Childhood Cancer Research: Paediatric Brain tumours

Information for The Jack Mylam Foundation – April 2013

Chris Jones PhD FRCPath

Research achievements in the field of High Grade Gliomas including Glioblastoma and Diffuse Intrinsic Pontine Glioma (DIPG)

Dr Chris Jones and his team concentrates on scanning the genome of paediatric brain tumours to create a catalogue of all the molecular alterations present. Their aim is to find the genes that are driving the development of these cancers, and those allowing the tumours to become resistant to therapy. His team are particularly interested in looking at mutations in genes for which drugs have already been developed for other diseases, as well as identifying potential new treatment targets. The goal is always to turn laboratory-based hypotheses into real, molecularly based treatments for malignant paediatric gliomas.

Dr Jones' research focusses on the more aggressive high grade gliomas (HGG); in children these tumours tend to be associated with a poor clinical outcome. This includes research on glioblastomas (glioblastoma multiforme or GBM) and Diffuse Intrinsic Pontine Gliomas (DIPGs).

Glioblastomas are malignant high grade gliomas that usually grow quickly and are invasive. There are currently no drug treatments available for these cancers. DIPGs are high grade gliomas that are universally fatal. They occur in the Pons structure within the brainstem and are exceptionally difficult to treat.

Historically, high grade gliomas are a very under-researched area. However, a critical mass of research is building and the ICR's Chris Jones is an international leader and driving force in HGG and DIPG research.

HGG tumours in general:

- The team at ICR have developed the most detailed picture to date of the genome of these aggressive cancers. As these tumours are rare, Dr Jones has forged collaborations with other international organisations in order to collect samples that cover the spectrum of potential variations, and to conduct the most comprehensive possible analysis. Dr Jones' work has already revealed some significant genetic differences between the adult and child form of the disease, and has highlighted potential new drug targets.

Glioblastoma:

- In a recent landmark publication (March 2013), Dr Jones' team describe the discovery of a genetic mechanism driving the development of childhood glioblastoma. Drugs targeted at this genetic mechanism have already been

developed for use in other cancer types, and the researchers plan to test these in clinical trials of children within the next two to three years.

The researchers showed that mutation of a histone protein called H3F3A – which acts as a gene scaffold – unleashes a chain of genetic activity that can lead to the development of glioblastomas. Specifically, this mechanism switches on a gene called MYCN which is known to cause cancer.

There are drugs currently in clinical trials for other types of cancer which can block MYCN's activity, and it is possible these could become effective treatments for glioblastoma, and help extend the lives of the young patients affected.

Study author Dr Chris Jones, leader of the glioma team at The Institute of Cancer Research (ICR), said: "Our research greatly improves our understanding of the genetic origins of childhood glioblastoma, and identifies key targets for drug treatment of the disease. At present, childhood glioblastoma is an almost certain death sentence for those who develop it, but we now have some hope that effective treatments may be on the horizon. We want to start testing out our ideas in clinical trials as soon as we can – within the next two to three years."

DIPG specific research:

- Dr Jones is the Chair of the SIOPE HGG/DIPG Biology Group – the International Society of Paediatric Oncology Europe, a position for which he was voted for by his peers.
- Development of worldwide collaborations to allow researchers to pool their knowledge and samples. This is important given the relative rarity of these types of cancer.
- Dr Jones is the Principal Investigator (genomics) on a North American DIPG collaborative grant.
- An increasing number of DIPG publications, an area where few others have yet published.
- Of particular note, Dr Jones' team performed the first study to comprehensively analyse the genomes of DIPG biopsy samples taken at diagnosis. This analysis allowed the researchers to identify key biological / genetic features which distinguish DIPG tumours from other paediatric high grade gliomas. Furthermore, the research uncovered the existence of two distinct subgroups of DIPG, and patients in one of these subgroups were found to have a significantly more aggressive cancer. Being able to classify these tumours by virtue of their different genetic features may be particularly valuable for the development of therapies targeted towards these very features.

Thomas Bland – *Deputy Director of Development (Trusts and Corporates)*
E: thomas.bland@icr.ac.uk, Tel: +44 (0) 20 8722 4200, W: www.icr.ac.uk

Registered Address: The Institute of Cancer Research: Royal Cancer Hospital
123 Old Brompton Road, London, SW7 3RP