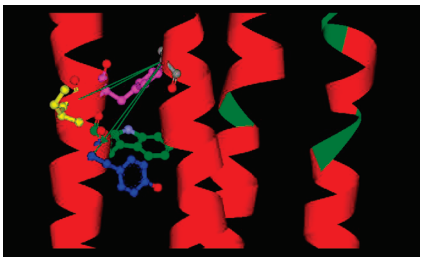
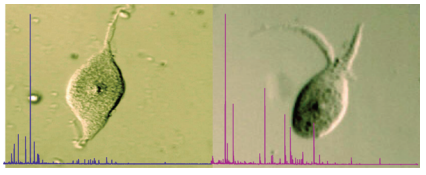
Binding in Glycine Receptor Transmembranes

Glycine receptors are ligand-gated chloride channels mediating inhibitory neurotransmission in the brain and spinal cord. These receptors are molecular targets of alcohols and volatile anesthetics. It is thought that these compounds augment receptor function by binding an intrasubunit hydrophilic cavity within the transmembrane (TM) domain, which is composed of four α-helical segments. Previously, it has been shown that that segments 1−3 of the TM domain likely participate; however, little was known about the orientation of amino acid residues in TM domain segment 4. Now, McCracken et al. (DOI: 10.1021/cn100019g) use site-directed mutagenesis and chemical cross-linking to provide evidence that amino residues of TM segment 4 face into the intrasubunit binding cavity.



Mapping neuropeptides in a Nematode

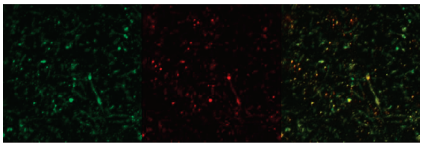
Single neuron mass spectrometry is a useful tool for determining the structure and cellular localization of neuropeptides, and the resulting single-cell mass spectra are often easier to interpret than mass spectra from ganglia containing multiple neurons. Jarecki et al. (DOI: 10.1021/cn1000217) have utilized this technique for interrogating single neurons from the nematode *Ascaris suum*. The authors analyzed the simplest ganglion from this animal, which contains only two neurons, and found that this approach was useful in discovering new peptides. In the process, the authors reported the structures of six novel peptides. An extension of this method may be useful in mapping neuropeptides from the entire nematode nervous system.



Insulin Signaling and Dopamine Neurotransmission

Dopaminergic regions of the brain regulate physiological functions such as motivation, movement, food intake, and pleasure. An important regulator of dopamine homeostasis is the dopamine transporter, which terminates synaptic transmission by clearing synaptic dopamine. Recent studies hint at the involvement of insulin signaling in the regulation of dopamine transporter function through the activity of the downstream effector protein kinase B (Akt). Speed et al. (DOI: 10.1021/cn100031t) examined how Akt signaling modulates dopamine transporter function by examining the isoform specificity.

With the help of isoform-specific inhibitors, the authors determined that basal activity of one of the isoforms of Akt, Akt2, is responsible for maintaining dopamine transporter cell surface expression in cell culture and in striatal tissue. Studying isoform-specific modulation of dopamine transporter function might help in learning more about how abnormal insulin signaling contributes to neurological disease.



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