

Aquaporin-4-Blockers for the Treatment of Edema

Background: Edema (tissue swelling) results from various clinical conditions, including neurological conditions such as stroke or traumatic brain injury. Identifying molecular targets that perpetuate edema in brain conditions, like stroke, is an extremely valuable tool to create drugs that can treat and reduce deaths related to these diseases. Stroke afflicts more than 700,000 Americans annually, and the degree of brain edema is a major determinant of patient survival after a stroke event. Managing edema from stroke can potentially extend the window of treatment – approved t-PA therapy must be administered within 3 hours of ischemic stroke occurrence. Aquaporin 4 (AQP4) is a molecular target that is being explored as one such target for adjunct treatment of stroke. AQP4 is expressed abundantly in the perivascular endfeet of brain astrocytes, suggesting these channels regular brain water balance.

The Technology: Researchers at the University of Arizona identified two known compounds that block AQP4 and have used these to make improved derivatives for pharmacological use in the treatment of edema. This is the first demonstration of any compound that can block AQP4 channels. Another purpose of this technology is to provide a water permeability assay expression system that is useful for screening and characterizing compounds that block AQP4 and other aquaporin channels.

Applications:

- *Therapeutic application in the treatment of brain edema resulting from diseases such as stroke and traumatic brain injury*
- *Assay to characterize and screen compounds that block aquaporin channels*

Advantages:

- *A novel group of AQP4 blocking agents have been designed, synthesized, characterized—when no publicly known blockers of AQP4 have been currently identified*
- *Potential drugs would likely extend the therapeutic window for stroke patients as edema would be targeted (rather than clot lysis). Also, a drug targeting edema would likely treat hemorrhagic as well as ischemic stroke.*
- *Mechanism of action for these blockers have been defined, making these lead compounds excellent candidates for preclinical testing*
- *Demonstrated a beneficial effect in an animal stroke model in vivo using these blockers*

Status: US utility patent and PCT applications have been filed.

Refer to Case # UA07-029

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