Analysis of neuropeptide secretion

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The long term goal of this project is to identify factors that regulate secretion of neuropeptides generally, and to determine how these peptides regulate behavior. The motivation for this project is two-fold. First, insulin secretion, and its misregulation, plays a pivotal role in aging, diabetes, and obesity. Second, while a great deal has been learned about mechanisms regulating secretion of classical neurotransmitters, far less is known about those regulating secretion of neuropeptides and hormones. Classical neurotransmitters are packaged in synaptic vesicles (SVs), which are clustered at active zones. Neuropeptides are packaged into large dense core vesicles (DCVs), and are distributed throughout axons and dendrites. Secretion of SVs occurs at active zones, in a rapid, phasic manner. Secretion of DCVs occurs typically after trains of depolarization, fusion events occur far from active zones, and they occur relatively slowly following depolarization. Following exocytosis, the SV pool is rapidly reconstituted at nerve terminals by endocytic recycling of SV components, and refilling with neurotransmitters. By contrast, the releasable pool of DCVs must be reconstituted by anterograde transport of immature secretory granules from the soma. Relatively little is known about the biochemical basis for these differences.

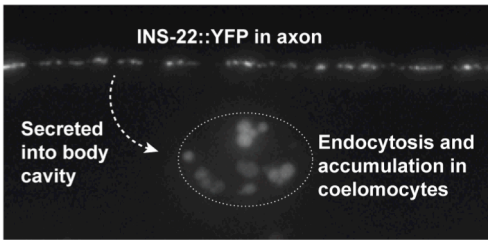

Fig. 1. An optical assay for neuropeptide secretion. YFP-tagged INS-22 expressed in motor neurons are secreted into the body cavity of worms. Secreted YFP is subsequently taken up by scavenger cells (coelomocytes). Coelomocyte fluorescence can be utilized to assess changes in peptide secretion. See Seiburth et al. (2007) and Ch'ng et al. (2008) for details.