

# Can microRNAs be useful biomarkers in ageing research?

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- Introduce microRNAs
- Highlight the current scope of microRNA in Neuroblastoma research
- Contrast this to the current findings in microRNA research in ageing
- Discuss future implications of microRNAs as biomarkers in ageing research

# Nomenclature

During this meeting I/ others may refer to microRNAs as miRs or miRNAs.

NB may be used in place of neuroblastoma.

NCC in place of neural crest cells.

OA in place of osteoarthritis.

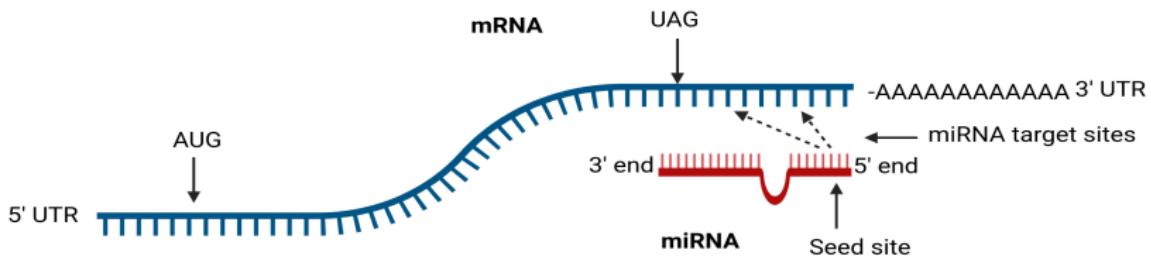
HD in place of huntington's disease.

CKD in place of chronic kidney disease.

nt in place of nucleotide.

# Background of microRNAs

- Short 16-22 nt long single strands of RNA which target specific mRNAs for degradation [1].
- Up to 60% of the mammalian protein coding genome are regulated by microRNAs [2].
- Highly conserved between species [1, 2].
- 7-8 nt region in the 5' end of the microRNA is known as the seed site.
- Responsible for complementary binding between the miRNA and mRNA.

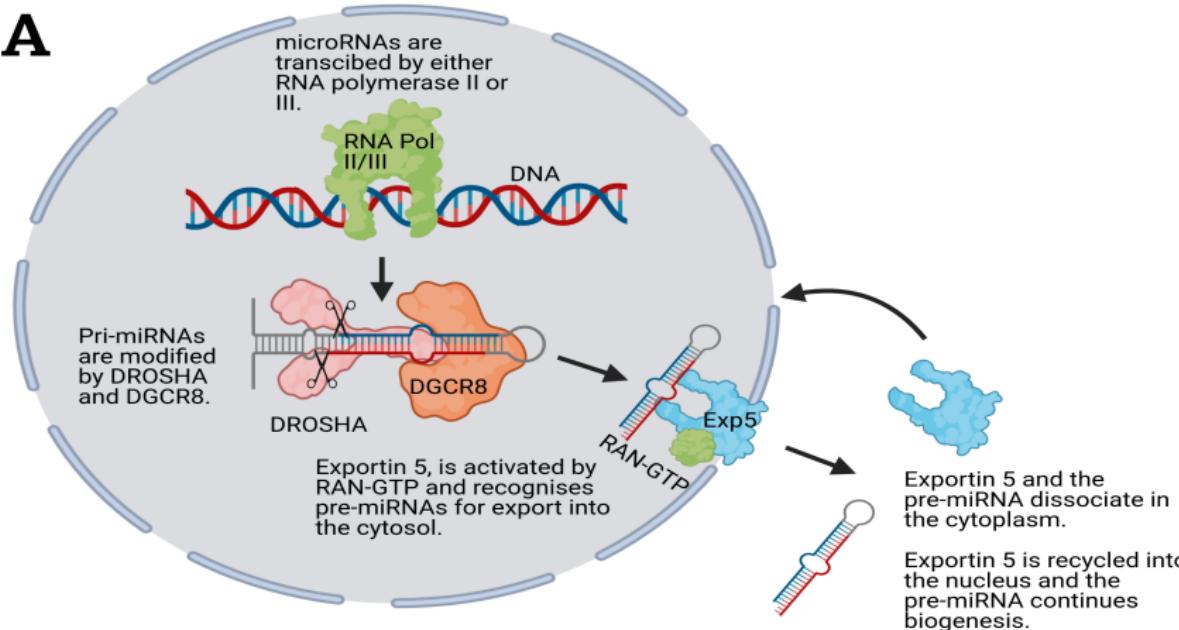


- There is a negative evolutionary pressure on DNA to not be complementary to seed sites.
- There is a positive evolutionary pressure on DNA to keep seed sites and seed site target regions as they are.

