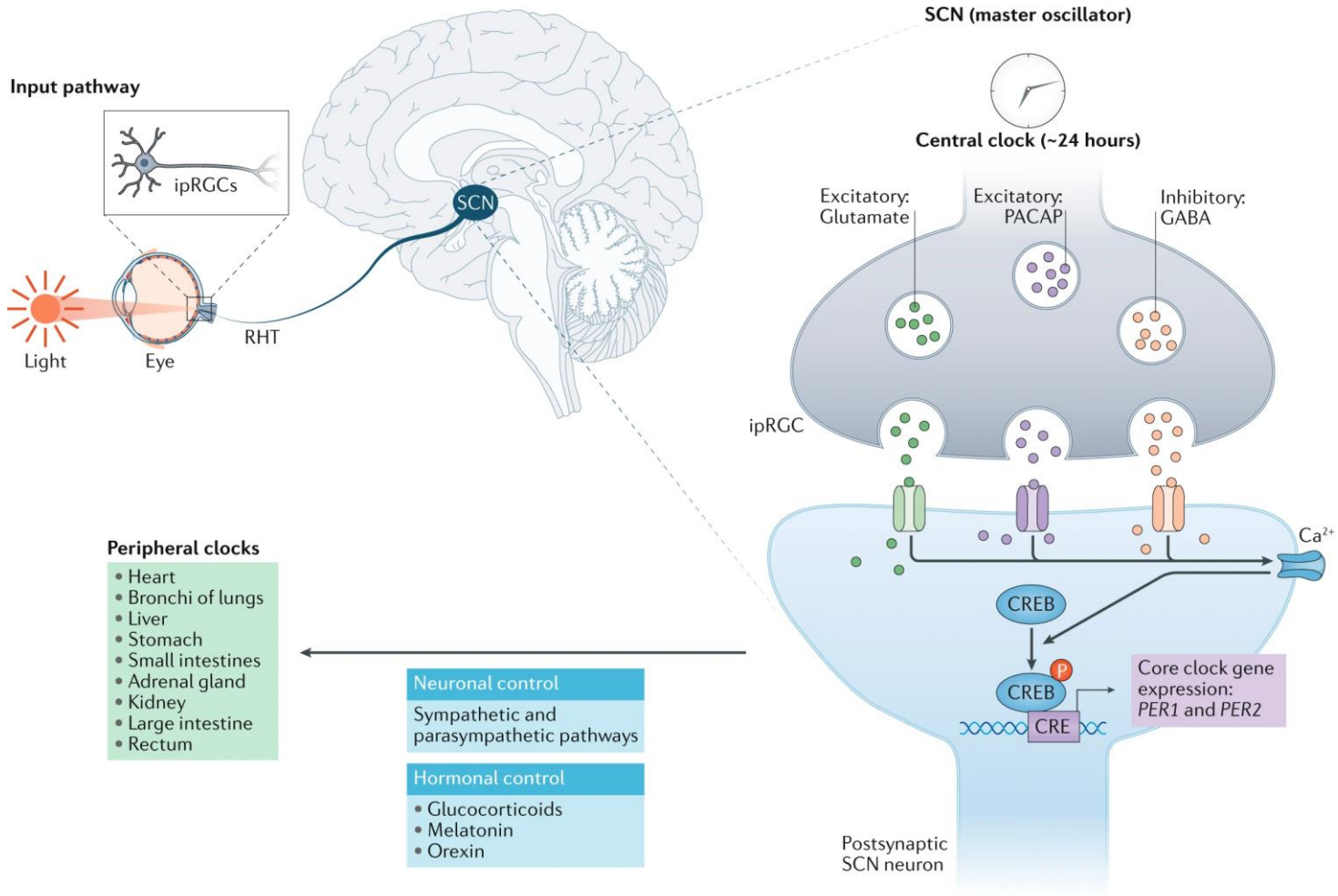
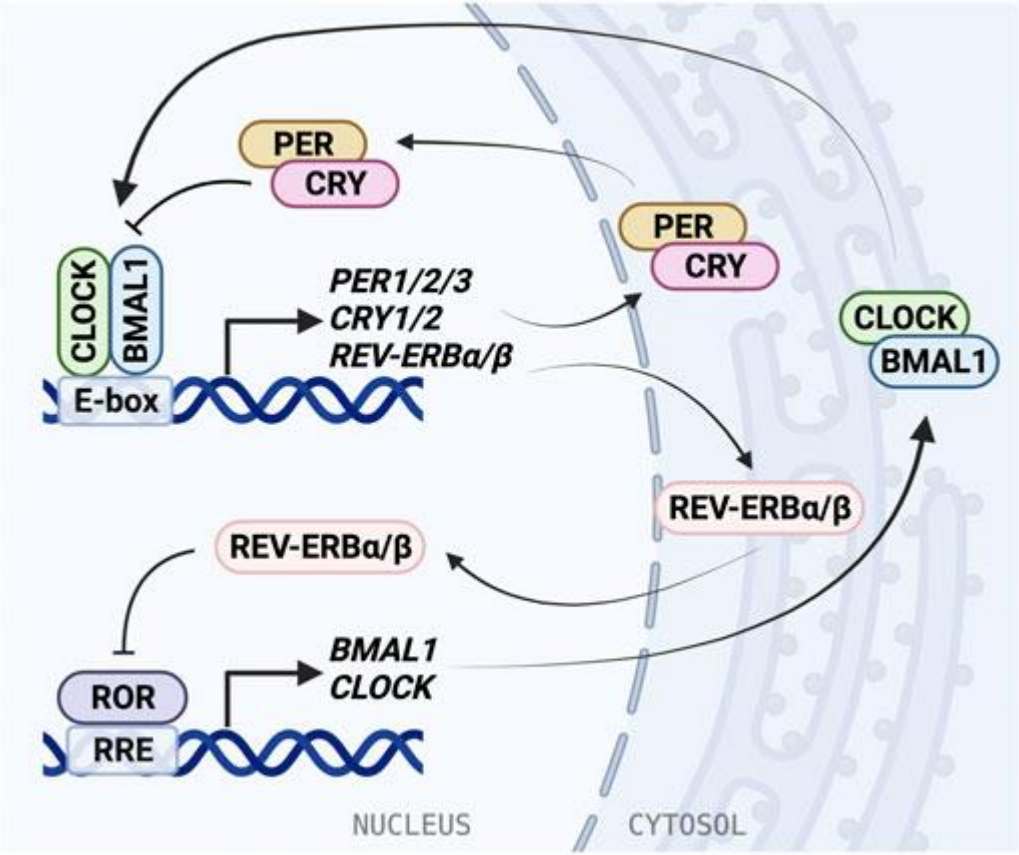
