Graduate Studies

Department of Physiology
MICHIGAN STATE UNIVERSITY

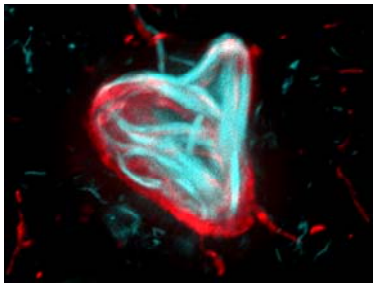
Glycobiology of Neural Development and Disease

Birgit Zipser, Ph.D.

While it is well-known that the surface glycans of neurons and glia correlate with different developmental and pathological states of the nervous system, the actual function of these glycans has only been extensively characterized for acidic forms, polysialic acid and glycosaminoglycans. We have focused on the function of neutral surface glycans that have received comparatively little attention.

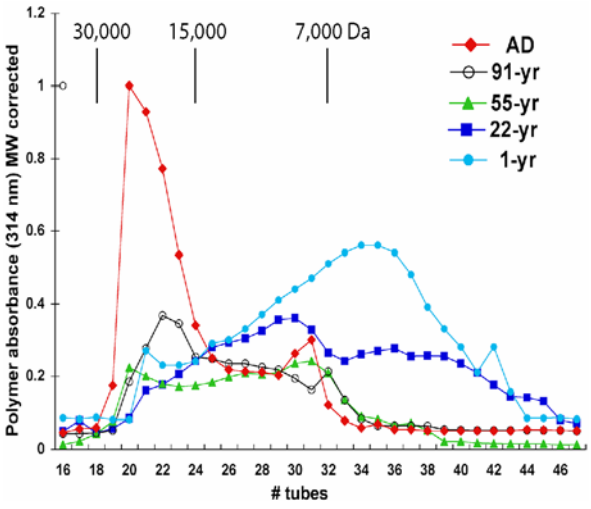
Previously, we investigated the early developmental function of neuronal surface glycosylations using an embryonic model system that is amenable to in vivo studies. In leech, as in mammals, sensory afferent neurons synapse their central processes in well-delineated laminae in the central nervous system, with each lamina corresponding to a particular sensory modality. The function of these neuronal glycans is as follows: A constitutive mannosidic glycosylation shared by all sensory afferents mediates early synaptic growth by facilitating axonal sprouting. Later appearing, different galactosidic glycosylations then divide the same neurons into subsets according to their different sensory modalities. These modality-specific glycosylations now oppose axonal sprouting and promote synapse formation thereby creating a laminated target region. Thus, the laminar distribution of sensory afferent synapses in the central nervous system is mediated by their different, sequentially expressed glycosylations with opposing functions.

Having learned about the critical role of neutral glycans during embryogenesis, we were curious about their possible functions during neurodegeneration. Two neuropathological hallmarks of the Alzheimer's disease brains are amyloid plaques and neurofibrillary tangles. We found that both stain with calcofluor, a dye commonly used for staining neutral glycans.



Neurofibrillary tangle double-labeled for glycans (blue) and hyperphosphorylated tau (red).

We isolated a novel type of polysaccharide from the human brain that is rich in N-acetylglucosamine. We named it chitinaceous polymers. Chitinaceous polymers are regulated by age and disease. Alzheimer's disease brains express higher molecular weight forms than age-matched control brains and young brains.



The molecular size of chitinaceous polymers is regulated by age and disease. Bio-Gel P10 chromatograph of polymers isolated from Alzheimer's disease and control brains.

Based on the observed regulation of molecular weight by age and disease, we hypothesize that small chitinaceous polymers plays a role in the development and high plasticity of early neuronal circuitry. The larger adult form may play a role in the maintenance and further sculpting of neuronal circuitry. The pathologically large form in brains afflicted with Alzheimer's disease could play neurotoxic or neuroprotective roles as both degenerative and repair mechanisms are found.