**Effects of Methamphetamine Pre-Exposure in C. Elegans Dopamine Levels**

Drug addiction is a serious and costly disorder that is poorly understood with few effective treatments. Methamphetamine is a known neurotoxin and is particularly harmful and destructive. Animal models have begun to provide important information about some aspects of the neurobiology of addiction, but the effects of methamphetamine on development has received almost no attention from the research community. Recent work indicates that the same basic types of behavior that define drug reward in mammals are also evident in invertebrates. Caenorhabditis elegans (C. elegans) is an excellent model to study the neurobiological basis of human behavior with: a surprisingly conserved, fully sequenced genome that can be easily manipulated; a completely mapped neuroanatomical system; and a short generation time with low maintenance costs for fast generation of data at a fraction of the cost of many other organisms. The purpose of this study is to determine if methamphetamines are a neurotoxin to DA in C. elegans and compare the neurotoxicity levels among the 4 strains.

The dat-1(ok157 or RM2702), cat-1(e1111 or CB1111) and cat-2(e1112 or CB1112) mutant strains along with the N2 wild-type (WT) worms were utilized in the present experiments. Worms were grown with E. coli (strain NA22) as a food source. A bleach and sodium hydroxide solution was used to lyse gravid adults and release the eggs into solution to age synchronize worm populations. The eggs were allowed to hatch overnight and plated 18 hr later as L1-stage larvae. Worms were washed off plates and extracted approximately 72 hr postplating the L1 worms. Adult worms were used for conditioning and testing to control for any effects of different sensitivities and responses to drugs at varying developmental stages. Sample tubes were weighed before and after placing worms into 1.5 ml Eppendorf tubes to determine worm tissue wet weight. Samples were kept on ice during all extraction procedures below to minimize DA degradation. DA concentrations were quantified by relating peak areas to those of calibrating DA standard solutions.

For the control group, the dopamine levels for the NS strain was 10 fmoles/mg tissue-wet weight. For the RM, CB1 and CB2 strains the dopamine levels were 5.5, 2.4, and 2.8 fmoles/mg tissue-wet weight, respectively.

Together these data indicate that C. elegans can serve as an excellent behavioral model system to study the neurotoxic and behavioral consequences of exposure to drugs of abuse with tremendous potential to uncover the underlying molecular events that lead to such outcomes. With the prospect of identifying new molecular targets, and the future application of this model to screen compounds for medications development, this project has a tremendous potential impact for the treatment of human drug addiction.