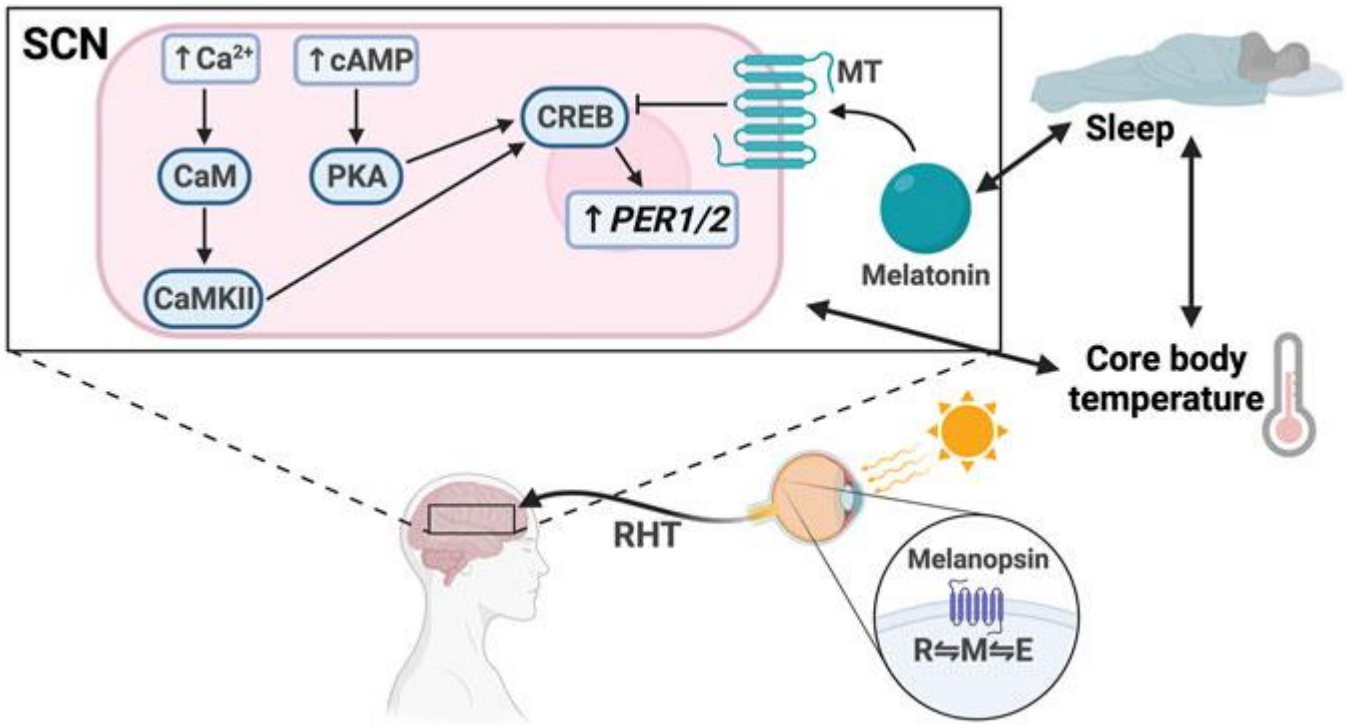


