# Intergenerational Substance Abuse Transmission - A Novel Testing Model: Impact of Parental Exposure to Nicotine or Alcohol on Conditioned Place Preference of Regenerated Offspring in Brown Planaria

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There is an unprecedented global mental health and substance abuse crisis including prescription drugs, affecting adults and youth. A recent FDA guidance requires abuse liability testing in animals and humans for neuro-active medicines. Although parental substance abuse could be a risk for children, health authorities do not require testing medicines for their potential to increase abuse liability in offspring. This unique research evaluated brown planaria as a novel model to test the intergenerational transfer of substance abuse potential. There are similarities between mammalian embryonic development and planarian regeneration, especially in development of nervous system. Planaria prefer dark but will go to light when conditioned to associate light with a reward. Adult planaria were conditioned to light in the presence of nicotine or ethanol, an hour daily for 10 days. After amputating the head of conditioned adult planaria, the tail was allowed to regenerate, with or without continued conditioning. Conditioned place preference (CPP) of parent and regenerated offspring planaria was evaluated by light preference and time spent in light. Parent planaria exposed to nicotine or ethanol showed CPP in a concentration and time-dependent manner. Exposure of regenerating planarian offspring to these substances during regeneration resulted in CPP at lower concentrations than parents, showing that offspring are more sensitive to conditioning by these substances. Interestingly, parental exposure to nicotine or alcohol led to CPP in regenerated offspring without direct exposure to the substances during regeneration. Overall, the results show that regenerating planaria is a promising alternative intergenerational abuse liability testing model and reduces time, cost, and mammal use.

**Awards Won:**