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Blood glutamate scavengers prolong the survival of rats and mice with brain-implanted gliomas

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In the last few years, an ever increasing body of data suggests that L-Glutamate (Glu) plays a crucial role in the growth of malignant gliomas, their invasiveness and ability to destroy neighboring brain tissue while being also the possible cause of the tumor-associated seizures that often occur in conjunction with gliomas.

In a paradigm shift in which neuroprotection takes place via blood, we have established the feasibility of accelerating a naturally occurring brain to-blood Glu efflux by decreasing blood Glu levels with intravenous oxaloacetate, the respective Glu co-substrate of the blood resident enzyme glutamate–oxaloacetate transaminase. We and others have also demonstrated that blood Glu scavenging provides highly significant brain neuroprotection at locations where Glu is in excess within the brain parenchyma extracellular fluids without affecting other brain areas.

We now describe the neuroprotective effects of blood Glu scavenging in a chronic and fatal condition such as brain-implanted C6 glioma in rats and brain-implanted human U87 MG glioma in nude mice. Animals drinking oxaloacetate with or without intracutaneous injections of glutamate–oxaloacetate transaminase display a smaller tumor volume, reduced invasiveness and prolonged survival than control animals are drinking saline. These effects are significantly enhanced by temozolomide, which increases survival by 237%. This is the first time that the blood Glu scavengers approach is used chronically, and because of their safety, is likely to be of clinical significance for the future treatment of human gliomas.

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