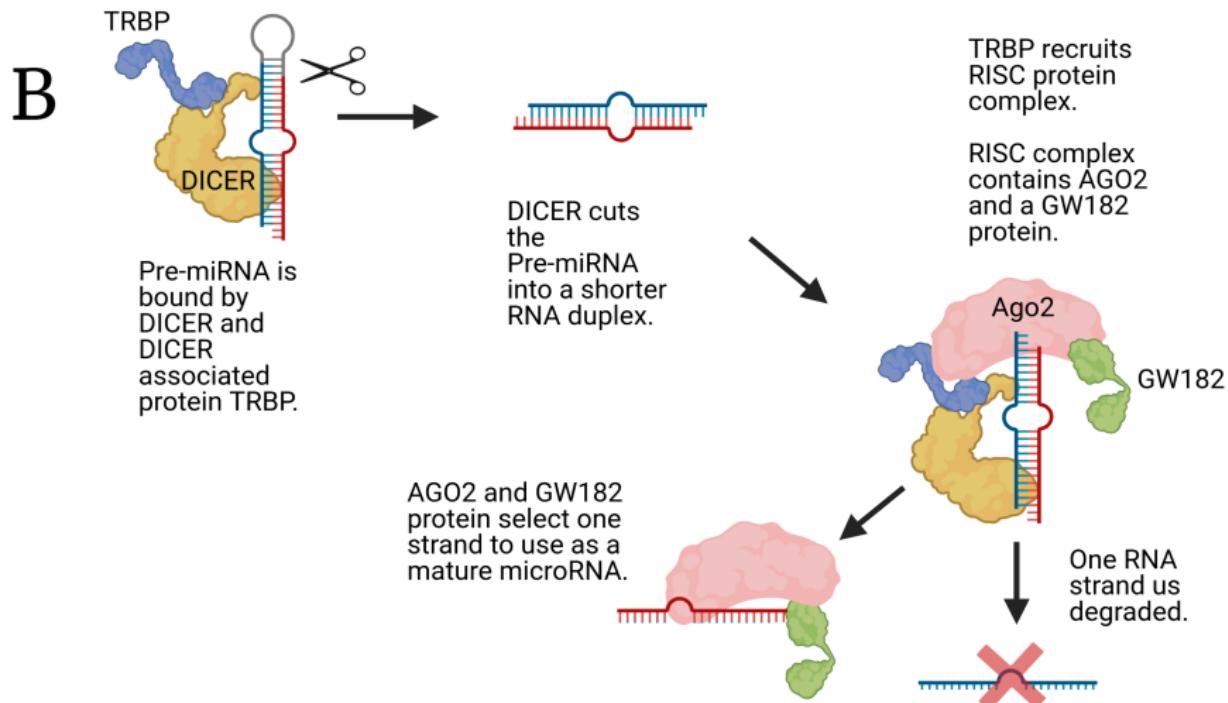
This implies miRNAs have special roles within organisms [3].

