Giorgia BENEGIAMO  
Chronobiology and Sleep Research Group, Institut für Pharmakologie und Toxikologie, Universität Zürich

“Role of the RNA-binding protein NONO in circadian gene expression and metabolism”

Host: Prof. Johan Auwerx

Abstract:
The mechanisms by which feeding and fasting drive rhythmic gene expression for physiological adaptation to daily rhythm in nutrient availability are not well understood. In my PhD work I found that, upon feeding, the RNA binding protein NONO accumulates within speckle-like structures in liver cell nuclei. Combining RNA-immunoprecipitation and sequencing (RIP-seq), I found that an increased number of RNAs are bound by NONO after feeding. I further discovered that NONO binds and regulates the rhythmicity of genes involved in nutrient metabolism post-transcriptionally. Finally, I found that disrupted rhythmicity of NONO target genes has profound metabolic impact. Indeed, NONO-deficient mice exhibit impaired glucose tolerance and lower hepatic glycogen and lipids. Accordingly, these mice shift from glucose storage to fat oxidation, and therefore remain lean throughout adulthood. In conclusion, my study demonstrated that NONO post-transcriptionally coordinates circadian mRNA expression of metabolic genes with the feeding/fasting cycle, thereby playing a critical role in energy homeostasis.