Systems Biology in a Toxic World: Two Case Studies with Cannabis and Hemp

Dr. Maxwell C. K. Leung

Project A: Adverse Outcome Pathways of Contaminant Exposure in Cannabis Use

Cannabis use is now legal for medical purposes in thirty-three states, including Arizona. There is growing concern that increased use of cannabis may result in increased exposure to contaminants on the cannabis, including pesticides, solvents, metals, and microbes. The focus of this project is to examine what may happen when teenagers, women of childbearing age, as well as patients with neurological disorders (e.g. Alzheimer's Disease, Parkinson's Disease, and epilepsy) are exposed to cannabis contaminated with neurotoxicants. We are using biomedical text mining, *C. elegans* toxicity testing, and mathematical modeling to develop quantitative adverse outcome pathways of cannabinoid/contaminant co-exposure. The outcome of this research will fill a key knowledge gap in public health regulations of legalized cannabis.

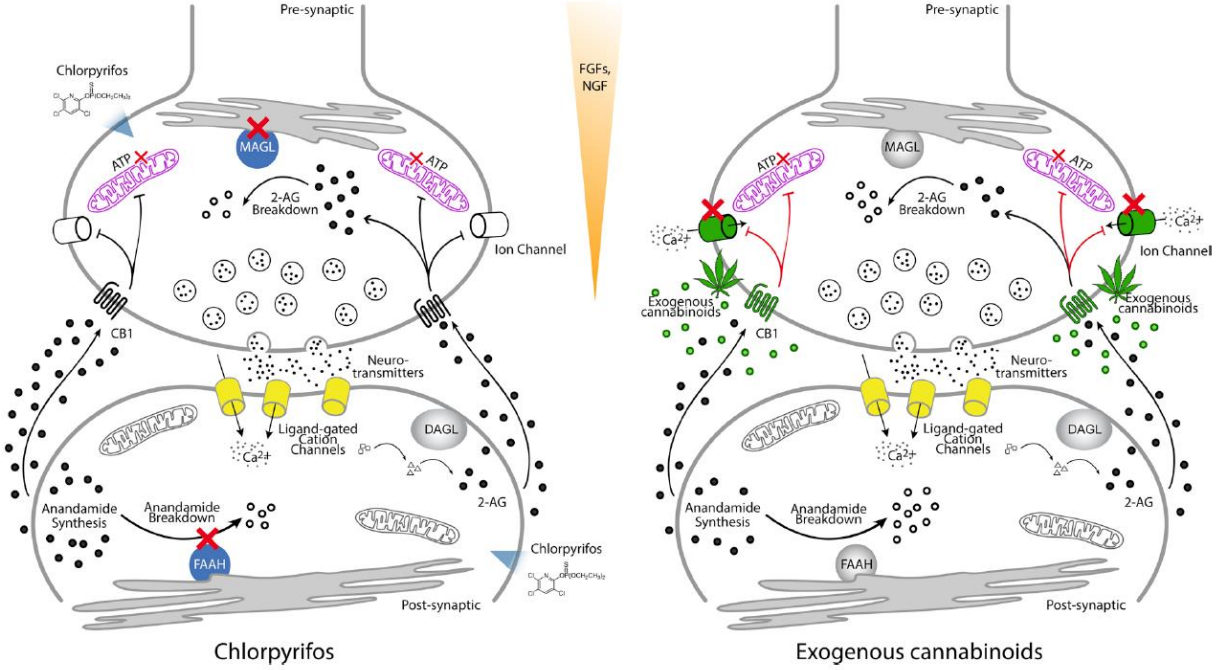

Figure 1. Disruption of post-synaptic retrograde signaling after exposure to the pesticide chlorpyrifos and cannabinoids. From Leung *et al*., Adverse outcome pathway of developmental neurotoxicity resulting from prenatal exposures to cannabis contaminated with organophosphate pesticide residues. *Reproductive Toxicology* 85 (2019) 12–18. *https://doi.org/10.1016/j.reprotox.2019.01.004*

Project B. Molecular Evolution of Plant-Parasitic Nematodes in Hemp Cultivation

Hemp is a variety of cannabis species that has a low concentration of tetrahydrocannabinol. It is grown for the industrial uses of fibers as well as a variety of derived products. Certain strains of hemp are resistant to plant-parasitic nematodes such as *Meloidogyne* spp. (i.e. root-knot nematodes) and *Pratylenchus* spp. (i.e. root-lesion nematodes). Yet, these nematodes have different virulence

characteristics and the mechanism of hemp's resistance is largely unknown. The goal of this project is to understand (a) the molecular evolution of plant-parasitic nematodes in overcoming hemp's resistance and (b) the environmental factors that influence the nematode infection of hemp in California and Arizona. This basic research will inform novel strategies of plant disease control, which is crucial to the growing hemp industry in the U.S.

Figure 2. Outdoor and indoor growing represents different challenges for plant-parasitic nematodes. Nematodes must compete with other free-living organisms outdoors. In comparison, modern greenhouses are a highly controlled environment. Sterilizing techniques are used to prevent nematode contamination.

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