The genetic and epigenetic architecture of behaviors related to drug seeking and abuse: The honey bee as a new animal model

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Honeybees have several advantages for studying the genetic and epigenetic architecture of behavioral traits, e.g. simple and complex types of learning and novelty seeking. Honey bees have a small genome with an extremely high recombination rate. This makes it straightforward to do forward genetics using QTL techniques in connection with selective breeding (including artificial insemination of queens). The honeybee genome has been well annotated and over the last couple of years reliable tools for genome manipulations have become available (dsRNAi, genetic transformation, CRISPR-CAS). Additionally, honey bees have human-like DNA methylation for developmental and and behavioral specializations. We have a large-scale breeding operation that can develop and maintain genetic lines of honey bees, so that we can take advantage of the honey bee for forward- and reverse-genetic screens.

Perhaps one of the biggest advantages is that in honey bees the male (drone) arises from an *unfertilized* egg alyed by the queen, which means that adult drones are haploid (i.e. they are the queen's gametes). We have shown that workers, queens and drones can be behaviorally conditioned in a well-controlled conditioning paradigm for traits such as reversal learning and latent inhibition. Those traits may also be correlated to novelty seeking behavior in the field as honey bees search for food. We take advantage of the haplodiploidy, and that individual worker queen and drone honey bees show genetic variation for learning and possibly novelty seeking within a colony. We have identified significant genetic variation for latent inhibition and reversal learning. We have mapped several loci in the genome that a linked to learning traits using RAPD- and SNP-based quantitative trait locus mapping[1]. At one locus we have identified a gene that affects expression of latent inhibition, and we have shown the *functional* link with pharmacological treatment and functional genomics (using ds- and si-RNA) to disrupt a biogenic amine receptor coded at that locus.

We propose to study the genetic and epigenetic architecture of novelty seeking (scouts versus recruits), reversal learning and latent inhibition. We will build this into a program designed to identify novel genes that regulate expression of these behavioral traits. We are also in a position to translate our discoveries into a rat model in the near future.

[1] Chandra SBC, Hunt G, Smith BH. (2001) Quantitative trait loci associated with reversal learning and latent inhibition in honeybees (*Apis mellifera*) *Behavior Genetics*. 31: 275-285. PMID: 11699600