adhesion in glioma and to their invasion⁷. Other proteins that are implicated in glioma growth may also be connected to glutamate systems in gliomas including Cl⁻ channels⁹ and Ca²⁺-activated K⁺ channels (BK channels)¹⁰. A better understanding of AMPA-mediated activation and Ca²⁺ influx will provide further insight into the invasion and migration of gliomas.

Much of the focus in glioma research has centered on 'conventional' mechanisms of tumor survival and growth: modulation of transcription factors, apoptotic cascades and blood vessel growth. All of these may be important targets for CNS oncologists. But this study and the recent studies by others should put a spotlight on CNS-specific approach to treatments that alter glutamate. A large body of knowledge about normal glutamate systems already exists—their receptors, enzymes and trans-

porters. And, many drugs are available to target these systems. So we clearly have the knowledge to tease apart glutamate's role in brain tumors and the tools to apply to therapy. A close collaboration between neuro-oncologists and glutamate neuroscientists—experts in previously unrelated specialties—is now warranted. The development of new therapeutics will depend on it.

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Endostatin turns heads

A two-headed tadpole emerged from the laboratory almost 20 years ago through investigations into Wnt signaling. Blocking components of the Wnt pathway in frog embryos results in a complete duplication of the embryonic axis. Now, researchers have used frogs to implicate the Wnt pathway as a target for endostatin, a potent anti-angiogenic fragment of collagen XIII.

Endostatin has been shown to block tumor growth in several animal models by inhibiting neovascularization and is currently being tested as a treatment for human cancers. However, the molecular mechanism by which endostatin prevents new vessel growth is still unknown. In the 5 August issue of *The Journal of Cell Biology*, Vikas Sukhatme and colleagues show that endostatin can antagonize the Wnt signaling pathway in both *Xenopus laevis* embryos and mammalian cells.

Previous studies demonstrated that endostatin has an important role in mammalian development and provided subtle hints that it might function in the Wnt signaling pathway. So the authors took a stab at the frog. Injection of endostatin RNA into early embryos resulted in the formation of an ectopic ectodermal organ called the cement gland, a phenotype comparable with embryos overexpressing glycogen synthase kinase-3 β , a Wnt signaling inhibitor. To further explore the tie between endostatin and Wnt, RNA encoding β -catenin, an essential mediator of Wnt signaling, was injected into embryos alone or with endostatin RNA. Overexpression of β -catenin alone resulted in frog embryos with two heads (top), whereas, coinjection with endostatin RNA partially rescued the phenotype (bottom).

Further studies showed that endostatin inhibits expression of a β -catenin-responsive promoter in mammalian cells and that it induces ubiquitin-mediated degradation of β -catenin. The team then showed that endostatin could inhibit endothelial-cell migration and entry into S-phase by preventing transcription of genes regulated by binding sites for TCF/LEF (T cell-specific factor/lymphoid-enhancer binding factor). TCF/LEF can function as a downstream component of the Wnt pathway. The results provide evidence that Wnt signaling is required for tumor neovascularization and reveals a molecular function for endostatin.

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