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The 13th International Multiconference

Bioinformatics of Genome Regulation and Structure/ Systems Biology

BGRS/SB-2022
NOVOSIBIRSK, RUSSIA
04–08 July, 2022

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BIOINFORMATICS OF GENOME REGULATION AND STRUCTURE/SYSTEMS BIOLOGY (BGRS/SB-2022)

The Thirteenth International Multiconference

Abstracts

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Evolution of protein regulators of circadian rhythm in mammals

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The Cry protein (cryptochrome) is an important target of anti-aging medicine mediating the effect of chronobiotics on lifespan, physical activity, and circadian rhythm. Chronobiotics are agents that can cause phase adjustment of the body clock. F-box and leucine-rich repeat protein 21 (Fbxl21), predominantly expressed in the hypothalamus, is associated with circadian rhythms by regulating the stability of the Cry protein, which binds to the CBD domain in Fbxl21. The same domain is present in Fbxl3 (an Fbxl21 paralog also involved in circadian rhythm regulation). The domain loss renders Fbxl21 and Fbxl3 nonfunctional. Both Cry and Fbxl3 are highly conserved in mammals. Thus, our findings of significant variation of the CBD domain in Fbxl21 certain species as well as of pseudogenization or loss of the Fbxl21 gene were unexpected. We used original programs to systemically screen such events for Fbxl21 and other protein factors of circadian rhythm regulation in mammals. Fbxl21 protein was missing in representatives of Metatheria and Prototheria as well as in certain placentals including human, gorilla, rabbit, hare, armadillo, etc. The Fbxl21 protein is shortened and lacks the domain in bison; stop codon is found within the domain in seal and elephant, and unique cysteine is replaced with tyrosine at position 364 in manatee. Interestingly, an experimental mutation at the same domain position in Fbxl3 modifies the period of biorhythms. Fbxl21 started to accumulate substantial modifications in the Homininae ancestor after the split of gibbons and great apes. Numerous independent Fbxl21 losses or pseudogenizations were demonstrated; for instance, the pseudogenization is observed only in the human and gorilla while other great apes have the functional gene. Among other things, the data obtained indicate the prevalence of positive selection on Fbxl21 in these taxa while its paralog Fbxl3 is under stabilizing selection in mammals.

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