

Media Release: Research Collaboration Agreement with Johns Hopkins School of Medicine

Public Information

“On (or as at) 23 September 2009 the Radiowave Therapy Research Institute (RTRI), Perth Australia entered into a ‘Research Collaboration Agreement’ with Johns Hopkins School of Medicine (JHM), Baltimore, USA.

The RTRI, established in 2005, is a non profit organisation committed to the research of radiowave cancer treatment protocols.

Under the Collaboration Agreement, RTRI has agreed to fund an in-vivo pilot brain cancer research project, to be conducted at Johns Hopkins in Baltimore.

This research will specifically assess two radiowave therapy protocols which are the basis of therapies founded by Dr John Holt.

The Agreement was developed following a proposal by Dr Gary L. Gallia, of Johns Hopkins School of Medicine.

Johns Hopkins will use its extensive medical research facilities to undertake the research whilst the RTR will provide the radiowave equipment necessary to undertake the project(s).

The following information describes the Radiowave Therapy Evaluation Project and is taken from the proposal prepared by Gary L Gallia MD, PhD of 12/03/2008:

“EVALUATION OF GMI/UHF and UHF/XRT THERAPY IN PRECLINICAL ANIMAL MODELS OF GLIOBLASTOMA

Malignant are the most common primary brain tumor in adults. In the Central Brain Tumor Registry of the United States (CBTRUS), the 2 year survival for patients aged 65 or older was less than 3% and for patients under age 45, less than 30%¹. Despite aggressive surgery, radiation and chemotherapy the median survival for patients with malignant gliomas treated with (i) surgery, (ii) chemotherapy with either locally implanted BCNU impregnated polymers or systemic temozolomide, and (iii) radiotherapy, is less than 15 months^{2,3}.

Numerous intracranial models systems are available for direct experimental testing of new drugs and modalities for glioblastoma. One of the best characterized model system is the 9L gliosarcoma model system. This system allows for efficient and highly reproducible evaluation of therapeutics.

In this system, rats are surgically implanted intracranially with a tumor piece and exposed to various therapeutics. We have extensive experience with this model system in the Brain Tumor Research Laboratory at Johns Hopkins Hospital.

While a fellow with Charles Teo, MBBS, FRACS at the Prince of Wales Hospital in Randwick, NSW, Australia, I learned of radiowave therapy and the Radiowave Therapy Clinic and Research

¹ CBTRUS. Statistical Report: Primary Brain Tumors in the United States, 1998-2002. Published by the Central Brain Tumor Registry of the United States 2005.

² Gallia GL, Brem S, Brem H. Local treatment of malignant brain tumors using implantable chemotherapeutic polymers. J Natl Compr Canc Netw 2005;3(5):721-8

³ Stupp R, Mason WP, van den Bent MJ, *et al*. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 2005;352(10):987-96

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Institute. After seeing several patients with glioblastoma treated with radiowave therapy and learning more about the outcomes following discussions with David Bonnin, I became interested in this treatment modality. Our brain tumor therapeutics laboratory at Johns Hopkins Hospital in Baltimore, MD, USA focuses on testing novel therapeutics for malignant brain tumors. The experiments outlined in this proposal, in collaboration with the RTRI, aim to investigate the effects of radiowave therapy in traditional and stem cell preclinical models of glioblastoma.

Specific Aim #1. Examination of safety of GMI, UHF, GMI/UHF and UHF/XRT therapy in rodents.

Hypothesis: GMI, UHF and XRT singly and in combination will be safe in rodents.

Given the clinical safety of radiowave therapy, it is likely safe in rodents. Prior to efficacy studies toxicity studies will be performed in immunocompetent rats.

Specific Aim #2. Examination of efficacy of GMI/UHF and UHF/XRT in a rodent intracranial model of glioblastoma.

Hypothesis: GMI/UHF and UHF/XRT therapy will prolong survival in an intracranial model of glioblastoma.

One of the the best characterized animal model for testing therapeutics is the rat gliosarcoma 9L model. In this model tumors are implanted intracranially in immunocompetent rats and the endpoint is death. The rats will then be randomized to receive either treatments (GMI/UHF or UHF/XRT) as determined in specific aim #1 or control treatments. Statistical analyses will be performed using the Kaplan-Meier method and the significance of survival differences will be evaluated. P-values of less than 0.01 will be considered statistically significant. The brains of all animals will be examined histopathologically.

Specific Aim #3. Examination of efficacy of GMI/UHF and UHF/XRT in human glioblastoma models.

Hypothesis: GMI/RF therapy will prolong survival in animals implanted with human glioblastoma tumors.

The 9L model system is one of the best intracranial glioblastoma model systems currently used. It is robust with high reproducibility. Its main drawback is that it is derived from a rat gliosarcoma model. Depending on the outcome of the 9L model system, additional human xenograft model systems will be considered including flank and intracranial xenografts from both traditional and stem-cell based tumors in immunocompromised rats following discussion with RTRI.

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Glossary

GMI: Glycolytic Metabolic Inhibitors

UHF: Ultra High Frequency (radiowave)

XRT: X-Ray Therapy (radiotherapy)

Other references

- § Lee J, Kotliarova S, Kotliarov Y, *et al.* Tumor stem cells derived from glioblastomas cultured in bFGF and EGF more closely mirror the phenotype and genotype of primary tumors than do serum-cultured cell lines. *Cancer Cell* 2006;9(5):391-403.
- § Bao S, Wu Q, McLendon RE, *et al.* Glioma stem cells promote radioresistance by preferential activation of the DNA damage response. *Nature* 2006;444(7120):756-60.
- § Kao GD, Jiang Z, Fernandes AM, Gupta AK, Maity A. Inhibition of phosphatidylinositol-3-OH kinase/Akt signaling impairs DNA repair in glioblastoma cells following ionizing radiation. *J Biol Chem* 2007;282(29):21206-12.
- § Liu G, Yuan X, Zeng Z, *et al.* Analysis of gene expression and chemoresistance of CD133+ cancer stem cells in glioblastoma. *Mol Cancer* 2006;5:67.

Please address any further enquiries about the John Hopkins School of Medicine and the Radiowave Therapy Research Institute collaboration, and/or their cancer research projects, to the following..... rtrimedia@the-institute.com.au

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