Report on Lions Kids Cancer Genome Project (Genome Power) to Australian Lions Childhood Cancer Research Foundation

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By Dr Marie Dziadek, Dr Joe Collins

Background

The Lions Kids Cancer Genome Project (Genome Power), funded by the LCIF and ALCCRF, contributes whole genome sequencing (WGS) and analysis to the Zero Childhood Cancer (ZCC) program run by the Kids Cancer Centre, Sydney Children's Hospital, and Children's Cancer Institute (CCI). The WGS and informatics analysis are undertaken at the Garvan Institute of Medical Research, through the Kinghorn Centre for Clinical Genomics.

The WGS of a child's tumour aims to identify mutations and structural changes in the DNA (e.g. variants in genes, structural rearrangements) that are 'actionable', meaning there are drugs available that target such specific genetic alterations. Other laboratory assays are also performed at CCI and collaborating research centres in Melbourne which provide more information about the molecular changes in the tumours to help identify an appropriate treatment plan.

The WGS of DNA in the child's blood also aims to determine whether the child has inherent mutations that predispose them to developing cancer at an early age. This aspect contributes to a major research program at the Garvan Institute to identify the full range of inherited mutations associated with the development of childhood cancers.

Progress

Over the first year of the project (2016-2017) a pilot program was undertaken by ZCC and LKCGP to develop all the collection and processing of tumour and blood samples from children with high risk cancers in Sydney (Kids Cancer Centre, Sydney Children's Hospital, Randwick, and Children's Hospital, Westmead), and the methodologies to analyse these samples at Garvan and CCI. A process for assessing the clinical significance of genomic and other data was also developed as part of the pilot, with the establishment of a Multidisciplinary Tumour Board (MTB) that assesses the data from each child presented by the clinical and research teams and makes a recommendation to the clinician of possible treatment options based on the data. This pilot program, called TARGET, analysed samples from 59 patients and was instrumental in establishing high quality analysis in a time-frame suitable for decision-making by the paediatric oncologists. Some children in this pilot program received a new treatment plan that resulted from genomic and other information.

The pilot program has now ceased and the actual nation-wide precision medicine program, called PRISM (PRecISion Medicine for Paediatric Oncology Patients), was launched towards the end of 2017 and now involves all 8 children's oncology centres across Australia. Seven of the sites have officially opened with Women's and Children's Hospital Adelaide to be opened soon (full local governance authorisation pending).

Since September 2017, 70 patients have been enrolled in PRISM, with an average of 9 new cases being enrolled each month. Approximately one third of enrolled children have a brain tumour, almost one third have sarcoma, and the remaining children have leukemia, lymphoma, neuroblastoma or other rare types of high risk aggressive cancers.

All patients have so far has WGS performed on their tumours and most have had other types of tests. To date 48 patients have been fully analysed and most of these have been presented to the MTB for recommendation on treatment options. Genetic changes were found in the majority of tumours and these changes led to a recommended alternative treatment of 21 patients to date. The PRISM program has been able to obtain access to a new drug from the USA for two of these patients, leading to a very significant slowdown in tumour growth for both children. Because the program has only been running for just over 6 months it is still too early to evaluate its impact, but the clinical and research staff are very excited by the early indications of good outcomes for some children considering these all had high risk cancers with poor prognosis.

In addition to the new treatment options resulting from PRISM, 12% of children in the pilot program (TARGET) were found to have known mutations in their blood DNA that have possibly predisposed them to developing the cancer in the first place. This type of information will be very important in the future for genetic screening of families at risk, enabling children and adults to be monitored frequently to pick up any developing tumours and remove and/or treat them at a very early stage when the chances of a full recovery are much higher.