Effects of a novel nonaddictive opioid on response to stress

Opioid drugs, such as morphine, are widely used in pain pharmacotherapy, however may also affect an organism's response to stress. Acting via receptors located on the surface of neuronal cells, opioids induce therapeutic effects, but also a range of side effects, including addiction and even potentially lethal respiratory depression. Recent discoveries indicate that it is possible to minimalize opioid side effects using novel compounds with innovative profile of action. In the present study we will use one of such compounds – PZM21. It is a functionally selective (biased) agonist of μ opioid receptor, therefore after binding to the receptor it does not activate β-arrestin, which is a protein considered to be responsible for some opioid side effects. Current results suggest that, unlike morphine, PZM21 does not have rewarding properties. Thus its potential use may be safer, as is not associated with high addiction risk.

The role of opioid system in the regulation of stress effects was profoundly studied. Research indicate that μ opioid receptor agonists may attenuate the effects of stress, as studies in animal models have shown that treatment with μ opioid receptor agonists (such as morphine), results in diminished stress response. Moreover, it was demonstrated that administration of morphine prevent the development of posttraumatic stress disorders in subjects with trauma exposure. Importantly, stress also affects people addicted to opioids and is one of the reasons for relapse. Therefore, it is especially important to look for substances that can minimize the negative effects of opioid withdrawal and abstinence.

The aim to the present project is to evaluate the action of PZM21 in animal models of stress-related behaviors. Effects of PZM21 will be compared with those induced by morphine. The implementation of research tasks will allow to answer the question whether and how PZM21 regulates the effects of stress. In addition, the characterization of molecular changes (expression of selected groups of genes) caused by PZM21 will be perform to study for possible mechanisms underlying action if this compound.

The anticipated results may ultimately help in determining whether PZM21 should be tested as a potential drug for stress-related disorders. Taking into account data suggesting that it is a compound with weak addictive properties, such interventions would be beneficial in the clinic.