SFB 960-/BZR – Kolloquium

Donnerstag 15. März 2018, 14.00 Uhr
H 53

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Daily oscillations in the liver

The mammalian timing system is composed of a master pacemaker in the suprachiasmatic nucleus (SCN) and peripheral oscillators in nearly all body cells (Schibler et al., 2015). It has long been thought that the master pacemaker in the SCN synchronizes circadian oscillators in peripheral organs. However, this has never been rigorously tested, since the appropriate technology was just not available. We have established a real-time monitoring technology, dubbed RT-Biolumicording, permitting us to follow circadian gene expression in peripheral organs of freely moving mice during months (Saini et al., 2013). Using this recording technology, we have shown that the phase coherence between organs is indeed compromised in SCN-lesioned animals, but that it can be re-established by imposed feeding cycles. Surprisingly, however, the phase coherence is maintained within the livers (i.e. between hepatocyte oscillators) of SCN-lesioned mice kept in constant darkness and fed *at libitum*.

The liver plays a pivotal role in metabolism and xenobiotic detoxification, processes that must be particularly efficient during the activity phase when animals feed. We observed that the size and macromolecular content of mouse hepatocytes follow a daily rhythm, whose amplitude depends on both feeding-fasting and light-dark cycles. In liver, ribosomes are rate-limiting for protein synthesis, and the daily oscillation of protein accumulation is indeed accompanied by a similar fluctuation in ribosome number. While the transcription of ribosomal RNA (rRNA) and ribosomal protein (RP) mRNAs remains nearly constant throughout the day, the translation efficiencies of RP mRNAs follow high-amplitude diurnal rhythms. Intriguingly, these RP synthesis cycles run in antiphase with rRNAs polyadenylation cycles in the nucleus. Based on studies with cultured fibroblasts we propose that rRNAs not packaged into complete ribosomal subunits are polyadenylated in the nucleus by the poly(A) polymerase PAPD5 and degraded by the nuclear exosome (Sinturel et al., 2017).

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