## DESCRIPTION FOR THE GENERAL PUBLIC

Benzodiazepines are psychoactive drugs with hypnotic, anxiolytic, anticonvulsant, amnestic and muscle relaxant properties. They potentiate $GABA_A$-evoked chloride currents resulting in hyperpolarization. Although clinical aspects of BZDs' actions including the high potential for dependence development are well-known, these drugs are still commonly abused. The long-term benzodiazepine use affects about 2–7.5% of the population in developed countries. Benzodiazepines are often prescribed in stress-related psychopathologies and difficulties in discontinuation of their use seem to be major clinical problem contributing to worsening the symptoms and lowering the quality of life. The exploration of neurobiological foundation of these phenomena is highly needed for implementing new methods of prevention.

Clinical data indicate that benzodiazepine abusers differ in their personality traits that may influence stress response and coping strategies. Similarly to humans, rats differ in their behavioural patterns, "emotionality" and coping strategies that are associated with differences in reactivity of many brain systems, i.a. reward system and hypothalamic-pituitary-adrenal (HPA) axis. Therefore, using of animal models may help to gain deep insight into molecular basis for individual differences in stress response and their contribution to benzodiazepine addiction susceptibility.

The aim of this project is to search for molecular features that distinguish subjects more prone to develop benzodiazepine addiction-related behavioural patterns and negative affective consequences of their long-term administration in animal chronic stress model. We plan to evaluate the neurobiological background of individual differences in chronic stress response, and its impact on the reaction to benzodiazepine as well as behavioural and molecular outcome following its long-term administration and persistency of these changes after its withdrawal. The project is intended to elucidate the mechanisms underlying GABA-ergic dysfunction and its possible associations with changes in activity of opioid system, HPA axis and dopaminergic system, as neurobiological background of benzodiazepine addiction susceptibility.

As stress may be a trigger factor in many psychiatric disorders, the epigenetic changes representing the key mechanism in which environmental factors may influence gene expression will also be examined. Particularly, the role of microRNAs, small non-coding RNAs, which control the gene expression on post-transcriptional level, seems to be worth investigation in this area. Searching for specific microRNAs as potential diagnostic and prognostic markers of e.g. stress-related psychopathologies and psychoactive drug abuse is a promising research field with high potential of clinical appliance.