Name: Taylor Elder
PI Name: Jill Turner

Email: taylor.elder@uky.edu
PI Email: jill.turner@uky.edu

Modulation of the Affective Withdrawal Phenotype in Nicotine Use Disorder: The Role of Intranasal Fingolimod

Elder T.[1], Adeluyi A.[2], Hessing M.[1], Keady J.[1], Pearson K.[3], Turner J.R.[1]

[1]University of Kentucky Department of Pharmaceutical Sciences, [2]Harvard Medical School, [3]University of Kentucky College of Medicine

Nicotine Use Disorder (NUD) is a major worldwide issue that has had multiple failed treatment plans in the past. NUD causes a high rate of relapse due to the adverse effects of withdrawal phenotypes. Withdrawal symptomology of the affective phenotype includes anxiety like behavior that has been exhibited in mouse models. Previous research within our lab has shown that the ventral hippocampus, of the central nervous system, is responsible for NUD withdrawal and has been the target of our ongoing treatment. The ventral hippocampus exhibits a negative feedback loop that contains excitatory glutamatergic pyramidal cells and inhibitory PV interneurons. A growing area in the field of NUD that is currently being studied includes glial cell dysfunction, which causes an increase in neuroinflammatory effects within the brain. Targeting glial cells directly, such as astrocytes and microglia, can dampen their activation and lead to balance within intended brain regions. A novel drug choice, Fingolimod, could be the answer to these problems. Fingolimod is sphingosine-1-phosphate functional antagonist that is currently on the market and being used for the treatment in Multiple Sclerosis. It has been shown to dampen microglia activation by antagonizing sphingosine-1-phosphate receptors located on astrocytes. Glutamate levels are depleted when undergoing NUD withdrawal, however the negative feedback mechanism of ventral hippocampus within the PV interneurons could lead to an increase in glutamate. Fingolimod's main objective to address ongoing issues within the ventral hippocampus could have significant efficacy in controlling neuroinflammation through an intranasal route of administration.