost in models of diet-induced obesity. By using an Adeno Associated Virus-delivered CRISPRa and CRISPRi system we have generated gain- and loss-of-function models for HNRNPH3 in the liver, to further investigate the metabolic role of this splicing factor. Interestingly, we find that HNRNPH3 plays a role controlling hepatic glucose production in vitro and in vivo, and more broadly, our results suggest that specific AS programs play an important role in metabolic regulation.

CON LA FINANCIACIÓN DE:



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