APPLICATION FOR A GOSHCC SURGICAL SCIENTIST PHD STUDENTSHP

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ICH Programme/Section: DBC/Developmental Biology of Birth Defects

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1. Title.

Improving treatment for relapsed brain tumours

2. Portfolio summary.

**Aim**
The aim of the project is to understand why brain tumours relapse and why they become difficult to treat at relapse. This will lead to better diagnostic tools and better treatments.

**Background**
Brain tumours are the most common cause of childhood cancer death (~120 deaths pa in the UK). While a high proportion of children can be treated successfully, many will relapse and at that point the tumour is rarely curable. We do not understand what makes the relapsed tumour resistant to treatment or how to predict the outcome for the child.

When a child first presents with a brain tumour, they will usually have surgery and the tumour tissue removed will be subjected to extensive histological and molecular investigation. This data provides a diagnosis that will predict outcome and response to treatment. This key step in planning treatment has also afforded an opportunity to understand the genetics of primary tumours. However, when the tumour relapses, it is equally critical to understand how to treat it but the same level of investigation is not routinely undertaken. Importantly, the tumours evolve over time and the molecular events that drive the tumour at relapse are different to those at presentation. Historically, patients have not undergone surgery at the time of relapse. This has been a major limitation to our ability to understand their biology but there are now a number of changes in practice that provide the opportunity to study relapsed disease. This involves increased use of surgery at relapse and undertaking autopsies (with parental consent). This means we are now in position to build a cohort of tissue samples at relapse and/or at the point of death.

**Proposed methodology to be adopted**
The trainee will build cohorts of high-grade brain tumours from primary surgery, relapsed surgery and at autopsy. They will undertake DNA methylation analysis, DNA sequencing and RNA sequencing to identify key molecular events occurring at relapse and use these to develop new diagnostic tests to predict outcome at relapse.

**Skills to be achieved by the PhD trainee**
The trainee will gain expertise in molecular biology (including DNA/RNAseq and DNA methylation arrays), histopathology, autopsy and oncological neurosurgery.

**Relevance to the area of paediatric surgery**
Neurosurgery is the primary modality of treatment for most brain tumours and is critical to obtaining tissue to inform diagnosis. In recent years, surgery has become critical to the management of relapsed brain tumours.
Reference
