The Sweet Smell of Success: Shilpa Swarup Completes Her Ph. D.

by Lauren M. Dembeck

On April 25, 2012, Shilpa Swarup successfully defended her doctoral thesis on the genetic architecture of natural variation in olfactory behavior in *Drosophila melanogaster*. Co-advised by Drs. Robert Anholt and Trudy Mackay, Shilpa examined the roles of odorant binding proteins (OBPs) in olfactory behavior and identified networks of polymorphic genes that contribute to natural variation in olfactory behavior. She also studied epistatic effects of pleiotropic genes affecting both olfactory behavior and sleep.

Shilpa's first project utilized RNAi lines from the Vienna *Drosophila* RNAi Center to systematically test the contributions of 17 OBPs in mediating olfactory behavior when exposed to a panel of 16 ecologically relevant odorants. This work took advantage of the ability of RNAi to knock-down expression of specific *Obp* transcripts. She then quantified the effectiveness of RNAi-mediated suppression by quantitative RT-PCR and used mass spectrometry to demonstrate target specific suppression of two OBPs expressed at high concentrations in the antennae. Flies in which expression of a specific OBP is suppressed often show a sex-dependent alteration in behavioral responses to more than one, but not all odorants. Similarly, responses to a specific odorant are frequently affected by suppression of expression of multiple, but not all OBPs. These results show that OBPs are essential for mediating olfactory behavioral responses, and suggest that OBP-dependent odorant recognition is combinatorial. By comparing her results with previously published electrophysiological studies, Shilpa showed that there is no simple relationship between OBPs and odorant receptors in their responses to odorants, but that the combinatorial patterns of odorants interacting with OBPs and odorant receptors are complex, yet appear based on an underlying logic.

Shilpa used two complementary approaches, genome-wide association analysis and extreme-QTL mapping, to identify alleles that affect natural variation in olfactory behavior using the *Drosophila melanogaster* Genetic Reference Panel (DGRP), a population of inbred wild-derived lines with fully sequenced genomes. Her results show that there is substantial phenotypic variation and sexual dimorphism in the DGRP for behavioral responses to the odorant benzaldehyde. Polymorphisms in or near chemosensory, developmental and signal transduction genes were found to be associated with natural variation in olfactory behavior. A subset of these genes forms a network that includes members of the inositol triphosphate and cyclic nucleotide signaling pathways. Results from both her genome-wide association analysis and extreme-QTL mapping studies indicate that variation in olfactory behavior depends not only on peripheral chemoreception, but also on information processing and decision making in the central nervous system. Further, polymorphisms in different chemosensory genes contribute to sexually dimorphic responses to benzaldehyde in nature.

Epistasis is an important feature of the genetic architecture of quantitative traits. In collaboration with Dr. Susan Harbison, Shilpa studied the effects of epistatic modifiers. They used DGRP chromosome substitution lines to study the effect pleiotropic genes have on P-element insertions that affect olfactory behavior, startle behavior and sleep phenotypes. The results show substantial suppressing epistasis and significant variation in the magnitude of this epistasis among the chromosome substitution lines. They conclude that epistasis may buffer the effects of new mutations, but that there are different epistatic modifiers that can suppress the effect of mutations in the same pleiotropic genes.

Shilpa has moved to St. Louis, Missouri, where she is hoping to pursue a position in the Emerging Leaders in Science Program with Monsanto. Dr. Shilpa will be greatly missed in the Anholt and Mackay laboratories. Congratulations Dr. Swarup!