Amine neurotransmitter signaling in *C. elegans*

**Summary**

cAMP response element binding protein (CREB) is a signal-activated transcription factor, which induces gene expression downstream of CRE upon its activation to control a broad range of biological processes. In *C. elegans*, the CREB activation can be visualized using a transgenic strain carrying a transcriptional reporter in which CRE is fused to a GFP reporter (*cre::gfp*). Using the *cre::gfp* reporter strain, we found that starvation induces CREB activation in the SIA neurons. The octopamine-deficient mutant *tbh-1* did not show CREB activation upon starvation and the exogenous application of octopamine resulted in CREB activation in well-fed animals, indicating that octopamine is responsible for the starvation-mediated CREB activation. We also found that the octopamine receptor, Gq, and CREB work in the SIA neurons to activate the CRE-mediated gene expression while Go and CaMKII suppress it.

Dopamine in *C. elegans* is shown to be involved in food (bacteria) sensing. Mechanosensory dopaminergic neurons sense bacteria and activate dopamine signaling in the presence of food. We tested whether dopamine signaling interacts with the octopamine signaling. Exogenous application of dopamine suppressed the exogenous octopamine-mediated CREB activation. Moreover, dopamine-deficient mutant *cat-2* showed spontaneous CREB activation in SIA neurons in the presence of food while *cat-2;tbh-1* double mutants did not. We also found that Gi/o-coupled dopamine receptors were involved in the dopamine signaling. The results suggest that the dopamine signal is suppressing the octopamine signal in the presence of food and the octopamine signal is activated when the dopamine signal ceases in the absence of food. We also demonstrate that the dopamine-octopamine signaling regulates the acetylcholine release likely through the regulation of CREB in the SIA neurons.

This study provides new insight in the *in vivo* molecular mechanisms of the amine neurotransmitter-mediated signaling and describes the interaction between the neurotransmitter signalings that allows animals to respond to environmental stimuli.