Final report form
Cancer Council ACT Research Grant 2019

Please submit electronically to cancer.information@actcancer.org

Report due date	16 March 2023	
Project Lay Title	Finding a more specific and efficient treatment for Hodgkin Lymphoma	
Grant Amount	$61,265	
Chief Investigator	Tatiana A Soboleva	
Project dates	Start: 1 July 2021	End: 15 December 2022

Project description Please explain the purpose of your research (including background and rationale). Please use language that the general public will understand. Word limit is approximately 250 words.	We have identified a novel molecular driver of Hodgkin Lymphoma (HL), DNA-binding protein, H2A.B. We have recently shown that H2A.B becomes highly active in all subtypes of HL where it binds to the DNA and overactivates genes that sustain cancer. Moreover, we have discovered why H2A.B is such an effective gene activator. These findings inspired an exciting new research avenue that we are pursuing in this project. Our research specifically aims to: (i) to identify the enzyme (the kinase) that phosphorylates H2A.B and (ii) identify the small molecule inhibitor that would inhibit this H2A.B-specific kinase

Major results of this research project As this project is now complete, please explain the major results of your research, and what it means for advancing cancer control. Please use language that the general public will understand. Word limit is approximately 500 words.	We have successfully concluded first aim by performing SILAC and IP experiments. Through this effort, we have identified a group of potential H2AB-specific kinases, including WNK family of kinases. For the second aim, we have done many extensive optimization experiments testing 10 H2A.B-specific antibodies in parallel with using some kinase inhibitors. However, we have identified that our antibodies did not produce high enough signal in the immunofluorescent assay for sufficient detection of small differences. We are now moving to a an alternative high through put approach using an alpha screen and Forster resonance energy transfer that is more sensitive.

Moderating Issues Please describe any challenges that you faced and/or that have impacted upon intended activity, progress and outcomes. Please explain your strategies for any aspects of the project that are incomplete. (Limit 300 words)	The antibody specificity and sensitivity are common inherit issue for most applications that rely on antibodies as a major tool. We have done multiple validations and control experiments, that allowed us to conclude that immunofluorescent approach is not optimal in our assay. However, the funding was crucial to establish the HTP approach to find kinases that specifically phosphorylate H2A.B. Nevertheless, during that optimization process WNK kinase family inhibitors produced important results, showing that WNK family is the likely writer of H2A.B phosphorylation. Therefore, the main aim of the project, identification of H2A.B-specific kinase was achieved, bringing us step closer to finding a more specific and efficient treatment for Hodgkin Lymphoma.

Publications and presentations Please list any publications and/or abstracts produced as a result of the project. Include manuscripts in preparation or in submission/under review.	1. Lorne Genome 2021, Victoria – CIA Soboleva, oral presentation 2. ComBio 2022, Melbourne – CIA Soboleva, invited speaker 3. "Identification of H2A.B post-translational writers and their inhibitors" Manuscript in preparation

Further studies and/or funding Please outline any further studies or funding which have arisen as a result of the project.	This funding allowed us to move forward with our investigation into the biology and function of H2A.B in Hodgkin Lymphoma, and as an important outcome, we have received NMHRC funding through the Ideas Grant scheme for 2022-2025 worth $1 million dollars.

Other Comments Please outline any other items of general interest which have arisen as a result of the project.	This project has opened several novel avenues for our research, and we are looking forward to further collaboration with ACT Cancer council who has been a very inspiring and reliable partner.

Signed Chief Investigator	Tatiana A Soboleva
Date	2/03/2023