Submitter Name: Kyung-An Han
Submitted email: khan@utep.edu

Unbiased genetic screen identifies the novel molecules critical for inhibitory control

Paul Sabandal[1], Erick Saldes[1], Abraham Arzola[1], Nathaniel Andersen[1] and Kyung-An Han[1]

[1]Department of Biological Sciences, University of Texas at El Paso

Inhibitory control is a core cognitive function and its dysfunction causes impulsivity that underlies addiction. Inhibitory capacity is not uniform in all individuals nor constant all the times but is affected by genetic and environmental interplay. We found that social context interacts with dopamine activity to impact inhibitory control in *Drosophila*. In the go/no-go test that measures action restraint, wild-type flies sustain movement suppression whereas the flies with enhanced dopamine neurotransmission loose inhibition and exhibit impulsive movements in the presence of peers. This dysfunctional inhibitory control requires D1 dopamine receptor and cAMP signaling in the mushroom bodies. Consistently, mushroom body activation is sufficient to provoke impulsivity without dopamine input nor social context. We conducted an unbiased genetic screen using X chromosome deficiency lines to uncover novel molecules important for social context-sensitive impulsivity and found 33 positive deficiency lines. The study is in progress to identify the candidate genes in the positive deficiency lines. The genes that we have uncovered to date include the homologs of the GWAS genetic loci linked to human brain diseases. The progress on *Scully* (mitochondria HSD17B10), *Frequenin 1* (neuronal calcium sensor 1 homolog), *kekkon5* (cell adhesion molecule; Lrfn homolog), *easily shocked* (ethanolamine/choline kinase), *highwire* (E3 ligase) and *Roc1a* (E3 ligase) will be presented. Overall, genetic association studies of inhibitory control often reveal inconsistent findings. Our study underscores the impact of social context in task performance that is largely overlooked and provides a unique opportunity for mechanistic study of social and genetic influence on inhibitory control.