C. elegans sensory neurons regulate a transgenerational developmental response to osmotic stress via insulin and MAP kinase signaling

Nick Burton¹, Swathi Arur², and H. Robert Horvitz¹

¹ Howard Hughes Medical Institute, Department of Biology, Massachusetts Institute of Technology, Cambridge, MA, USA
² UT MD Anderson Cancer Center, Department of Genetics, Houston, TX, USA

In the late 19th century August Weismann proposed that information about the environment could not pass from somatic cells to germ cells, a model now known as the Weismann barrier. Recently, several studies have observed that parental environment can alter progeny phenotype. However, it remains unclear how parental environment affects progeny phenotype or if these observations represent somatic signaling to the germline. Here we describe a novel C. elegans developmental arrest in response to osmotic stress. This developmental arrest can be bypassed if parental animals are exposed to low levels of osmotic stress and is regulated by the release of the insulin-like peptide INS-3 from sensory neurons. We found that the INS-3 receptor DAF-2 functions in the germline to regulate progeny development in response to osmotic stress. In addition, the MAP kinase MPK-1/Erk is required for animals to arrest their development in response to osmotic stress, and parental MPK-1/Erk activity regulates progeny development in response to osmotic stress. MPK-1/Erk is activated in the germline in response to osmotic stress, and this activation depends on both sensory neurons and DAF-2 activity in the germline. Finally, animals lacking several targets of MPK-1/Erk exhibit abnormal development in response to osmotic stress, including the deubiquitinase Target-Of-Erk 3 (TOE-3), which is known to regulate development and H2A ubiquitination in Xenopus. Based on these observations, we propose that sensory neurons regulate MPK-1/Erk activity in the germline via insulin signaling and that altered MPK-1/Erk activity in the germline can enhance progeny survival in response to osmotic stress. This model would represent the first case in which a parental neuronal signal crosses the Weismann barrier to heritably regulate progeny development and progeny response to stress.