



**SAMANTHA DICKSON
BRAIN TUMOUR TRUST**

Head to head with brain tumours

Research update August 2011

SDBTT Research Centre of Excellence at University College London

Thanks to the donations from all of our supporters, the past year has seen significant advances in our understanding of brain tumours, much of which has been achieved through our award-winning research programme, not least by the team of talented researchers at our Research Centre of Excellence at University College London, the Samantha Dickson Brain Cancer Unit.

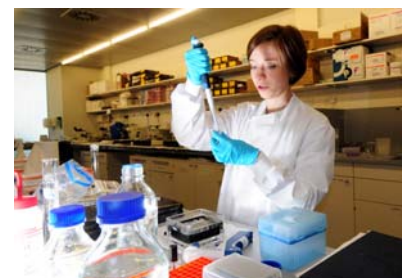


“We at the Centre aim to make laboratory discoveries which can contribute to patient care in the clinic. Our programme aims to shed light on the origins and development of brain tumours, and to reveal why some cancer cells are resistant to therapy and to identify new ways of overcoming this.”

Professor Paolo Salomoni, Programme Lead at Samantha Dickson Brain Cancer Unit

Inhibiting autophagy in glioma brain tumours - a way to combat drug resistance?

The cells in our bodies break down their worn out components to produce energy using a process called autophagy. Research has shown that cancer cells use autophagy to repair their DNA, thereby resisting the effects of cancer drug treatments which would normally work by attacking cancer cell DNA. The team has shown that blocking autophagy in glioma brain tumour cells in the lab can make the cells easier to kill.



Dr Maria Dvorkina in the lab

Experiments are underway to determine exactly how common autophagy is in glioma cells, and precisely what effect blocking autophagy has on the behaviours of these cells. Research into drugs that could be used to block autophagy in glioma cells may lead to improved treatments for patients with brain tumour types such as glioblastoma multiforme, low-grade astrocytoma and oligodendroglioma.

Based on this idea, clinical trials using the autophagy-inhibitor chloroquine to treat patients with glioblastoma multiforme (GBM) brain tumours are in development. Chloroquine has been used for decades against malaria, and more recently rheumatoid arthritis, so is known to be safe; this means that much of initial safety testing that would be needed for a new drug has been done already, so chloroquine could benefit people with brain tumours even sooner. This is a great example of how fundamental research can be translated into new treatments for patients.

The role of 'PML' protein in brain tumours – a target for treatment?

All cells in the human body, including those in the brain, have a number of checks in place to ensure they grow and are replaced in a controlled, ordered fashion. If these checks fail, uncontrolled cell growth can ensue, leading to the formation of a brain tumour. Professor Salomoni and his team are examining the role of cell growth controls in the development of the normal brain and in medulloblastoma brain tumours. This will allow them to reveal more of the mechanisms by which a normal brain cell becomes a brain tumour cell.

They are looking at 'promyelocytic leukaemia protein' or PML, a protein found in human cells that is already known to be critical in controlling growth in several different cancers such as leukaemia. The team have found that loss of PML in a particular type of cell in the healthy brain, called a 'granule cell progenitor', appears to fast-forward the cells' internal clocks, causing rapid cell growth and maturation.

The researchers are currently experimenting to see if this phenomenon is mirrored in medulloblastoma brain tumour cells. This could provide clues as to how these tumours develop, and how to slow or stop their growth by targeting the relevant pathways with new treatments.



Researcher Dr Joanne Betts-Henderson at work at the Unit

Investigating control mechanisms in cancer stem cells – how do they grow?

Most cells within a brain tumour are specialised cells which cannot grow. However, particular subpopulations of cells, termed cancer stem cells, can grow continuously and perpetuate the tumour. Dr Steve Pollard and his team aim to understand the genes involved in determining whether and when glioma stem cells (GSCs) either grow and multiply, or mature ('differentiate') into specialised cells that are unable to grow and multiply. Working towards this goal they have now identified a set of proteins called transcription factors that are likely to be involved in driving the uncontrolled growth of cancer stem cells.

The team are now using SDBTT funding to determine the importance of four of these transcription factors, and whether any of them are necessary or sufficient alone to cause normal and cancer stem cells to divide and multiply.

The first step in this process has been to confirm that the cells on test are producing the transcription factors being investigated. This has involved developing fluorescent antibodies against the transcription factors, in order to 'label' them (if they are present) in the test cells.



*Team Leader
Dr Steven Pollard*

The next step, currently underway, is to better understand the specific role of these transcription factors in these cells by blocking their production, using a technique called 'RNA knockdown', and observing the effects. If the transcription factors do prove to be important in the growth and survival of these cancer cells, they may make a suitable target for new treatments.

Furthermore, the team has found that the lab-grown brain tumour cells being used for these experiments have retained the characteristics of those in the original brain tumours, meaning the results of this work will be all the more relevant to the clinic.



*Research Assistant Ms Sara Galavotti
at work at the Unit*

Photographs courtesy of the Eastern Daily Press.

For more information about our Research Centre of Excellence at UCL or on any of our current research projects can be found at: www.braintumourtrust.co.uk/research

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