MicroRNA-1246 as a potential biomarker for the detection of brain metastasis in melanoma patients

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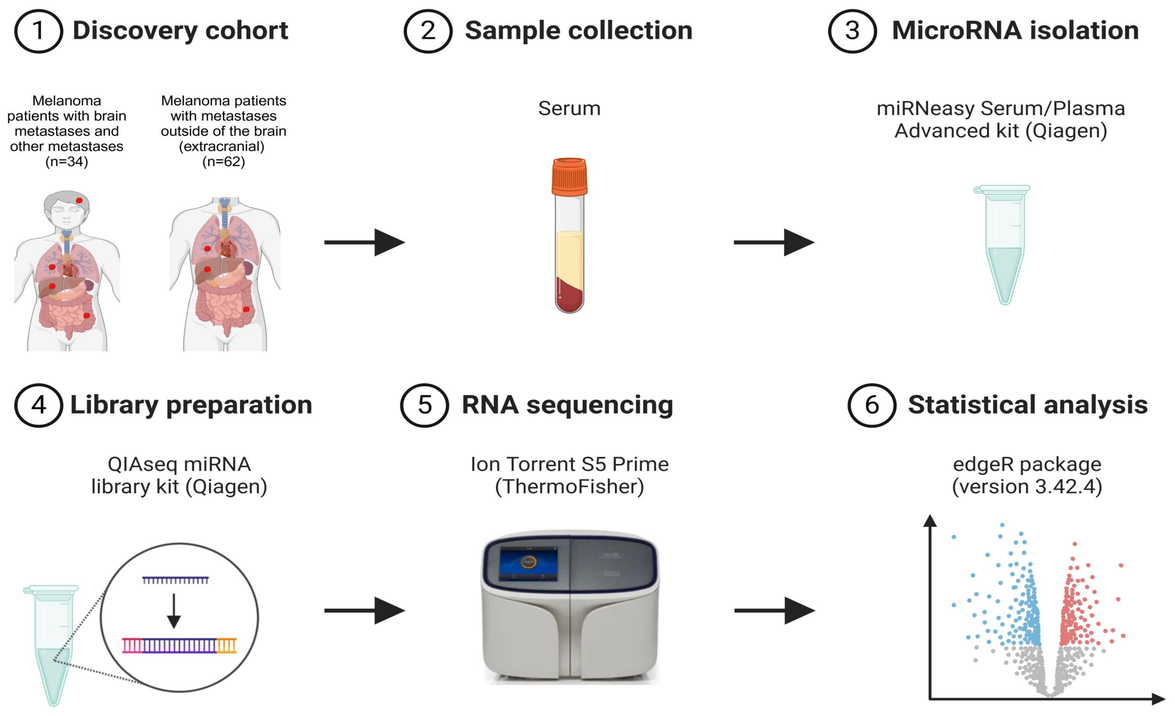
Background

- Cutaneous melanoma is an aggressive type of skin cancer that is responsible for the majority (80%) of skin-cancer related deaths[1].
- The screening for melanoma brain metastasis is not a standard of care in asymptomatic patients and MRI scans remain underused in the advanced melanoma clinical setting (<40%)[2,3].
- There is an urgent need for a blood test that can be used to detect brain metastasis early, when tumour burden is low and more responsive to therapy.
- **This project aims to identify and validate biomarkers, such as miRNAs, for the detection of brain metastasis in melanoma patients.**

#1
cause of death in advanced melanoma patients[4]

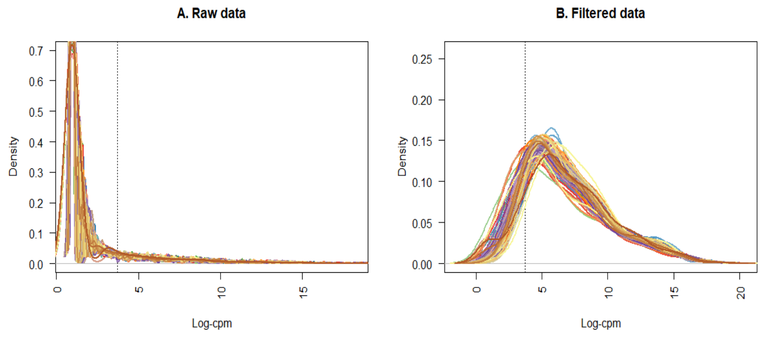
60%
of advanced melanoma patients may develop brain metastasis[5]

