



**SAMANTHA DICKSON
BRAIN TUMOUR TRUST**

Head to head with brain tumours

Research update August 2011

Research into high-grade tumours

Thanks to the donations from all of our supporters, the past year has seen significant advances in our understanding of high-grade brain tumours in children and adults, much of which has been achieved through our award-winning research programme.

SDBTT-funded researchers at the Institute of Cancer Research in London and at the University of Nottingham are making headway into the genetics of and treatment monitoring for high-grade gliomas in children. Genetic testing at the National Hospital for Neurology and Neurosurgery built on research at the University of Cambridge means that adult patients across the UK with high-grade gliomas are receiving more tailored treatment and care. Our research Centre of Excellence at UCL is uncovering the genetic pathways and treatment targets in oligodendroglioma. SDBTT-funded research at the University of Wolverhampton has led to the early-stage development of a potential new treatment to improve chemotherapy for glioblastoma multiforme (GBM), while clinical trials co-funded with Cancer Research UK are testing new treatments for adults and children with different types of high-grade glioma.

We examine three of these research projects in more detail here.

Identifying and studying the role of key genes in high-grade brain tumours in children

Dr Chris Jones, Institute of Cancer Research, Royal Marsden NHS Foundation Trust

In our last research update we told you about six new research grants we had awarded thanks to your help. Since then, we have been able to award two further research grants, one of which was to Dr Chris Jones at the Institute of Cancer Research, to identify the key genes underlying glioblastoma multiforme in children and how they work. Using a unique collection of primary brain tumours that have been surgically removed, he is focussing on genes that are present in increased numbers of copies in comparison with healthy cells. The findings will provide valuable cues for the development of specifically-targeted drugs to improve outcomes for children with GBM.

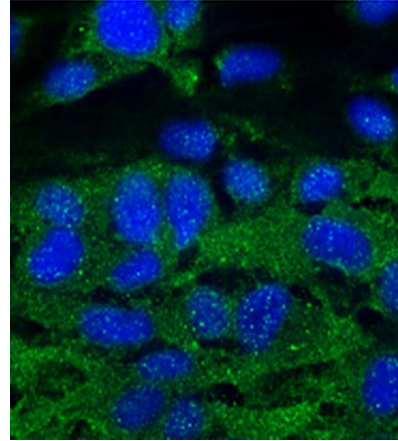


Dr Chris Jones in his lab at ICR

Improving the efficacy of chemotherapy for glioblastoma multiforme patients

Dr Weiguang Wang, University of Wolverhampton

Drug resistance is a major obstacle in successfully treating people with glioblastoma multiforme (GBM). This research looks to improve the efficacy of anti-GBM chemotherapy. GBM cells are resistant to drugs partly because they have high levels of a protein called nuclear factor kappa B (NF- κ B). Early findings suggest that the drug disulfiram, which is conventionally used to treat alcoholism, can stop GBM cells from growing by blocking the effect of NF- κ B.



Brain tumour cells fluorescing under the microscope

The team has developed a new fat-enveloped formulation of disulfiram that is stable in the body and has shown a strong anti-cancer effect on GBM cells in the lab. It is hoped that in future this research will contribute to the development of new therapies to help treat patients with GBM more effectively.

Researching alternatives to invasive monitoring procedures for children with brain tumours

Dr Nada Al-Saffar, Institute of Cancer Research, Royal Marsden NHS Foundation Trust

Dr Al-Saffar is using Magnetic Resonance Spectroscopy (MRS) to look at how a new class of anti-cancer drugs for treating high-grade gliomas in children affects a specific pathway in the brain. MRS measures the levels of metabolites - the chemical 'fingerprint' that cellular processes leave behind. Dr Al-Saffar is using this technique to see how these drugs affect the levels of metabolites in a particular chemical pathway in brain tissue.



Dr Nada Al-Saffar explains her work at ICR

Comparing treated to non-treated cells in high-grade glioma cell models, Dr Al-Saffar and her team have observed a decrease in the levels of phosphocholine (PC) and lactate; chemicals are required for maintaining growth in cancer cells. This interesting discovery means that levels of PC and lactate could be monitored as a means of tracking the effectiveness of chemotherapy drugs, without resorting to invasive measures such as biopsies. This has great potential for improving treatment monitoring of children and adolescents with malignant gliomas, for whom invasive techniques such as biopsies can be very distressing and potentially high risk.

A list of all our current and recent research projects into high-grade brain tumours with scientific and lay titles is included overleaf.

More information on our current research projects can be found at:

www.braintumourtrust.co.uk/research

Or please contact us:

Email: enquiries@sdbtt.co.uk

Call: **01252 749990**

High-grade projects funded this year

Institute of Cancer Research, Royal Marsden NHS Foundation Trust (Dr Nada Al-Saffar) (2009 – 2012), Establishing non-invasive biomarkers of the efficacy of novel phosphoinositide 3-kinase inhibitors in paediatric high-grade glioma by magnetic resonance spectroscopy: Researching alternatives to invasive monitoring procedures for children with brain tumours

Institute of Cancer Research, Royal Marsden NHS Foundation Trust (Dr Louis Chesler) (2010 – 2012), Systematic analysis of the role of MYCN in the formation and progression of high-grade, anaplastic medulloblastoma: Analysing the role of 'MYCN' in medulloblastoma

Institute of Cancer Research, Royal Marsden NHS Foundation Trust (Dr Chris Jones) (2010 – 2012), Systematic characterisation and functional assessment of amplified genes in paediatric glioblastoma: Identifying and studying the role of key genes in high-grade brain tumours in children

University of Nottingham (Professor Richard Grundy) (2008 – 2011), Genome-wide molecular characterisation of supratentorial PNET (sPNET) – II: Investigating the genetics of CNS PNET brain tumours in children

Royal Victoria Infirmary, Newcastle (Dr Simon Bailey) (2010 - 2012) – A phase II multi-centre study of the concomitant and prolonged adjuvant temozolomide with radiotherapy in diffuse pontine gliomas: A phase II study of temozolomide with radiotherapy for diffuse pontine gliomas in children
Jointly funded with Cancer Research UK

University of Cambridge (Dr Colin Watts) (2011 – 2013), An Evaluation of the tolerability and feasibility of combining 5-Amino-Levulinic Acid (5-ALA) with Carmustine Wafers (Gliadel®) in the surgical management of primary glioblastoma: A Phase I trial of 5-ALA with Gliadel® for glioblastoma multiforme
Jointly funded with Cancer Research UK

Institute of Neurology, London (Professor Sebastian Brandner) (2008 – 2011), Analysis of LOH 1p/19q and MGMT methylation in patients with malignant gliomas: Researching genetic testing for patients with malignant gliomas

Recently completed high-grade projects

University of Nottingham (Professor Richard Grundy) (2007 – 2009), Comprehensive mapping of gene expression and genomic gains and losses in paediatric high grade gliomas: Identifying important molecular abnormalities in high-grade gliomas

University of Wolverhampton (Dr Weiguang Wang) (2008 – 2011), Targeting the Nuclear Factor kappaB (NF-kB) pathway to improve chemotherapy of glioblastoma multiforme: Improving the efficacy of chemotherapy for glioblastoma multiforme patients