Background: for amandas honours proposal it came to 2,450words.

Caveolae, Caveolin and Cavins; Basic molecular biology intro:

Caveolae, flask-like invaginations of the plasma membrane, exosome and microvesicle biogenesis and regulation have been linked to Caveolin family activity and expression. These vesicles allow for intercellular transport of proteins, Ribonucleic acids (RNA) and lipids which previously been attributed to a range of biological processes. Hereby, finding that disrupting this regulation has been attributed to multiple diseases is not unexpected. Namely, prostate cancer (PC) cells exemplify the range of negative effects that occurs when Caveolins are abnormally expressed. These Caveolins, particularly caveolin-1 (CAV1), facilitate vesicle formation by associating with cholesterol-enriched membrane microdomains on the plasma membrane. However, in the case of prostate cells where no Caveolin is usually expressed, CAV1 is upregulated to stimulate cancer-like properties, due to stimulating signalling processes attributed to tumour progression, invasion and metastasis. In contrast, typical function of CAV1 requires the introduction of coat proteins called Cavins (named 1-4) that stabilise Caveolae.

Exosomes and microvesicles:

Long range intercellular communication takes advantage of membrane bound vesicles, exosomes and microvesicles, secreted from a cell to allow for cell-specific homing of cargo and enhanced stability in interstitial fluid. These extracellular vesicles, which only differ by route of release, require cholesterol, sphingolipid and ceramide rich lipid microdomains to recruit a two main families of proteins to mediate release. Once released, the cytoplasmic contents, which also contains selectively exported ribonucleic acids (RNA), proteins and lipids, can be reabsorbed by other cells to facilitate biological function.

You’re floundering into other sections. Start again.

Significance and broad field: 96w excl. references.

Prostate cancer intro and significance; current stats for PC and why they are so sucky. Eg, prostate cancer currently rates as the second most diagnosed cancer, with its progression resulting in a high incidence of death in males. Once an advanced stage is reached, these tumours begin to exhibit androgen independence, uncontrolled proliferation, angiogenesis and general metastasis to adjacent bone and lymph nodes. Such negative affects occur due to dysregulation of molecular entities, namely proteins and ribonucleic acids (RNA). Some prostate cancers exhibit abnormal expression of proteins related to caveolae and exosome formation, which have been implicated in the progression of prostate cancer. Furthermore, this occurrence reveals gaps in knowledge regarding caveolae, caveolae-associated proteins and their molecular consequence.

Exosomes and microvesicles: 200w

Exosomes are defined as 40-100nm diameter extracellular vesicles formed by exocytosis of multivesicular bodies. Whilst similar in size and biochemical markers, microvesicles differ from exosomes by being released directly from budding of the plasma membrane. Despite being two different vesicle subtypes, their similarities make these difficult to distinguish experimentally. These vesicles contain cytoplasmic material with selectively exported ribonucleic acids (RNA), proteins and lipids due loading mechanisms with integral surface proteins. As such, this secretion facilitates long range intercellular communication, benefiting from homing mechanisms by surface proteins and enhanced stability of the contents due to being membrane bound. The membrane composition, being lipid raft like and cholesterol rich, recruits the caveolin family proteins to mediate its formation. Additionally, cytoplasmic coat proteins, from the Cavin family, regulate the caveolin interaction.

Caveolin: 120w

What are caveolin, name the 3 and their usual function. Detail why we only look at cav1 in this report.

Caveolin in Cancer: 100w

Introduction sentence, eg Caveolin 1 expression has been assosciated with aggressive late stage PC. Evidence of this (eg expression in cancer normally, effects of knocking it down or enhancing it expression (this could link into the fact that its not the only protein that will mediate the aggressiveness of cancer)). Introduce that their function when associated with cavins indicates their role in cancer.

Cavins: 100w

Introduce cavins, introduce the 4 different types and their cell specificity, and why we only assess 1-3. Introduce that that form complexes with each other in order to facilitate caveolae/exosome secretion.

Cavins role in exosomes/caveolae: 200w

Establish that cavin-1 is the important one: why? State experimental evidence. Explain what the other cavins do.

Cavins for cancer therapy: 200w

Reiterate that cavins are involed in the stabilisation of interactions. Explain that when cavins are introduced it attenuated the cancer progression. Introduce that recent evidence reveals that cavin differential expression in regards to cancer caused a flux of miRNAs (miR148a). add unpublished info about the pellet changes, and that cavins are strongly linked to this flux. Follow up with info about why we study the exosomes in respects to mirnas and cavins. (eg. Hereby this may indicate that Cavins may play a role in selectivity of miRNA export.)

microRNAs in Cancer: 100w

State what miRNAs are. Provide evidence that miRNAs appear to be playing part in cancer progression.

Cavins and miRNAs: 200w

Include evidence that miRNA148 supports this and that it is selectively exported. That cavins may be recruit or taking part in selection of exported material. This may be where we include info from our lab.

INCLUDE CRITICAL REVIEW OF RELAVNT LITERATURE (60% of the report so ~2400words)