Cancer Council Western Australia
Research Fellowship

Cancer Council WA

Fellowship title	Improving the cure rates for the childhood brain cancer, medulloblastoma
Fellow	Clin/A/Prof Nicholas Gottardo
Institution	Telethon Kids Institute
Research description	This project is focused on medulloblastoma (MB), the most common malignant childhood brain cancer, which accounts for 1 in 5 brain tumours. Current treatment consists of surgery to remove as much of the tumour as is safely possible, followed by radiotherapy (high-energy x-rays) and chemotherapy (anti-cancer medication). The exception to this is infants where radiotherapy is avoided due to the damage it causes to the developing brain. Using these approaches approximately 70% of children in developed countries can be cured; however, long-term treatment-related health problems continue to be a major issue for survivors, significantly impacting upon their quality of life. New therapeutic interventions are sorely needed in the clinic for these patients. Currently, only a handful of chemotherapies are used worldwide for the treatment of MB, highlighting the need to identify additional effective drugs for this disease. To address this, our laboratory has devised a drug discovery and research strategy to identify and evaluate new drugs to treat MB. This workflow includes using robotics to screen thousands of drugs for their ability to kill MB cells in vitro (in test tubes), then prioritising the drugs found to enhance the activity of the chemotherapeutics currently used in the clinic, to treat children with MB. The efficacy of the best drug combinations are then tested in vivo (in a living organism) in our “clinic of mice”, which are unique mouse models we have established that represent a range of different human MBs. Chemotherapy for MB principally works by damaging the DNA of cancer cells but these cells also have repair mechanisms that impede the effectiveness of treatment. One of the most promising drugs we identified in our work blocks the DNA damage repair system (a class of drugs known as CHK inhibitors) and thus enhances the effect of chemotherapy. This research aims to further validate CHK inhibitors as promising new treatments for MB. This work will identify the best CHK inhibitor to take into the clinic with the potential long term benefit to cure more children with MB.
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