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Identification of candidate susceptibility genes for Acute Myeloid Leukaemia.

Ruth Spearing Cancer Research Trust

In 2022 I was accepted into the University of Otago Future Health Researchers summer program, sponsored by Ruth Spearing Cancer Research Trust. I have been investigating acute myeloid leukaemia and identifying inequity drivers for Māori and Pasifika individuals with cancer. The Future Health Researchers summer program has provided a unique experience with which to appreciate the groundwork of research and improve my own personal skills. Throughout this program, I have learnt about the role of health research, the involvement of Te Tiriti O Waitangi, methodological practices, teamwork and communication within research in Aotearoa. I aim to utilize the competencies I have gained throughout this program in the future research I will conduct.

Acute myeloid leukaemia is a form of blood cancer which disrupts development of cells within the bone marrow. Malignant myeloid stem cells develop into abnormal myeloid blast cells which over-crowd the bone marrow, preventing normal red and white blood production. Incidence of acute myeloid leukaemia are estimated to be roughly 3-4 cases per 100,000, with this statistic remaining relatively stable for the past two decades. However, inequities in recorded incidences across ethnicities have also remained static. Pairing the 2013 New Zealand census with the 2013 New Zealand Cancer Registry, Māori and Pasifika had higher incidence of acute myeloid leukaemia compared to other ethnicities (1.53 and 1.24, respectively). Throughout my summer studentship, I aimed to investigate candidate susceptibility genes for acute myeloid leukaemia and potential for copy number deletions across those genes. Copy number deletions are where between 50 base pairs to 1 million base pairs are removed from the gene, which can alter the ability of the gene to function or delete the gene entirely. I investigated genes throughout the genome that are intolerant to copy number deletions. Copy number deletions can reduce gene expression, causing cancer related molecular pathway(s) to behave abnormally, which may promote a cancer phenotype. I analysed the tolerance for copy number deletions in 55 candidate susceptibility genes for acute myeloid leukaemia. From that analysis, I selected the top 10 genes with the highest intolerance for copy number deletions and further explored their impact on gene function. These 10 genes included those involved in regulation of inflammation, cell migration and cell death. Further exploration of the prevalence of copy number deletions overlapping candidate susceptibility genes in acute myeloid leukaemia patients may also help identify targets for the development of novel therapies.

I used statistical population data and publicly available datasets to investigate candidate genes of interest for acute myeloid leukaemia. I originally used Rstudio, using computer coding language R, to extract gene expression and copy number data from a dataset. However, this dataset did not contain the full copy number data that I required and thus I would be unable to explore my aim. I decided instead to extract information from a previous study and utilize online programs such as the Human Protein Atlas, the Genome Aggregation Database and cBioPortal to further explore my aim to investigate candidate susceptibility genes in acute myeloid leukaemia. Throughout this program I have improved my skills in extracting, collating and interpreting bioinformation to determine if it is relevant for my research. Learning and understanding bioinformatic methodology allows me to utilize previously conducted health research further to gain novel information.

Health research in Aotearoa is crucial to expand not only local but worldwide knowledge gaps across multiple fields. Our health care outcomes, treatments and diseases are constantly evolving, with new research shedding light on health areas previously unknown or undeveloped. As a student within biomedical research, I have learnt that health research is imperative to understanding complex diseases, investigating new treatments and identifying inequity where we need to do better.

Te Tiriti O Waitangi is the founding document of Aotearoa and I have learnt through this program about its involvement in health research and the negligence of the document within the past. When signing the Te Tiriti, Māori agreed to the three articles; Kawanatanga, Tino rangatiratanga over taonga and Oritetanga. Kawanatanga indicates that Māori will share the power and decision making with that of the crown, as long as Māori interests are protected. Tino rangatiratanga shows that Māori will possess autonomy over items of values such as lands, food supplies and possessions. Finally, Oritetanga states that Māori and Europeans should have equal rights and equity in outcomes. Within the current health and cancer research in New Zealand, the final article of Te Tiriti O Waitangi has yet to be achieved. The inequities do not adhere to Te Tiriti O Waitangi and the right of Māori to be treated equally to Europeans within healthcare. As a future health researcher, the professional development sessions have highlighted a requirement for ethnic inclusion within the research that is produced. In many of the acute myeloid leukaemia datasets I have explored, Māori patients are often excluded, or make up less than 2% of the overall patient percentage. The field of acute myeloid leukaemia in New Zealand requires more population representative datasets by ensuring that Māori are included and Europeans are not over-represented. To offset the current inequities, Māori-specific health research should be conducted and promoted within the health research space. Care must also be taken when research is conducted to respect Māori customs and practices. Health researchers must take care when acquiring samples that are considered tapu and ensure the correct methodology is used for testing and disposal. Te Tiriti O Waitangi is thus an integral part of health research and must be used as a guide to not only respect Māori beliefs but to achieve equitable health care within Aotearoa.

Collaborating with others has allowed me to improve my interpersonal skills such as communication, group planning and teamwork. I have presented the study containing the 55 candidate susceptibility genes for acute myeloid leukaemia to the members of my research group during journal club. This required a breakdown of aims, methods, findings and conclusions into 5-minute talks, utilizing time-management, organization and my communication skills. The summer studentship program has also provided me with individual development by allowing a level of independence. I am able to investigate and troubleshoot both my R code and dataset sources with the support of my supervisor. Writing reports and other media products on the results of my summer studentship has meant communicating my bioinformatic methods and outcomes in simplified language so it can be understood by the general public, patients and stakeholder/sponsors who are supporting my research.

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