**Supplementary material**

### 2.6. RNA extraction and cDNA synthesis

Total RNA, containing small RNAs, was extracted from frozen liver and from cell culture using a mi/mRNA extraction kit (miRNA kit, E.Z.N.A., Omega Bio-tek, Norcros, U.S.A), according to the manufacturer's protocol. To isolate both total RNA and miRNA 1 equivalent of absolute ethanol was added instead of recommended 0.33 equivalent at step 7. The washing step was performed according to the protocol for isolating large RNAs. The concentration of the purified RNA was determined using a Nanodrop 1000 Spectrophotometer (Fischer Bioblock Scientific, France).

### 2.7. mRNA quantification by RT-qPCR

To analyse the expression of each mRNA, reverse transcription was performed using TaqMan mRNA reverse transcription kit (Fisher Scientific, Madrid, Spain). For the reverse transcription a My gene L series Peltier Theraml Cycler was used; the reaction was performed at 25 °C for 10 min, 37°C for 120 min and 85 °C for 5 min. The final total concentration was 50 ng/µL. We used 22.5 µL of the resulting diluted cDNA solution for subsequent RT-qPCR amplification using the hydrolysis probe (Taqman pPCR master mix; Applied Biosystem, Madrid, Spain). The following probes were used for each gene: *Bmal1* (Hs00154147_m1) and *Nampt* (Hs00237184_m1). The results where normalized to cyclophilin (PPIA: Hs99999904_m1), which was used as *reference gene*. Amplification was performed using the ABI Prism 7300 SDS Real-Time PCR system (Applied Biosystems, Madrid, Spain) at 50 °C for 2 min, 95 °C for 10 min followed by 40 cycles of 95 °C for 15 s and 60 °C for 1 min. The fold change in the mRNA level was calculated by a log 2 scale according to the equation $2^{-\Delta\Delta Cq}$, being Cq quantification cycle.

### 2.8. microRNA quantification by real-time quantitative real-time polymerase chain reaction (RT-qPCR)

To analyse the expression of each miRNA, reverse transcription was performed using TaqMan microRNA reverse transcription kit (Fisher Scientific) and the miRNA-specific reverse transcription primers provided with the TaqMan microRNA assay (Fisher Scientific). For the reverse transcription a "My gene L series" Peltier thermal cycler was used; the reaction was performed at 16 °C for 30 min, 42 °C for 30 min and 85 °C for 5 mi. 1.33 µL of resulting diluted cDNA were used in a subsequent RT-qPCR amplification using a hydrolysis probe (Taq-Man universal PCR master mix; Applied Biosystem) and the associated specific probes provided in the TaqMan microRNA assay kit (Applied Biosystem). The following specific hydrolysis probes were used for each gene: microRNA-27b-3p (MI0000440), a microRNA target of *Bmal1* (NM_001030272.2) and microRNA-34a (MI0000268), target of *Nampt* (NM_005746.2). The results were normalized to the expression of the U6 small nuclear RNA (NR_004394), which was used as *reference*. Amplification was performed using the ABI Prism 7300 SDS Real-Time PCR system (Applied Biosystems) at 95 °C for 10 min, followed by 40 cycles of 95 °C for 15 s and 60 °C for 1 min. The fold change in the miRNA level was calculated by a log 2 scale

according to the equation $2^{-\Delta\Delta Cq}$, where ΔCq=Cq miRNA−Cq U6 and ΔΔCq=ΔCq treated samples−ΔCq untreated controls.

Table S1. Individual phenolic compounds of the grape seed proanthocyanidins extract determined by reverse-phase HPLC-MS.

| Phenolic compounds | m/z | total amount mg/g extract* |
|---|---|---|
| Gallic acid | 169.01 | 35.16 ± 2.85 |
| Protocatechuic acid | 153.01 | 2.19 ± 0.14 |
| Vanillic acid | 167.03 | 0.15 ± 0.2 |
| Procyanidin dimer [a] | 577.13 | 87.51 ± 2.71 |
| Catechin | 289.07 | 58.36 ± 2.7 |
| Epicatechin | 289.07 | 50.35 ± 1.26 |
| p-coumaric acid | 163.03 | 0.14 ± 0.08 |
| dimer gallate [b] | 729.14 | 4.64 ± 0.49 |
| Epigallogatechin gallate | 457.07 | n.d. |
| Procyanidin trimer [a] | 865.19 | 9.77 ± 0.5 |
| Procyanidin tetramer [a] | 1153.26 | n.d. |
| Epicatechin Gallate [b] | 441.08 | 1.86 ± 0.07 |
| Quercetin-3-O-galactoside | 463.08 | 0.20 ± 0.01 |
| Narigenin-7-glucoside | 433.11 | 0.25 ± 0.04 |
| Kaempferol-3-glucoside | 447.09 | n.d. |
| Quercetin | 301.03 | 0.20 ± 0.11 |

*Values are expressed as mg compound/ g extract ± standard deviation. n.d.: non detected. [a] quantified using calibration curve of proanthocyanidins dimer. [b] quantified using the calibration curve of epicatechin gallate

Table S2. Comparative analysis of the estimated circadian rhythm of *Bmal1*, *Nampt*, miR-27b-3p, miR-34a expression obtained by cosinor-based method.

| Groups | p | d_Amplitude | p(d_Amplitude) | d_Acrophase | p(d_Acrophase) |
|---|---|---|---|---|---|
| | | | ***Bmal1*** | | |
| CD vs. CJL | 0.000 | -4.857 | 0.891 | 0.480 | 0.292 |
| CD vs. TJL | 0.000 | -6.938 | 0.842 | 0.327 | 0.456 |
| CJL vs. TJL | 0.000 | -2.081 | 0.930 | -0.152 | 0.685 |
| | | | **miR-27b-3p** | | |
| CD vs. CJL | 0.273 | 0.228 | 0.243 | 0.024 | 0.978 |
| CD vs. TJL | 0.004 | 0.599 | 0.013 | 0.299 | 0.778 |
| CJL vs. TJL | 0.004 | 0.371 | 0.219 | 0.274 | 0.508 |
| | | | ***Nampt*** | | |
| CD vs. CJL | 0.000 | 0.224 | 0.009 | -0.218 | 0.163 |

| | | | | | |
|---|---|---|---|---|---|
| CD vs. TJL | 0.000 | -0.006 | 0.947 | -0.204 | 0.207 |
| CJL vs. TJL | 0.000 | -0.230 | 0.002 | 0.013 | 0.895 |
| **miR-34a** | | | | | |
| CD vs. CJL | 0.152 | -0.083 | 0.792 | 0.268 | 0.697 |
| CD vs. TJL | 0.220 | -0.208 | 0.482 | 2.389 | 0.097 |
| CJL vs. TJL | 0.835 | -0.125 | 0.736 | 2.121 | 0.168 |

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