

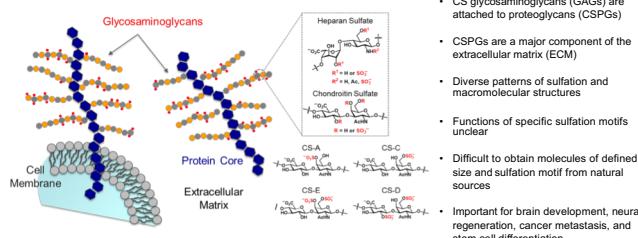
CHEMICAL APPROACHES TO STUDY CHONDROITIN SULFATE IN NEUROPLASTICITY AND NEURODEGENERATION

Hsieh-Wilson Laboratory*

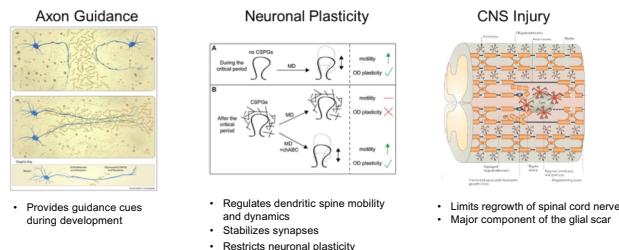
California Institute of Technology, Division of Chemistry & Chemical Engineering, 1200 E. California Blvd, Pasadena CA 91125

CHONDROITIN SULFATE (CS) GLYCOSAMINOGLYCANs

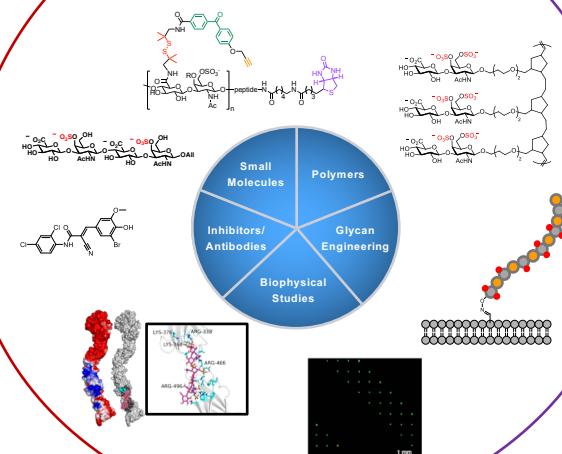
Chondroitin Sulfate is a Sulfated Polysaccharide Found in the Extracellular Matrix



Chondroitin Sulfate Regulates Important Neuronal Processes

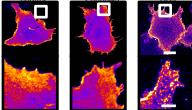
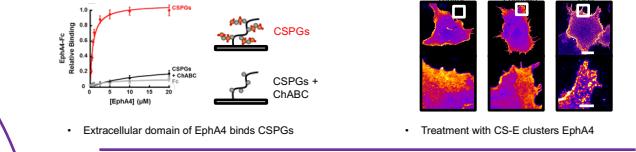


CHEMICAL TOOLBOX FOR STUDYING CS BIOLOGY



CSPGs CLUSTER AND ACTIVATE CELL-SURFACE RECEPTORS

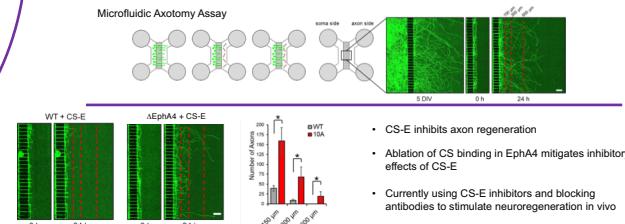
Cell-Surface Receptor EphA4 Binds CS and Induces Clustering



Proposed Molecular Mechanism:

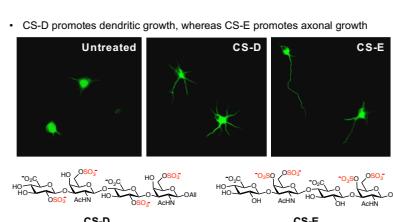
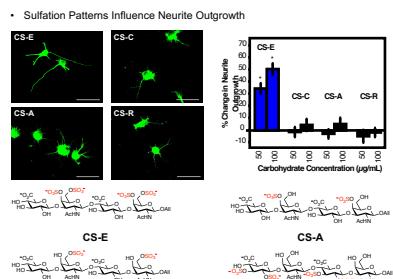
- CS-E sulfation motif binds EphA4
- CS binding is independent of soluble protein ligands
- CS chains cluster EphA4 and induce auto-phosphorylation
- Downstream signaling is activated

Loss of EphA4 CS-Binding Capacity Promotes Axon Regrowth

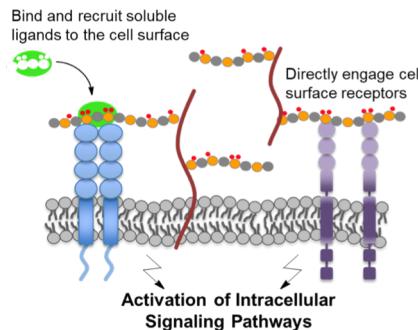


CS BIOLOGY INFLUENCED BY 'SULFATION CODE'

Different Sulfation Patterns Elicit Different Outcomes



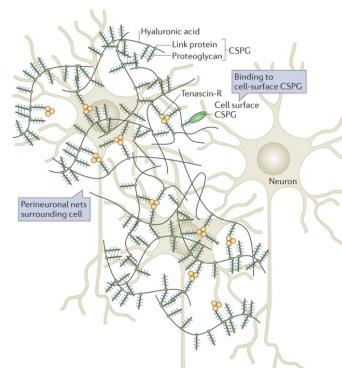
CS-Binding Proteins Recognize Specific Sulfation Motifs



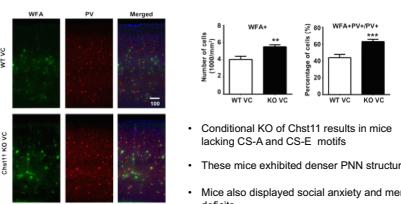
UNDERSTANDING THE ROLE OF CS IN NEUROPLASTICITY

CSPGs in Perineuronal Nets (PNNs)

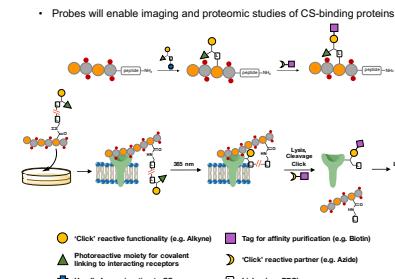
- Neuroplasticity is the ability of the brain to adapt and form new neural connections
- Neuroplasticity is critical in processes related to learning, memory, aging, injury, and disease



CSPG Sulfation Regulates PNNs and Behavior



Developing Multi-Functional Chemical Probes



- CSPGs and other ECM components form perineuronal nets (PNNs) around neurons
- CSPGs are a major component of the ECM in the brain and regulate neuroplasticity
- Molecular mechanisms involved remain elusive