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Photoaffinity Tools for Understanding Neuroplasticity

Understanding how the brain dynamically reorganizes itself and establishes neural connections is critical for helping patients recover brain function. Despite the increasing prevalence of neurodegenerative diseases such as Alzheimer’s, there are no effective treatments to prevent neurons from degenerating. A major priority in the field, therefore, is to understand the molecular mechanisms underlying neuroplasticity, the ability of the brain to adapt and form new neural connections. Such an understanding would enable the development of therapeutic strategies that promote axon regeneration.

Recently, chondroitin sulfate (CS) glycosaminoglycans (GAGs) and their associated proteoglycans (CSPGs) have been shown to regulate receptor-mediated signaling events that underlie axon regrowth and neuroplasticity. Importantly, a specific CS sulfation motif, called CS-E, inhibits neuroplasticity and axon regeneration after central nervous system injury through its interactions with multiple protein receptors, such as PTPσ. Mapping CS-protein interaction networks and deciphering the structure-function relationships of these polysaccharides in their physiological context is therefore key to elucidating molecular mechanisms underlying neuroplasticity. However, the identification of GAG binding proteins is challenging. To address these challenges, we have developed for the first time GAG polysaccharide photoaffinity probes to map the GAG-protein interactome in live cells. Overall, our studies outline a general chemical approach for the discovery of GAG-binding proteins in their native extracellular context.

Hosted by Professor Matthew Pratt

The scientific community is invited

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