The central pacemaker is located in the suprachiasmatic nucleus (SCN) of the anterior hypothalamus. In the input pathway to the SCN, light is received by the intrinsically photosensitive retinal ganglion cells (ipRGCs) expressing melanopsin, which sends electric signals to the SCN through the retinohypothalamic tract (RHT). Neurotransmitters released by ipRGCs, such as excitatory glutamate and pituitary adenylate cyclase-activating polypeptide (PACAP), cause membrane depolarization in postsynaptic SCN neurons. Changes in Ca^{2+} and cAMP levels, in turn, induce phosphorylation of cAMP-response element (CRE)-binding protein (CREB) and expression of immediate early genes including the core clock genes, *PER1* and *PER2*, thereby resetting SCN cellular oscillators. Meanwhile, the inhibitory neurotransmitter γ-aminobutyric acid (GABA) decreases the sensitivity of non-image-forming behaviours at low light levels. The SCN neurons are tightly coupled and control peripheral clocks in other brain regions and throughout the body via neuronal and hormonal signals.



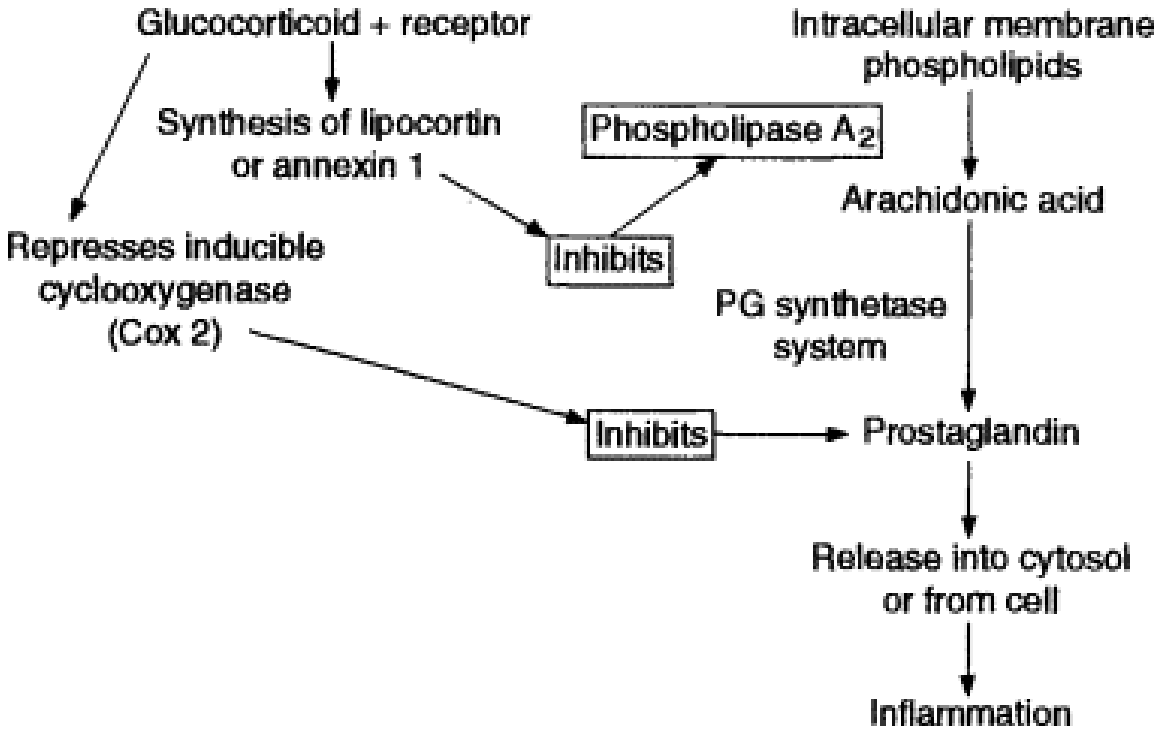
The molecular mechanism of the mammalian circadian clock. The molecular clock is based on a transcriptional/translational negative feedback mechanism and consists of the core loop and two interlocking loops. In the core loop, the BMAL1/CLOCK heterodimer binds to the E-box cis-elements and drives transcription of targeted genes, including PER1/2/3, CRY1/2, and NR1D1/2 (REV-ERBα/β). PER and CRY inhibit BMAL1/CLOCK activity and therefore repress their own expression. In the RRE loop, REV-ERB repressors and ROR activators bind to RRE to regulate BMAL1 and CLOCK expression.



