The Development of Cell Line Models of Childhood Brain Tumours

Richard Grundy

Human Development, University of Nottingham Medical School, Queen’s Medical Centre, Nottingham, UK

Summary — Childhood brain cancers have a significant impact on society. Currently, it is possible to make sophisticated diagnoses, but the treatments do not reflect patient differences and are out-dated. In order to develop better therapies and improve the outcome, we must first understand the underlying biology of brain cancer and how cells influence the disease process. For that purpose, several lines of brain cancer stem cells have been isolated, which have retained the characteristics of their original tissues. These in vitro human cell models are a much-needed addition to research on childhood brain cancers.

Key words: brain tumour, cancer stem cell, childhood tumour, tumour model.

Address for correspondence: Richard Grundy, Human Development, University of Nottingham Medical School, Queen’s Medical Centre, Nottingham NG7 2UH, UK.
E-mail: richard.grundy@nottingham.ac.uk

Introduction

There are several reasons why research into children’s brain tumours is important. Paediatric oncology is one of the success stories of the last 20–30 years, but the outcome for children with brain tumours is still poor. For example, 85–90% of children with leukaemia are being cured, but, at most, only 50% of children with brain cancer are successfully treated (1). Although the number of new cases is relatively small (500/year), 60% of survivors have some sort of disability, which has a significant impact on society (2). This shows the need to improve our understanding and treatment of these tumours.

At the moment, it is possible to make complex diagnoses by using histopathology and immunohistochemistry. However, there are some cases where molecular biology is crucial to obtaining a more sophisticated and accurate diagnosis. The ability to correctly predict disease progression and individual outcomes may positively change the approach to treatment. Rather than giving the most intensive therapy to every child, it will be possible to more-effectively stratify treatment and assess when it can be stopped, thereby reducing the impact and burden of the treatments.

Trying to Understand Cancer

Cancer is an interplay of a variety of elements, which is different in adults and children. In order to develop better therapies, we need to understand what those differences are and what impact they have on the disease. Unfortunately, cancer is a complex disease. When the human genome was sequenced, it was assumed that scientists would be able to select the genes playing a role in the disease process and easily treat patients. The present approach to cancer treatment, both for children and adults, is far from ideal and can be compared to a forest fire — after the forest has been destroyed, a few surviving trees will reproduce and form the new forest.

Brain tumours in children are relatively rare, and it is mainly for this reason that they have been a relatively low priority for research. There is a poor understanding of their biology, there is no accurate disease stratification, and the treatments used have been around for a long time. Associated with a lack of specific therapies, these factors contribute to the higher morbidity and mortality seen with childhood brain tumours. Understanding the biology of children’s brain tumours at the molecular level aids the development of treatments and the chance of a positive outcome.

A large amount of our research involves collaborations, for example, with the Children’s Cancer Leukaemia Group (UK) and with St Jude Children’s Research Hospital (Memphis, TN, USA). These studies are helping us to build up a picture of the underlying genotypes and gene expression profiles of a number of major childhood brain tumours. DNA microarray technology has been essential to these studies, and it has revolutionised our understanding of the diseases. Gene expression analysis of different tumours has enabled us to pick out different histological subtypes more reliably than would have been possible with histopathology and immunohistochemistry alone. However, it is not feasible to perform gene expression analysis for each new diagnosis, and we