In addition to being widely investigated as a marker of neuronal activity, expression of c-Fos has also been shown to be closely linked to synaptic plasticity, learning and memory. We hypothesized that c-Fos driven synaptic plasticity in neurons in the central amygdala is essential for appetitive but not for aversive learning. To test this hypothesis we injected lentiviral vector (LV_PGKeGFP_sh_c-fos) which blocks c-Fos expression in neurons to the central amygdala of mice. The animals learned the appetitively and aversively motivated place preference and avoidance tasks in the automated IntelliCage system. Learning of the appetitively motivated place preference has been previously shown to increase c-Fos expression in the mouse central amygdala, whereas the aversively motivated place avoidance learning did not result in such increase (Knapska et al., *Learning & Memory* 2006). We showed that blocking c-Fos expression impairs appetitive but not aversive learning which is consistent with our hypothesis.

Understanding c-Fos-dependent molecular underpinnings of the synaptic plasticity may be achieved by following its transcription-regulatory function, i.e., by identifying the genes it controls. MMP-9 (matrix metalloproteinase-9), an extracellular endopeptidase which cleaves extracellular matrix proteins and plays an important role in synaptic plasticity, learning and memory, have been documented to be c-Fos/AP-1 regulated at the transcriptional level, also in the activated neurons. We hypothesized that following the extracellular release of MMP-9 supply, c-Fos upregulation is necessary for MMP-9 replenishment. To test this hypothesis we injected PLGA nanoparticles releasing TIMP-1 (tissue inhibitor of matrix metalloproteinases-1, a specific inhibitor of MMP-9) to the central amygdala of mice. Then, the animals learned the appetitively motivated behavioral task in the IntelliCage system, which had been previously shown to specifically increase c-Fos expression in the central amygdala. We showed that blocking MMP-9 results in significantly decreased expression of c-Fos protein. This result is consistent with the hypothesis of the role of c-Fos in MMP-9 replenishment.