Circadian clocks: more beyond neurons

Circadian astrocytes: Networked in cortex and cancer
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Circadian rhythms in the brain regulate sleep-wake, feeding-fasting and other daily behaviors. The cells of the suprachiasmatic nucleus play a central role in coordinating daily rhythms in the brain. This talk will explore how daily rhythms in the neurons and astrocytes of the cortex arise and synchronize to local time in health and in glioblastoma, the most common and deadly form of brain cancer.

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Tso, C.F, Simon, T., Greenlaw, A.C., Puri, T., Mieda, M., Herzog, E.D. (2017) Astrocytes Regulate Daily Rhythms in the Suprachiasmatic Nucleus and Behavior. Curr Biol. 27,1-7.

Exploring mechanisms of microRNA rhythms in the mouse cerebral cortex
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Post-transcriptional mechanisms control daily oscillations of protein abundance in the mouse liver. Whether this occurs in brain is unknown. MicroRNAs are small noncoding RNAs with post-transcriptional regulatory capacity. Analysis, around the 24 hours, of transcriptome/miRNome indicated that ~19% of the miRNAs are circadian in cerebral cortices of adult mice. Most of oscillating miRNAs peak in the active phase (between ZT10-ZT18), therefore ‘in phase’ with the Per and Cry circadian repressors, and were compromised upon the deletion of Bmal1 gene in astrocytes, which impairs brain circadian rhythms, cognition and lifespan. We will discuss mechanisms of miRNA oscillations in cortical cell subpopulations and relevance of miRNA rhythms in circadian circuits.

Barca-Mayo O, Pons-Espinal M, Follert P, Armirotti A, Berdondini L, De Pietri Tonelli D. Astrocyte deletion of Bmal1 alters daily locomotor activity and cognitive functions via GABA signalling. Nat Commun. 2017 Feb 10;8:14336. doi: 10.1038/ncomms14336.

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How fish “sense” the light? Fish as model to study the deep brain photoreception
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During the Cambrian explosion animal body plans evolved very rapidly and image-forming eyes and visual systems emerged. However, in the pre-Cambrian era early organisms already evolved photoreceptors that were capable of light detection to mediated simple behavioral responses as the phototaxis. For this reason, extra-retinal photoreceptors represent the most basal form of light reception. Fish represent the most fascinating model to study deep brain photoreception because they colonized all aquatic habitats characterized by different photic environments including the subterranean waters in perpetual darkness. Comparative studies on pigeon and hypogean fish species could help to shed light on key genetic and physiological mechanisms whereby animals directly or indirectly respond to light.

Calderoni, L., Rota-Stabelli, O., Frigato, E., Panziera, A., Kirchner, S., Foulkes, N. S.,Fuselli, S. (2016). Relaxed selective constraints drove functional modifications in peripheral photoreception of the cavefish Phreatichthys andruzzii and provide insight into the time of cave colonization. Heredity.

Cavallari N., Frigato E., Vallone D., Fröhlich N., Lopez Olmeda J.F., Foà A., Berti R., Sánchez Vázquez F.J., Bertolucci C., Foulkes N.S. (2011) A Blind Circadian Clock in Cavefish Reveals that Opsins Mediate Peripheral Clock Photoreception. PLoS Biology 9(9): e1001142.

Cryptochrome: the dark side of a circadian photoreceptor comes to light

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In Drosophila, Cryptochrome acts as the main circadian photoreceptor in the central pacemaker neurons and as component of the circadian repressor complex in the peripheral clocks. While the light-activation mechanism is being thoroughly studied, the nature of the transduction signaling that activate CRY in the dark remains largely unknown. We hypothesize a novel mechanism regulated by Ca2+/CaM, that could be involved in the light-independent activation of Drosophila and act in consolidating the light-response stimulation.

Mazzotta GM, Bellanda M, Minervini G, Damulewicz M, Cusumano P, Aufiero S, Stefani M, Mammi S, Costa R and Tosatto S (2018). Calmodulin enhances Cryptochrome binding to INAD in Drosophila photoreceptors. Frontiers in Molecular Neuroscience. 11:280. doi:10.3389/fnmol.2018.00280

Schlichting M, Rieger D, Cusumano P, Grebler R. Costa R, Mazzotta GM*, Helfrich-Förster C* (2018). Cryptochrome interacts with actin and enhances eye-mediated light sensitivity of the circadian clock in Drosophila melanogaster. Frontiers in Molecular Neuroscience 11:238. doi: 10.3389/fnmol.2018.00238. eCollection 2018. (* Co-corresponding Author)