

Internship Proposal Academic Year 2019-2020

1. Host team :

Research Unit (e.g. Department or Institute) : Cognition Action Group
Research Unit Director: Dr Pierre Paul Vidal
Research Team Director: Dr Eric Krejci
Team name: Sensorial bases for behavior based on mice models

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2. Internship project title:

Acetylcholine function and dysfunction: Alterations of respiration by inhibition of cholinesterases

3. Internship Description:

Respiration is a vital function that is severely impacted when acetylcholine (ACh) is not properly hydrolyzed by cholinesterases. Inhibitors of cholinesterase are pesticides, drugs to treat Alzheimer or myasthenia diseases, drugs used for anesthesia or nerve agents. ACh is a well-known neurotransmitter at the neuromuscular junction (NMJ), in central and peripheral cholinergic synapses. At the NMJ, acetylcholinesterase (AChE) is clustered by Colq and in the cholinergic synapses of the central nervous system by PRiMA. Physostigmine a reversible ChE inhibitor triggers very long pause after inspiration, apnea, attributed to the inhibition of AChE in the respiratory centers in brain. Unexpectedly, Colq KO mice that have a normal level of AChE in brain do not pause the breathing when injected with physostigmine. In mice, the duration of the pauses after inspiration is related to the stimulation of sensory neurons by irritant molecules and can be reduced by eucalyptol, the duration of the pauses triggered by physostigmine is also reduced by eucalyptol. The aim of this internship is to decipher how ACh can trigger this reflex, the pauses after inspiration.

The pauses are recorded in double chamber plethysmography, in which we precisely measure the flux of air that pass through the nostril and the movement of the body over the time. You will use WT and mice with partial deficit in cholinesterase and drugs.

ACh acts on ACh receptors and preliminary results support that atropine, a muscarinic antagonist, can prevent the pauses. A first aim will be to know if the pauses result from the activation of muscarinic receptors and possibly which type of receptors. Methacholine is very specific agonist of muscarinic receptors used to provoke exacerbated response in asthmatic patients. When injected in mice, methacholine triggers apnea as physostigmine and thus allows deciphering how the reflex is generated.