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Genetic basis of Nicotine seeking behaviors in *C. elegans*

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The identification of genetic mechanisms underlying behavioral traits is an important strategy to understand the fundamental biological mechanism underpinning nicotine addiction, pivotal role in smoking behavior. To overcome this limitation in population genetics in humans, it is reasonably obligated to develop fast genetic workflow for the validation of functional alleles.
For rapid functional characterization and effectively accomplish, we exploit *C. elegans*, established genetic model, and propose approach of cross-species validation of vulnerable target genes and functional alleles associated with nicotine dependence.
We developed the approach to determine nicotine seeking by nicotine-paired cue preference, corresponding to Conditioned-Place Preference (CPP) paradigm, a form of associative learning used to study the rewarding and aversive effects of drug. We demonstrated that *C. elegans* develops nicotine-paired cue preference after prolonged time of association in time dependent manner. The single-session of prolonged conditioning of Hexane (CS), an alkane volatile odorant, and nicotine (US) leads to the development of nicotine-paired cue preference, although Hexane is a neutral olfactory stimuli to naive *C. elegans*. The conditioning of nicotine-paired cue preference was validated by pretreatment of US only or CS only. Additionally, we represent conditioned-cue seeking over the aversive chemical barrier as a proxy measurement of compulsive nicotine-seeking. The simplest and the most completely defined connectome with the rapid genetic workflow of *C. elegans* give us feasible tool for high throughput (HTP) cross-species validation of functional alleles including candidates, which are not enough for significance but valuable, and characterization of highly complex neuromodulation to progress nicotine seeking behavior.