DESCRIPTION FOR THE GENERAL PUBLIC

Stress is defined as conditions that seriously perturb the psychological and physiological balance of an individual. However, the impact of stressful life events on physical and psychological well-being is highly variable, and does not affect everyone in the same manner – there are susceptible individuals who poorly adapt to stressors and express inappropriate responses that can become persistent states of stress, while resilient individuals can perceive adversity and develop adaptive psychological and physiological responses. The underlying mechanisms of these responses are not fully understood as yet, although they are known to depend on a combination of genetic and non-genetic factors that interact in complex ways. Finding molecular markers underlying the different stress coping strategies will help in the future to improve the quality of life of people, who cannot otherwise cope with serious demands of the modern society. We strongly believe that animal models used in the present project (see below) are the most suitable to achieve this goal, since they mimic well the responses characteristic for human society and the observed individual differences in sensitivity to adverse and chronically present stimuli. At the same time, it is an experimental animal model, so more factors can be measured, compared, validated and verified at different levels of complexity. Only such complex approach will help to delineate the right track, which then can be transferred to clinical practice.

The idea of microRNAs (miRNAs) as mediators of the brains genomic response to stress is quite new, although recently many studies have been devoted to this subject, and various miRNAs or miRNAs families have been shown to be regulated in the response to different kinds of stress. In the present project we plan to use animals differentially reacting to stress stimuli. We plan to use mice with knock-out of the gene encoding norepinephrine transporter (NET-KO), which are well characterized as displaying stress-resistant phenotype, as well as two strains of mice displaying two different stress-coping strategies, i.e. C57BL/6J and SWR/J. The procedure of restraint stress has been shown to induce uncontrollable aversive situation that produces both physical and psychological consequences leading to neuronal and behavioural alterations. The aim of the project is to identify the molecular markers differentiating these three strains of mice (control and subjected to restraint stress). We plan to search for such markers at the level of miRNA in blood as well as in the selected brain regions, and to characterize their target genes. At the final stage of the project we plan to administer the selected miRNA(s), using lentivirus vector, to one of the studied strains of mice in order to reverse their behavioural phenotype (e.g. to alter the passive coping strategy of C57Bl/6J mice into an active one, as displayed by SWR/J mice). Additional goal of our project is to contribute to the further understanding of the mechanisms underlying stress responses. Successful realization of the project will have profound economic and societal impact, since various forms of psychological and physical pressure is practically omnipresent in the modern world, and some people are not able to cope with it, what leads to various forms of stress-induced mental illnesses, affecting not only the life of the patients but also of their families, and – in consequences – has also an impact on the economical outcome.