

Child Health Research CIO

CHILD HEALTH RESEARCH CHARITABLE INCORPORATED ORGANISATION (CHR CIO) PROGRESS FORM – VACATION STUDENT - 2018

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Project title(s):	Targeting DUSP6 in neuroblastoma

Summary

What are you trying to do in this studentship?

Protein tyrosine phosphatases are a family of phosphate hydrolysing enzymes that are essential for normal development and physiology. Aberrations in protein phosphorylation are associated with the pathogenesis of several diseases, including cancer. Protein tyrosine phosphatases have been shown to play an important role in signalling pathways that are dysregulated in cancer, and have been attributed to both oncogenic and tumour-suppressor roles, depending on the type of cancer.

My studentship project focused on Dual Specificity Phosphatase 6 (DUSP6), which can remove phosphate from both phosphotyrosine and phosphoserine/phosphothreonine residues in its protein targets.

The significance of this enzyme in carcinogenesis has been highlighted in the literature with evidence of both loss and gain of function in various cancers. It is therefore currently a target of crucial interest for researchers, who work to improve our understanding of the pathophysiology of neuroblastoma and eventually contribute to the development of potential therapies.

With the hypothesis that DUSP6 may be overexpressed in neuroblastoma, our aim was to investigate the role of DUSP6 in neuroblastoma and whether it does have an oncogenic role. We studied the response to DUSP6 inhibition in various neuroblastoma cell lines, compared to a control cell line. We also wanted to explore the nature of its target interactions downstream of its activation, by looking at protein phosphorylation on target proteins following DUSP6 inhibition.

Why is this research important?

Neuroblastoma is a type of childhood cancer that forms from immature nerve cells in the developing sympathetic nervous system. It is an embryonic tumour and is the most common malignancy diagnosed in the first year of life as well as the second most common solid tumour in childhood. It is most common in children under five years old and extremely rare after the age of 10 years.

The causes of neuroblastoma are still unknown and this cancer is a particularly complex one which presents many challenges.

There is still a lot of contradicting information found in the literature, especially regarding the nature of DUSP6 implications in carcinogenesis, and whether it plays a positive or negative role.

The prognosis is variable and outcomes are mainly related to age, cancer stage and molecular pathology. It can sometimes almost be considered benign, with spontaneous regression of the tumour seen in some infants. However, older patients diagnosed with high-risk neuroblastoma, which is usually fatal, have a 5-year survival rate of around 40 to 50%.

Treatments currently available include surgery, chemotherapy and radiotherapy, depending on the age of the patient, and the size and position of the tumour, as well as the tumour biology and stage. The risk of relapse in high-risk patients is estimated at 50-60%.

With current advances, survival rates have improved but are still unacceptably low. Moreover, current treatments are associated with many side effects, which could be reduced with a better understanding of the disease. Defining ways in which DUSP6 is implicated in tumorigenesis is a crucial aspect of the current research undertaken to improve our knowledge of the disease, in an effort to develop more optimal therapies.

Value of Your Experience

This vacation studentship was my very first actual work experience in research. It not only allowed me to put into practice the theory I had been taught in my course, but also gave me an insight into the scientific research process. For instance, I got to appreciate how the efforts of each scientist contribute to the overall progress of one bigger project. I wasn't familiar with the way research is actually undertaken in a research institute, and how scientists collaborate and work together to bring about progress in Science. I now have a better understanding of what being a scientist really entails and I can consider my future career in medical sciences with more awareness of the different approaches I could take.

Working independently in the lab allowed me to improve my practical skills, as I became increasingly confident in the work I was doing and my responses to unforeseen experimental complications. I had the opportunity to attend seminars and team meetings, observing and learning from scientists with different backgrounds and skills. This broadened my vision and allowed me to put the project I was working on into perspective, understanding how it fit within a wider enterprise. Practicing how to interpret experimental results in context tremendously improved my critical thinking and my adaptability. Although I thought I knew how unpredictable and difficult the scientific research process is, I got to experience it first-hand and I now feel better equipped to face challenges that are part of a scientist's work.

This experience was a unique opportunity for me to acquire and improve a broad range of skills, both practical and theoretical.

The insight I got into the scientific research world gave me the tools and motivations I needed to define which direction to take with my studies and career.