

Project Title: Mechanisms and targets of protein synthesis dysregulation in cancer

Grant Awarded: \$600,000 over 3 years: \$200,000 in 2016-17

Principal Investigators: Prof Thomas Preiss, John Curtin School of Medical Research, The Australian National University.

Work on this project commenced in early 2017 as follows:

A multi-institutional agreement was signed with the Peter MacCallum Cancer Centre to formalise the involvement of CI Prof R Pearson and PI Dr G Poortinga. A PhD student (Ms Y Janapala, started in May) and postdoctoral researcher (Dr S Wagner; due to commence in July) were recruited to the project. The Preiss and Hannan groups commenced collaborative work (coordinated by Dr N Shirokikh and Dr K Hannan, respectively). To support these efforts a monthly 'work-in-progress' meeting involving all Canberra based researchers was established (with the Melbourne-based co-investigators being updated on relevant content).

Drs Shirokikh and Hannan have performed experiments to identify suitable conditions for generating polysomal material from E μ -Myc lymphoma cells. Furthermore, efforts have begun to adapt Translation Complex Profile Sequencing (TCP-seq) for use in mammalian cells (required for aims 1 and 2 of the project). A series of biochemical parameters (cell fixation, extraction, preparative separation of ribosomal complexes, and purification of protected messenger RNA fragments) were optimised and a working version of the approach is now close to being established. A first set of high-throughput sequencing libraries will be generated, soon. The resulting data will allow for the adaptation of appropriate bioinformatics analysis methods, a major focus for the coming months. At this early stage, there are not yet any publications that have arisen from this project.