Reactive Gliosis

- Investigation of Poststroke Depression Following a Nucleus Accumbens Infarct in Mice
- KChIP3 fosters neuroinflammation and synaptic dysfunction in the 5XFAD mouse model of Alzheimer's disease
- Functional-guided frameless stereotactic biopsy of highly eloquent brain tumors
- Targeting glial fibrillary acidic protein in glaucoma: a monoclonal antibody approach to modulate glial reactivity and neuroinflammation for neuroprotection
- Diet-incorporated saracatinib, a Src tyrosine kinase inhibitor, counteracts diisopropylfluorophosphate (DFP)-induced chronic neurotoxicity in the rat model
- Exposure to a nanoplastic-enriched diet for fourteen days increases microglial immunoreactivity in the zebrafish telencephalon
- Modulating inflammatory prostaglandin E2 signaling to mitigate neurobehavioral comorbidities associated with seizure disorders
- Seizure Circuit Activity in the Theiler's Murine Encephalomyelitis Virus Model of Infection-induced Epilepsy Using Transient Recombination in Active Populations

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Reactive gliosis is a response of glial tissue to different types of injury such as brain abscess, trauma, hemorrhage, or even neoplastic process.

Glial cells, including astrocytes, microglia, and oligodendrocytes, play essential roles in supporting and maintaining the function of neurons in the CNS.

When the CNS is damaged, whether due to injury, infection, neurodegenerative diseases, or other insults, glial cells undergo reactive changes as part of the inflammatory response. The two main types of glial cells involved in reactive gliosis are astrocytes and microglia.

Astrocytes:

Activation: Astrocytes become activated in response to injury or damage. They undergo hypertrophy (increase in cell size) and hyperplasia (increase in cell number) as a part of the response. Formation of Glial Scar: Astrocytes also contribute to the formation of a glial scar, which is a dense network of astrocytes and extracellular matrix molecules. The glial scar serves as a physical barrier that helps to contain and isolate the damaged tissue, preventing the spread of injury. Microglia:

Activation: Microglia, which are the resident immune cells of the CNS, become activated in response to injury or inflammation. They undergo morphological changes and release various signaling molecules, including cytokines and chemokines. Phagocytosis: Activated microglia also play a crucial role in phagocytosing (engulfing and digesting) cellular debris, dead neurons, and other harmful substances in the damaged area. Reactive gliosis is a double-edged sword. On one hand, it is a protective response aimed at containing damage, removing debris, and promoting tissue repair. On the other hand, excessive or prolonged gliosis can lead to the formation of a dense scar that may inhibit the regeneration of neurons and contribute to long-term functional deficits.

Understanding the mechanisms underlying reactive gliosis is crucial for developing therapeutic strategies to modulate this process in various neurological conditions, such as traumatic brain injury, stroke, and neurodegenerative diseases. Researchers are actively exploring ways to harness the

beneficial aspects of gliosis while minimizing its detrimental effects to promote neural repair and recovery.

The specific intermediate metabolites contributing to reactive astrogliosis remain unknown. This study investigated how glioblastomas induce reactive astrogliosis in the neighboring microenvironment and explores 11C-acetate PET as an imaging technique for detecting reactive astrogliosis.

Through in vitro, mouse models, and human tissue experiments, we examined the association between elevated 11C-acetate uptake and reactive astrogliosis in gliomas. We explored acetate from glioblastoma cells, which triggers reactive astrogliosis in neighboring astrocytes by upregulating MAO-B and MCT1 expression. We evaluated the presence of cancer stem cells in the reactive astrogliosis region of glioblastomas and assessed the correlation between the volume of 11C-acetate uptake beyond MRI and prognosis.

Elevated 11C-acetate uptake is associated with reactive astrogliosis and astrocytic MCT1 in the periphery of glioblastomas in human tissues and mouse models. Glioblastoma cells exhibit increased acetate production as a result of glucose metabolism, with subsequent secretion of acetate. Acetate derived from glioblastoma cells induces reactive astrogliosis in neighboring astrocytes by increasing the expression of MAO-B and MCT1. We found cancer stem cells within the reactive astrogliosis at the tumor periphery. Consequently, a larger volume of 11C-acetate uptake beyond contrast-enhanced MRI was associated with a worse prognosis.

The results highlight the role of acetate derived from glioblastoma cells in inducing reactive astrogliosis and underscore the potential value of 11C-acetate PET as an imaging technique for detecting reactive astrogliosis, offering important implications for the diagnosis and treatment of glioblastomas [1)].

Reactive (astro)gliosis is a highly heterogeneous and also context-dependent process that aims at the restoration of homeostasis and limits tissue damage. However, under some circumstances, dysfunctional (Astro)gliosis can become detrimental and inhibit adaptive neuroplasticity mechanisms needed for functional recovery [2)].

The CNS is prone to heterogeneous insults of diverse etiologies that elicit multifaceted responses. Acute and focal injuries trigger wound repair with tissue replacement. Diffuse and chronic diseases provoke gradually escalating tissue changes. The responses to CNS insults involve complex interactions among cells of numerous lineages and functions, including CNS intrinsic neural cells, CNS intrinsic nonneural cells, and CNS extrinsic cells that enter from the circulation. The contributions of diverse nonneuronal cell types to outcome after acute injury, or to the progression of chronic disease, are of increasing interest as the push toward understanding and ameliorating CNS afflictions accelerates. In some cases, considerable information is available, in others, comparatively little, as examined and reviewed here [3)].

Astrogliosis in epileptic brain is a peculiar condition showing epileptogenesis and is thought to be

different from the other pathological conditions. The aim of a study was to investigate the altered expression of astrocytic receptors, which contribute to neurotransmission in the synapse, and channels in Hippocampal sclerosis (HS) lesions.

Aoki et al., performed immunohistochemical and immunoblotting analyses of the P2RY1, P2RY2, P2RY4, Kir4.1, Kv4.2, mGluR1, and mGluR5 receptors and channels with the brain samples of 20 HS patients and 4 controls and evaluated the ratio of immunopositive cells and those expression levels.

The ratio of each immunopositive cell per glial fibrillary acidic protein-positive astrocytes and the expression levels of all 7 astrocytic receptors and channels in HS lesions were significantly increased. We previously described unique astrogliosis in epileptic lesions similar to what was observed in this study.

This phenomenon is considered to trigger activation of the related signaling pathways and then contribute to epileptogenesis. Thus, astrocytes in epileptic lesion may show self-hyperexcitability and contribute to epileptogenesis through the endogenous astrocytic receptors and channels. These findings may suggest novel astrocytic receptor-related targets for the pharmacological treatment of epilepsy. [4].

Differential diagnosis

Reactive gliosis differential diagnosis.

1)
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