Drug delivery for the treatment of brain tumors

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The development of applicable brain tumor models in the laboratory setting is crucial to the success of treatments utilized clinically. We have used various brain tumor models to test the technology of local delivery and to target multiple pathways for brain tumor therapy. Through the combination of Gliadel, radiation therapy and oral temozolomide (TMZ), median patient survival has increased from 9 to 21 months. To further increase survival, we are exploring the local delivery of TMZ and have shown that in animal models we can achieve 37.5% long term survival. This benefit dramatically increases when combined with radiation therapy. Paclitaxel, a mitotic inhibitor, when incorporated into a thermosensitive gel depot provides local delivery, enhances efficacy, and limits systemic toxicity. In combination with TMZ and radiation therapy, this survival can significantly increase. This data led to a Phase 1 clinical trial for brain tumor patients as well as a Phase 2 dose escalation study in patients with inoperable esophageal cancer. The timing regimen of chemotherapeutics and radiation therapy was also explored. Rapamycin, an MTOR inhibitor, anti-angiogenic agent, and anti-proliferative agent has been efficiently incorporated and delivered using biodegradable, controlled release beads which are safe and effective for CNS delivery. Combination of anti-VEGF therapy and temozolomide in human glioma models have been investigated and showed that the intratumoral concentration of temozolomide was not adversely effected and that the combination can improve overall survival. It has been shown that manipulating the modulation of glutamate may provide a therapeutic benefit in the treatment of gliomas. Additionally, various imaging techniques to better track angiogenesis may provide a therapeutic benefit in the treatment of gliomas. Biopsy and optical coherence tomography might be helpful in imaging blood vessels in vivo are being used.

Biography

Betty Tyler is an Assistant Professor of Neurosurgery at Johns Hopkins University. She runs a highly successful and productive laboratory and has a national reputation for stellar science in the field of translational research and local delivery of chemotherapeutic agents for brain tumor therapy. In addition to publishing over 95 peer-reviewed articles she has mentored and taught over 250 neurosurgical residents, medical students, and undergraduate students in research design, surgical techniques and statistical analysis. She is particularly interested in bringing promising new therapies to patients with brain tumors and making a difference in the brain cancer research field.

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