Project 1.17. Deciphering activity of CA1 region during alcohol seeking and consumption

Supervisor: dr hab. Katarzyna Radwańska Laboratory: Molecular Basis of Behavior

WWW: https://radwanskalab.eu/

Background: Development of drug addiction involves functional alterations within brain areas controlling reward-driven behaviour and memory processes. In this context, remodelling of the glutamatergic synapses has gained a lot of attention (Hanse et al, 2013; Lüscher et al, 2011; Wolf, 2016). Still the molecular processes which contribute to the remodelling of the synapses and circuits in addicted individuals are poorly understood**. Our aim in this project is to test the hypothesis that regulation of activity of CA1 pyramidal neurons by Arc/Arg3.1 protein controls addiction-related behaviours.** Arc/Arg3.1 protein is rapidly upregulated by strong synaptic activity and critically contributes to weakening glutamatergic synapses by promoting AMPA receptor endocytosis (Plath et al, 2006; Tzingounis and Nicoll, 2006). The hypothesis is also based on our observations showing that Arc knockout mice (Arc KO) are impaired in alcohol seeking during relapse induced by alcohol-associated cues, while alcohol consumption and seeking in wild-type animals affects expression of Arc protein in the area CA1 of the hippocampus.

To verify the hypothesis we plan to realize the following tasks:

Task 1. To test the role of Arc/Arg3.1 in CA1 in regulation of addiction-related behaviours. To this end we will use novel methods of genetic manipulations *in vivo* (CRISR/Cas9 system).

Task 2. To test the role of Arc/Arg3.1 in regulation of alcohol-induced plasticity of CA1 neurons. To this end we will use electrophysiology ex vivo.

Task 3. To test the dynamics of CA1 neurons during alcohol consumption and seeking. To this end we will use *in vivo* imaging of CA1 neurons in mice drinking alcohol with mini-endoscopes.

Alcohol addiction-related behaviours will be characterised in mice leaving in automated cages, IntelliCages (Radwanska and Kaczmarek, 2012).

Aim: Our aim in this project is to test the hypothesis that regulation of activity of CA1 pyramidal neurons by Arc/Arg3.1 protein controls addiction-related behaviours.

Requirements: The students should have MSc in Biology (Molecular), Neurobiology, Biotechnology, Bioinformatics or Biophysics. Only highly motivated students with outstanding academic record and fluent English will be accepted. Strong background in mathematics/bioinformatics/image analysis will be an asset of the successful candidate. The project involves experiments with laboratory animals.