# MECHARESIST

Project title: Identification of cellular and molecular resistance mechanisms to develop innovative strategies in pest insect control

Acronym: MECHARESIST

Project duration: 36 months – Start date: 2017/ 09/01 End date: 2020/ 08/31

Key-words: Pest insects - insecticide - resistance - nicotinic acetylcholine receptors

Coordinator: Pr Valérie RAYMOND, RCIM (SiFCIR), UPRES EA 2647 / USC INRA 1330 SFR 4207 QUASAV
valerie.raymond@univ-angers.fr

PhD student : BANTZ

Financial support from « Objectif Végétal »: 116 k€ (PhD grant INRA / Région Pays de la Loire, running costs 25 k€ Région Pays de la Loire)

**Summary:**

***Context:*** Agriculture is facing an important challenge: it must be ensured that enough high-quality food is available to meet the needs of a continuously growing population. Even if chemical pesticides such as insecticides have been used successfully in controlling a number of pest insects, their uses, however, during several decades have lead to resistance emergence resulting in a decrease in the insecticide effects. Consequently and in accordance with Ecophyto 2 program, current and future agronomic production of food requires innovative solutions for existing and future changes and challenges, like counteract the setting-up of resistance of pest insects. Thus, it becomes necessary to consider the key cellular and molecular elements involved in the environmental adaptation of the insect such as the insecticide target conformation and calcium-dependent intracellular signaling pathways. Indeed, recent studies have demonstrated that the subunit composition of nicotinic acetylcholine receptors (nAChRs) could influence their affinity to insecticide neonicotinoids and the major role of calcium and calcium-dependent pathways in the modulation of insecticide responses in insects.

***Goal:*** The aim of the project is to use for the first time the original insect model developed in the laboratory to explore how long it would take for an insect to adapt to chronic exposure to sublethal doses of neonicotinoid insecticide and how resistance factors are developed sequentially in this insect population during chronic exposure. Thus, this innovative project is not to study the mode of action of insecticides but to identify the cellular and molecular mechanisms developed by the insects for their environmental adaptation. We will focus our study on the characterization of cellular and molecular mechanisms, that include 1) the subunit composition of nAChRs, and 2) the intracellular signaling pathways involved in the modulation of the nAChR sensitivity to neonicotinoid and therefore involved in the modulation of the neonicotinoid efficacy. The insect model, the cockroach *Periplaneta americana,* which is a well-known suitable model to examine the influence of a chronic exposure to sublethal doses of insecticides will allow to better understand the resistance mechanisms involved 1) to develop innovative strategies in the circumvention of resistance to insecticides and 2) to improve the management of pest insect resistance. The knowledge obtained with these studies could be transposed to other insects such as the pea aphid to optimize pest control.

***Methodology:*** Experiments will be carried out on adult dorsal unpaired median (DUM) neurons isolated from the central nervous system of *P. americana* cockroaches exposed or not to a sublethal dose of the neonicotinoid, imidacloprid during 30 days. Electrophysiological studies, using the patch-clamp technique, combined to the single cell RT-PCR technique, will bring new correlated insights between electro-pharmacological profile of nAChRs and their subunit composition. Then, we will determine in heterologous system (Xenopus oocytes) if the composition of nAChR subunits modulates the amplitude of the current induced by imidacloprid and therefore the sensitivity of nAChRs to insecticides. Moreover, the identification of calcium- dependent intracellular signaling pathways including kinases or phosphatases involved in increase of the sensitivity of nAChRs to insecticide will be performed by single cell RT-PCR. Finally, using calcium imaging technique combined with the technique of RNA interference, we will be able to block the previous identified kinases or phosphatases and to determine their involvement in this modulation.