BRAIN-TO-GONAD-TO-EMBRYO ADRENERGIC SIGNALING MODULATES INTERGENERATIONAL TRACE LEARNING IN *C.ELEGANS*.

Eugene L.Q. Lee, H. Robert Horvitz
HHMI, MIT, Dept. Biology, Cambridge, MA

The ability to process temporal patterns of stimuli is crucial to organismal behavior and survival. How cellular and molecular components coordinately interact across different tissues to produce temporal context-appropriate behaviors across multiple timescales is a fundamental unsolved problem. We have shown that the nematode *Caenorhabditis elegans* is responsive to the patterning of timed events. Worms learn to associate a neutral odor stimulus with a noxious aversive light stimulus specifically when these stimuli are paired in an ordered temporal pattern. Notably, *C. elegans* is capable of trace-conditioning – a form of learning in which there is a delay between the presentation of a neutral (odor) stimulus and the presentation of a noxious (light) stimulus. Thus, worms have the ability to detect and distinguish timing durations. Remarkably, these sensitivities to temporal durations can be modulated intergenerationally: worms display enhanced trace-conditioning abilities if their parents were primed with the training stimuli in a specified temporal pattern. We identified adrenergic neuromodulators as key molecules in the regulation of temporal processing. The adrenergic axis not only modulates the behavioral aspects of trace-conditioning abilities (in parental worms) but also controls the transmission of such altered temporal sensitivities to the progeny of trained parents. Apart from two pairs of adrenergic neurons, the only other source of adrenergic signals in the worm is the somatic gonad. Forming part of the somatic gonad are the gonadal sheath cells that surround oocytes and support oocyte maturation. Inhibiting adrenergic signaling from the adrenergic neurons but not from the gonadal sheath cells abolishes trace conditioning. By contrast, inhibiting adrenergic signaling from either the adrenergic neurons or the gonadal sheath cells abolishes inheritance of temporal sensitivities. We found that a brain-to-gonad-to-embryo communication relay flexibly coordinates intergenerational modulation of trace-conditioning. In short, our results demonstrate that adrenergic signaling functions as a central inter-organ communication system for tuning temporal processing within and across generations.