

Naslov projekta: Defining the role of circadian genes in behavioral sensitization to psychostimulants in *Drosophila melanogaster*

Trajanje projekta: 36 mjeseci

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Voditelj projekta: Rozi Andretić Waldowski

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Sažetak projekta:

Addiction to drugs is a brain disease characterized by changes in the brain functioning caused by repeated drug taking. Repeated drug taking leads to neuroadaptations which over time affect neural networks and change behavior. One such change induced by drugs and commonly studied in lab animals is behavioral sensitization. Regulation of gene expression is one important mechanism by which drugs change the plasticity of the networks which regulate behavior. A group of transcriptional regulators of the molecular circadian clock have been identified to function as regulators of behavioral sensitization to cocaine in *Drosophila*. Subsequent studies in rodents proved the universality of those genes in mediating drug responses. The genetic pathways and molecular interactions through which circadian genes regulate drug responses has remained undefined. We hypothesize that new genes which interact with circadian genes in the regulation of behavioral sensitization to psychostimulants can be identified in a genetic screen in *Drosophila*. This is a goal for which *Drosophila* is perfectly suited, because genetic screens aimed at defining new genes can be performed relatively easy, fast and cheap. Our first aim is to devise a high-throughput method for measuring behavioral sensitization in flies by modifying the existing method for measuring activity. Second, we will undertake a directed behavioral screen by pre-selecting candidates with reported molecular interaction with circadian genes. In the third aim we will use transgenic flies and other genetic tools to investigate neural mechanisms involved in behavioral sensitization. The proposed research is innovative and relevant for human health. New gene candidates isolated in this screen could easily be translated into mammalian research where they will help in further understanding of neuroplastic changes induced by psychostimulants. Given our expertise and available resources the project has great potential to advance the field.