Docket #: S24-196

Targeting Muscarinic Receptors CHRM1 and CHRM3 for Diffuse Midline Glioma Therapy

High-grade gliomas, including glioblastoma and diffuse midline glioma are the most common malignant brain tumor types and leading causes of brain-tumor-related death in adults and children, respectively. Diffuse midline gliomas commonly occur in the pons, thalamus, and spinal cord, and can spread throughout the brain. These tumors are universally fatal, highlighting the urgent need for new therapies.

The Monje and Deisseroth labs at Stanford have discovered important therapeutic targets for diffuse midline gliomas. The inventors demonstrated that the activity of cholinergic midbrain neurons modulates tumor cell proliferation in a circuit-specific manner at sites of long-range cholinergic projections. From this work, they found that acetylcholine exerts a direct effect on diffuse midline glioma cells, promoting increased proliferation and invasion through muscarinic receptors. The inventors thus invented a method to pharmacologically block specific acetylcholine receptors with antagonists, showing the abolishment of the activity-regulated increase in glioma proliferation in human-derived cholinergic neuron-glioma co-culture and in vivo. No current medication presently exists to block these specific receptors, enabling the invention to be the first of its kind for brain tumor therapy.

Applications

- Cancer therapy for diffuse midline gliomas, glioblastoma, medulloblastoma, oligodendroglioma, and ependymoma brain tumors
- Therapy for neurological disorders
- Evaluation of anti-glioma therapeutics using a novel co-culture comprising both cholinergic neurons and glioma cells

Advantages

- Targeted receptor blockage
- No currently available therapeutic for brain cancer therapy via targeted receptor blockage

Publications

- Richard Drexler, Antonia Drinnenberg, Avishai Gavish, Karl Deisseroth, Michelle Monje, et al. Cholinergic neuronal activity promotes diffuse midline glioma growth through muscarinic signaling. *Cell*, Open Access, Published online June 19, 2025.

Patents

- Published Application: WO2026055114

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