Brain tumour treatment hope

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Australian scientists have played a key role in the identification of a new biochemical mechanism that allows brain tumours to survive and grow, offering hope of new drug treatments for some of the most aggressive tumours.

The discovery offers new therapeutic perspectives and gives hope for the treatment of gliomas, the most common and aggressive type of brain tumour in both adults and children. Gliomas progress rapidly and the median survival time of patients is less than a year.

The research – by an international team from Germany, USA, Switzerland and Australia, led by Professor Michael Platten from the Department of Neurooncology at the University Hospital of Heidelberg – was recently published in the prestigious journal *Nature*.

In the study, the international team – including University of New South Wales researcher Associate Professor Gilles Guillemin – identified the key role played by kynurenine, a by-product of the metabolism of the essential amino acid tryptophan, in favouring brain tumour growth and at the same time suppressing anti-tumour immune response.

The researchers were also able to identify the receptor expressed by tumour cells that kynurenine acts through – the aryl hydrocarbon receptor (AhR).

While particularly relevant in the development and persistence of gliomas, the kynurenine pathway also has a role in other brain cancers, and is implicated in other neurodegenerative diseases. Associate Professor Guillemin said the breakthrough could potentially lead to viable therapeutics for a range of conditions, including Alzheimer's disease, motor neuron diseases, multiple sclerosis and Parkinson's disease.

"We are currently looking at all the molecules deriving from the tryptophan metabolism through the kynurenine pathway that can be linked to tumour persistence and immune suppression," said Associate Professor Guillemin, who is head of the Neuroinflammation Group in UNSW's School of Medical Sciences.

An oral drug able to block enzymes leading to kynurenine production has been developed and the drug could potentially be available for clinical trials within a few years, Associate Professor Guillemin said. The survival time for patients with gliomas, particularly the more aggressive tumours such as glioblastoma multiforme, has not changed in decades despite changes in therapeutic approaches. The mechanism elucidated here offers an entirely novel approach to therapy.

The finding is the latest in a series of related breakthroughs. In 2007,

Associate Professor Guillemin, UNSW conjoint Professor Bruce Brew (St Vincent's Hospital) and colleagues showed that tryptophan metabolism was significantly altered in another type of human brain tumour, neuroblastoma. This was a seminal study in the area and served as the foundation for further work. Since then the team, including PhD candidate Ms Seray Adams and postdoctoral scientist Dr Alban Bessede, has worked with neurosurgeon and UNSW conjoint Associate Professor Charlie Teo.

Dr Teo, who provided tumour samples to the researchers and funding through his charity Cure for Life Foundation, said the UNSW researchers could be on the brink of "an enormously powerful discovery".

"The stage is set to apply this discovery to the uniformly fatal disease of brain cancer and in so doing, potentially find an effective treatment," he said.

"Basic science breakthroughs such as this should give comfort to all those affected by brain tumours and confidence to those who have supported the Cure for Life foundation that their hard-earned dollars are being well spent."

Provided by University of New South Wales