

Understanding the role of Kleisin beta, a subunit of the condensin II complex, in T cell differentiation.

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The research stems from discovering a mutant mouse strain, called “nessy”, which has abnormal T cells. T cells are white blood cells critical for fighting infections and cancers. After many years of work, we were able to identify the mutated gene causing this white blood cell problem. To our great surprise, the gene (called kleisin beta) is important for chromosome structure and for cell division. We were able to prove that a single mistake in this gene caused the abnormal T cell problem in nesy mice. The aim of our research work during the last year has been to identify exactly what was wrong with the T cells, and to start to understand how this single change in the kleisin beta gene causes these problems.

The work is related to understanding the molecular causes of cancer in the following ways:

First, cancer arises due to the failure of the immune system, particularly T cells, to recognise cancer cells as foreign. Our work involves studying defective T cell development and function. Second, cancer arises due to defective cell division. The mutated gene we have identified is important for cell division, and reduction in the level of the protein has been shown to cause errors in chromosome separation during cell division. These sorts of errors are common in many types of cancer. Lastly, through searches of the scientific literature we identified a possible interaction between kleisin beta and the protein SCL (stem cell leukaemia). Over-expression of SCL is the most common genetic association with T cell acute lymphoblastic leukaemia.

Thanks to funding from the ACT Cancer Council, we have had a very successful 12 months of research. Our publication explaining our findings has been accepted for publication by the prestigious American journal, Proceedings of the National Academy of Sciences, USA. We have also submitted a second scientific publication to another international journal.

Funding by the ACT Cancer Council not only allowed this work to proceed for 12 months, it has also played a pivotal role in allowing four research students to complete their advanced studies. Lydia Makaroff completed her Ph.D. thesis in January, and has gone to the University of Washington in Seattle to continue her career in scientific research. Katharine Gosling completed her Ph.D. thesis in March, and is looking at working for the department of Health and Ageing, or in scientific publishing. Angelo Theodoratos plans to finish his thesis in October. Kim Yong-Hee successfully completed his honours research thesis in the lab, and has gone to the University of New South Wales to undertake a medical degree.

So thanks to the ACT Cancer Council, we have been able to successfully continue our research, which has identified a novel link between T cell function and Chromosome structure. The funding has also been important in completing the training of four research students, all of whom can go on to make important contributions to cancer research or treatment.

Thank you ACT Cancer Council!