Light entrainment of the SCN and sleep/wake regulation. Light strikes the retina and excites melanopsin, driving it to the M configuration. The signal travels along the retinohypothalamic tract (RHT), resulting in increased intracellular levels of Ca2+ and cAMP in the SCN. Ca2+ activates calmodulin (CaM) and CaMKII. cAMP activates PKA. CaMKII and PKA activate CREB, which drives PER1/2 transcription. Melatonin binds the melatonin receptor (MT), which inhibits CREB activation. There is bidirectional regulation between melatonin secretion and sleep, sleep and core body temperature, and core body temperature and SCN signaling.

Anti-inflammatory and immunosuppressive effect of glucocorticoids

- Lipocortin - inhibition of phospholipase A2 - inhibition of prostaglandin and leukotriene synthesis
- Decrease in the number of lymphocytes (T more than B) based on their redistribution to the spleen, lymph nodes and bone marrow
- Increase in neutrophil count
- Decrease in the number of eosinophils and basophils
- Inhibition of monocyte differentiation into macrophages
- Inhibition of immunoglobulin synthesis
- Inhibition of cytokine synthesis (IL-2)
- Inhibition of histamine and serotonin secretion from mast cells



Hormonal contraception

- Gestational contraceptives versus combination products (estrogenic component - ethinylestradiol, mestranol, estradiol valerate and gestagenic component - desogestrel, drospirenone, gestodene)
- Pearl index (PI)
- Monophasic preparations - fixed amount of gestagen/estrogen
- Biphasic preparations - constant amount of estrogen - increase gestagen dose in the second half of the cycle
- Triphasic - higher or equal dose of estrogen and progestin in the second third, lower dose of estrogen and higher dose of progestin in the third third
- Also combi-phasic, sequential (estrogen only in the first half!), dynamic
- **Mechanism of action**:
  - Suppression of FSH secretion - preventing the formation of a dominant follicle, inhibition of ovulation (gestagenic component)
  - Ensuring endometrial stability (E)
  - Decreased ability to nidate, increased viscosity of mucus in cervix, impaired sperm penetration, decreased fallopian tube motility
  - Postcoital contraception - high gestagen content
- Side effects of estrogens and contraceptives
- Increased risk of thromboembolic disease
- Mood changes
- Hypertriacylglycerolemia
- Hepatic disorders