**Modeling age-related alterations in the mouse liver circadian clock caused by an imbalance in the NAD + consumption system**

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A mathematical model of the interaction of the circadian oscillator in the mouse liver with the NAD+ consumption system, including the enzyme SIRT1, PARP1, CD38, whose activity changes with age, has been developed and tested on experimental data.

We included in our model the genes Arntl, Clock/Npas2, Per1/2, Cry1/2, Rora/g, Rev-Erbalpha/beta, Dbp, Nfil3, Nampt which are important for the functioning of the circadian oscillator in the mammalian liver (mouse). To verify the model, we used experimental data with various types of impacts, knowledge about the intervals of possible values of model parameters and the effect of knockout of various genes on the dynamics of the model and the oscillation period, the relationship between amplitudes, phases of model variables.

Modeling showed a pronounced circadian activity of CD38, PARP1 and SIRT1, as well as the fact that age-related changes in the activity of these enzymes lead to age-related disorders of NAD+ metabolism. Such disorders can be one of the causes of dysfunction of circadian oscillators in the liver and contribute to disruption of circadian rhythms in the body as a whole.

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