Antagonistic cGMP Signaling Pathways Regulate a Heritable Developmental Response to Pathogens

Nick Burton and Bob Horvitz
HHMI, Dept. Biology, MIT, Cambridge, MA 02139 USA

Recently a number of studies have linked environmental stress to changes in the physiology of an individual's progeny. To test whether maternal bacterial infection affects progeny physiology, we fed *C. elegans* either *Pseudomonas aeruginosa* (PA14) or *Serretia marcesens* (DB10). We found that wild-type parental (P0) worms slow their rate of development when fed either PA14 or DB10 in comparison to OP50. In the following generation, when again exposed to pathogen, the progeny (F1) exhibit a dramatically enhanced slowing of development compared to that of naïve worms. However, when the progeny of infected worms are fed OP50, they exhibit no difference in developmental rate compared to naïve worms, indicating that both the P0 and F1 require exposure to pathogen to result in enhanced slowing.

We showed that developmental slowing requires the guanylyl cyclase GCY-36 and the cGMP-dependent kinase EGL-4 as well as the insulin-like peptide INS-7. In contrast to worms unable to slow their development, worms lacking either the guanylyl cyclase GCY-33 or the serotonin biosynthetic enzyme TPH-1 exhibit an enhanced slowing of development. In the case of *gcy-33*, this enhancement can be suppressed by mutations in *gcy-36* and *egl-4*. Taken together, we interpret that *gcy-33* and *gcy-36* likely act in antagonistic signaling pathways.

Zimmer et, al. 2009, showed that *gcy-33* acts together with *gcy-31* to mediate responses to low oxygen and that *gcy-36* acts together with *gcy-35* to mediate responses to high oxygen. They also showed that *gcy-33, gcy-35* and *gcy-36* promoters drive expression in AQR, PQR and URX neurons. The *gcy-31* promoter, however, does not. Interestingly, we observed that mutations in *gcy-31* do not affect development in response to PA14. Furthermore, we found that genetic ablation of AQR, PQR and URX results in a similar phenotype to that of *gcy-33* mutants. These results suggest that the defect in developmental rate of *gcy-33* mutants is separable from the defect in the response to low oxygen and that the rate of development is controlled in part by the AQR, PQR and URX neurons. In summary, we have found that parental bacterial infection influences the development of progeny and that antagonistic cGMP signaling pathways regulate this response at least in part through the AQR, PQR, and URX neurons.