Good morning everyone. I’m Harley Robinson, and im currently completing honours at Diamantina institute in the Hill group, completing a project titled: the selective export of miRNAs via extracellular vesicles. This project will hopefully reveal mechanisms in fundamental cellular biology, particularly that relating to miRNAs.

These small non-coding nucleic acids, derived from spliced regions of RNA or as their own gene, facilitate pathway regulatory activities. This occurs as these miRs can form complementary base pairing to the 3’ end of messenger RNAs, specific to the mir sequence, recruit RNA induced Silencing complex and associated proteins, including Argonauts and Dicers. This complex then degrades the transcript or inhibits its translation to alter protein function and therefore pathway activity. These miRNAs can be excreted and taken into recipient cells to complete this function, which alters pathways in the recipient cell to establish the basis of intercellular communication. Secreted miRs has been attributed to heart diseases, diabetes and cancers.

Once method of secretion is through the use of extracellular vesicles, composed of microvesicles and exosomes as illustrated. Now this method has added benefits over paracrine systems as these vesicles can possess homing proteins on the surface to allow for cell specificity with the added benefit of stability due to being surrounded by membrane. These vesicles package particular proteins, RNAs and DNA which when taken into the recipient cell can regulate cellular activity. Hereby understanding the exported content can reveal important intercellular communications.

Protein EV sorting is well characterised. Typically the content will change based on cell type, stresses and in diseases. This can include the participation of ESCRT protein complexes which are involved in the formation and sorting of proteins into EVs. Tetraspanins, which involve the use of specialised lipid microdomains, sorts integral membrane proteins which span the membrane. However in respects to miRNA sorting, very little is known. Previously export of miRs was considered non-selective where the miRs within the vesicles are merely representative of total cellular RNA levels. A single miRNA export protein has been named in a neuronal model that’s been known to selectively export a small subset of miRs. However, methods of regulation, different conditions and the export of other miRs had not been explored.

Our lab focuses on the use of an advanced prostate cancer model, PC3, which may reveal a miRNA export protein. This cell line exhibits abnormal expression of caveolin-1 whilst lacking expression of cavins.