Methods



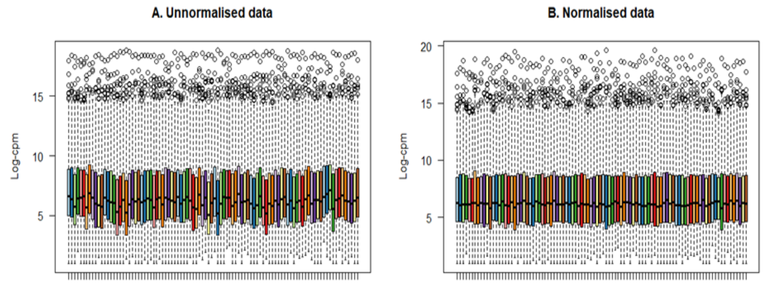
Results

Figure 1: Density plots of log-CPM values of raw and filtered data



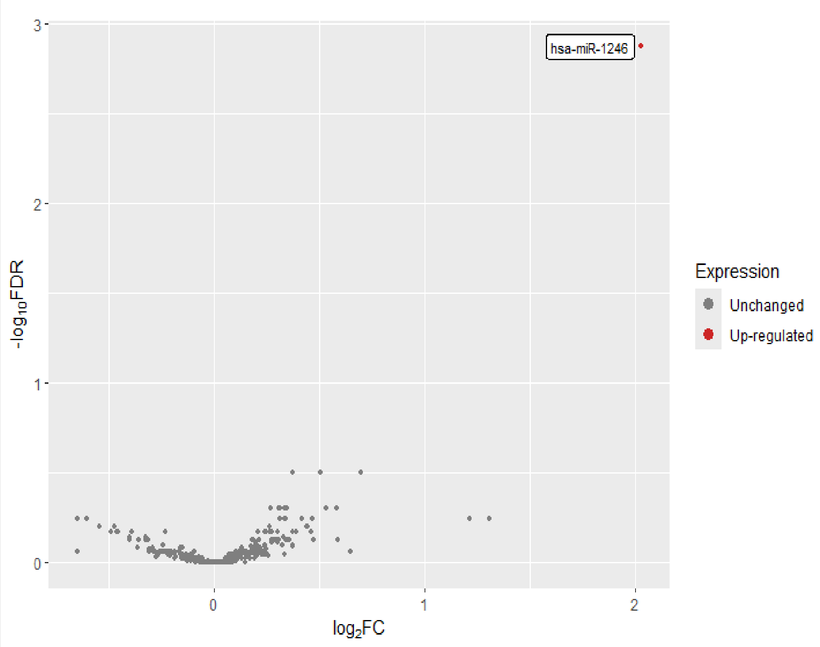
After filtering out miRNAs with very low counts, 336 miRNAs remained for further analysis from an initial set of 2,633. This indicates that a significant proportion of miRNAs were removed, leaving only those with higher expression levels for subsequent investigation.

Figure 2: Boxplots of log-CPM values prior and after to normalisation



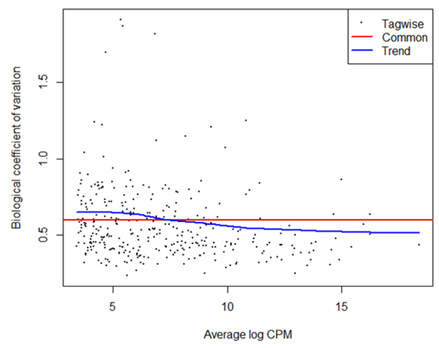
To normalise the miRNA expression count data, the Trimmed Mean of M-values (TMM) method was used.

Figure 5: has-miR-1246 was the only significant differently expressed miRNA in patients with brain metastasis.



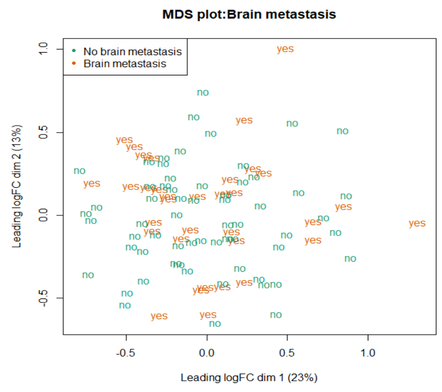
The volcano plot shows all non-significant and significant differentially expressed miRNAs in grey based on their measured log2 fold change difference (x-axis) and the significance of the change (y-axis). Grey dots represent non-significantly expressed miRNAs. Highlighted in red (upregulated) is has-miR-1246, which was the only significant differently expressed miRNA in patients with brain metastasis (logFC=2.028, FDR=0.0013) in patients with brain metastasis.

Figure 3: Scatterplot of the biological coefficient of variation (BCV) against the average abundance of each miRNA



Common dispersion was 0.355 and BCV was 0.596, implying that miRNA expression levels deviated from their average expression level across samples.

Figure 4: MDS plots of log-CPM values



Multidimensional scaling revealed that miRNAs are not consistently differentially expressed between melanoma patients with and without brain metastasis.

Conclusions and Future Directions

- miRNA-1246 was significantly enriched in advanced melanoma patients with brain metastases.
- miRNA-1246 has pro-oncogenic functions in multiple types of cancer[6] and is implicated in neuroinflammatory conditions[7,8].
- A TaqMan MicroRNA Assay (Thermo Fisher) will be performed in an independent validation cohort (n=90).
- Since the identification and quantification of specific combinations of circulating biomarkers may enable a more precise assessment for screening and prognostic purposes in metastatic melanoma patients, a multi-omic model will be established, based on the RNA-seq, methylation and tumour-associated autoantibodies data.

References

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Acknowledgements

This project is funded by research funds from Dr Aaron B Beasley and Professor Elin S Gray. Thanks to a collaboration with the IMPLEMENT study (Chief Investigator A/Project Lead Professor Rizos), already generated miRNA and methylated cfDNA data for the discovery phase will be used. D Sexauer is supported by an ECU Higher Degree by Research Scholarship and a Melanoma Institute Australia Postgraduate Research Top-up Scholarship.

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