# microRNA biogenesis I

A

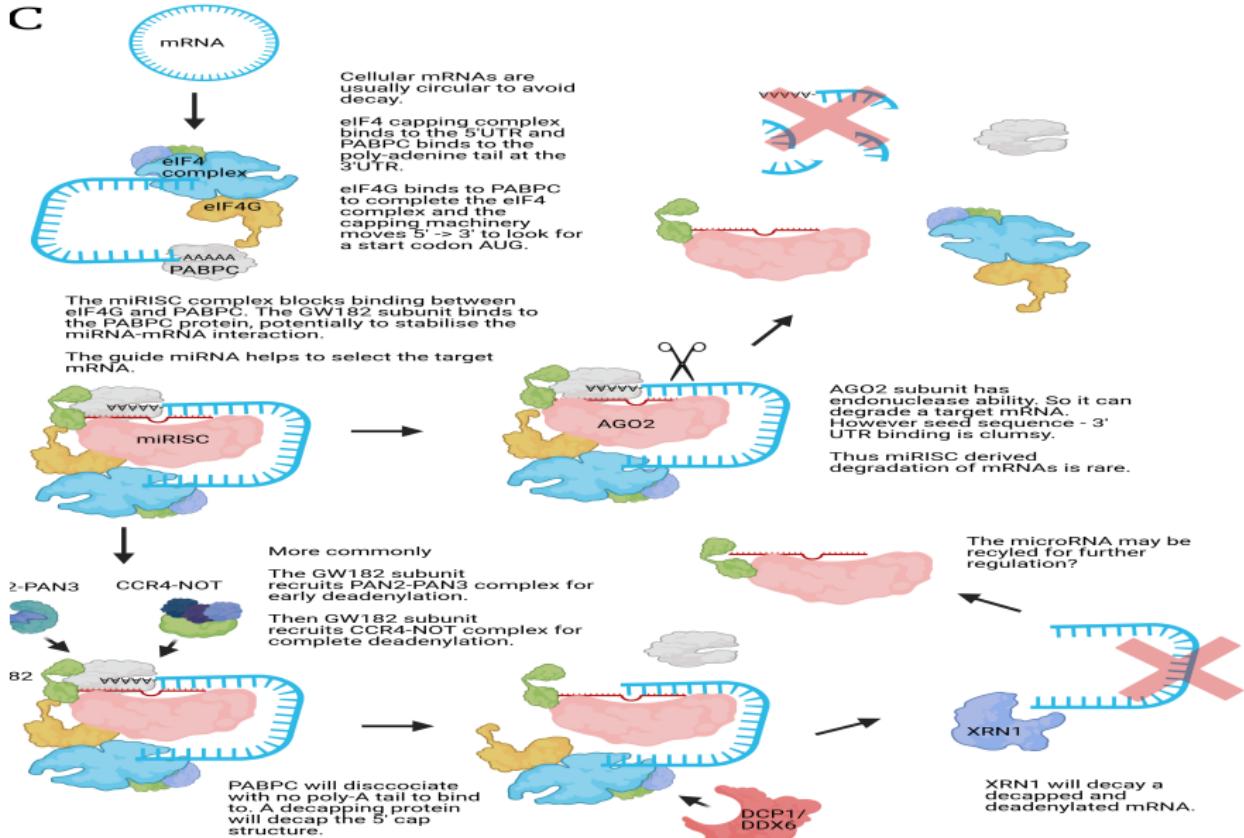


# microRNA biogenesis II



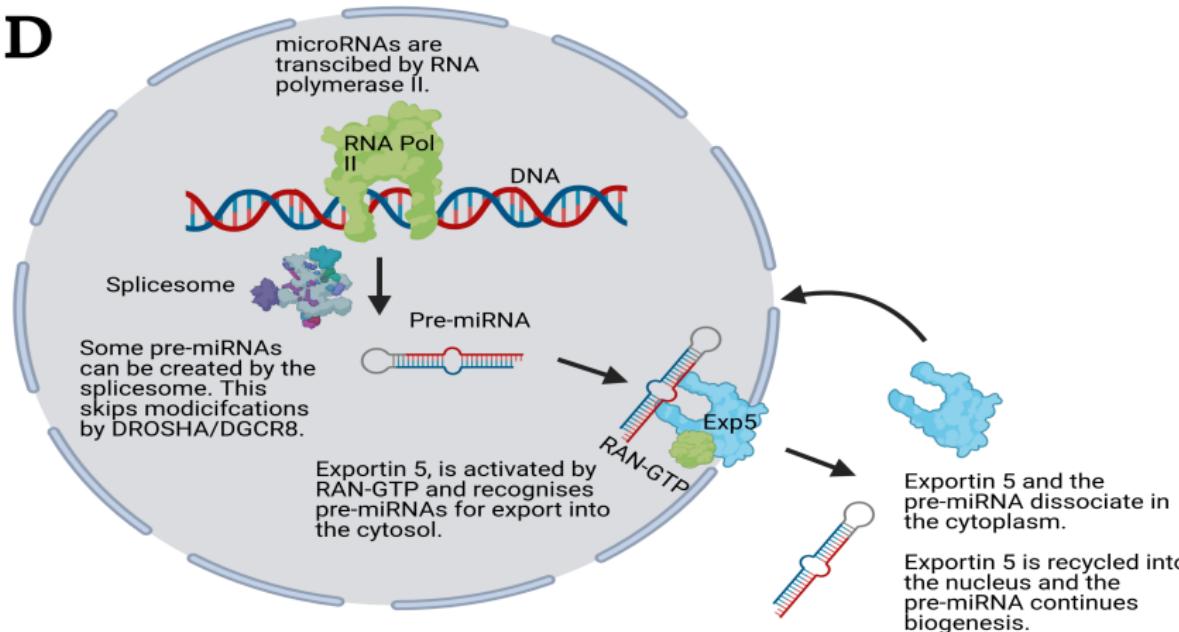
# microRNA biogenesis III

C



# microRNA biogenesis IV

D



# Circulating microRNAs

miRNAs have been found within fluids within extracellular vesicles [4].

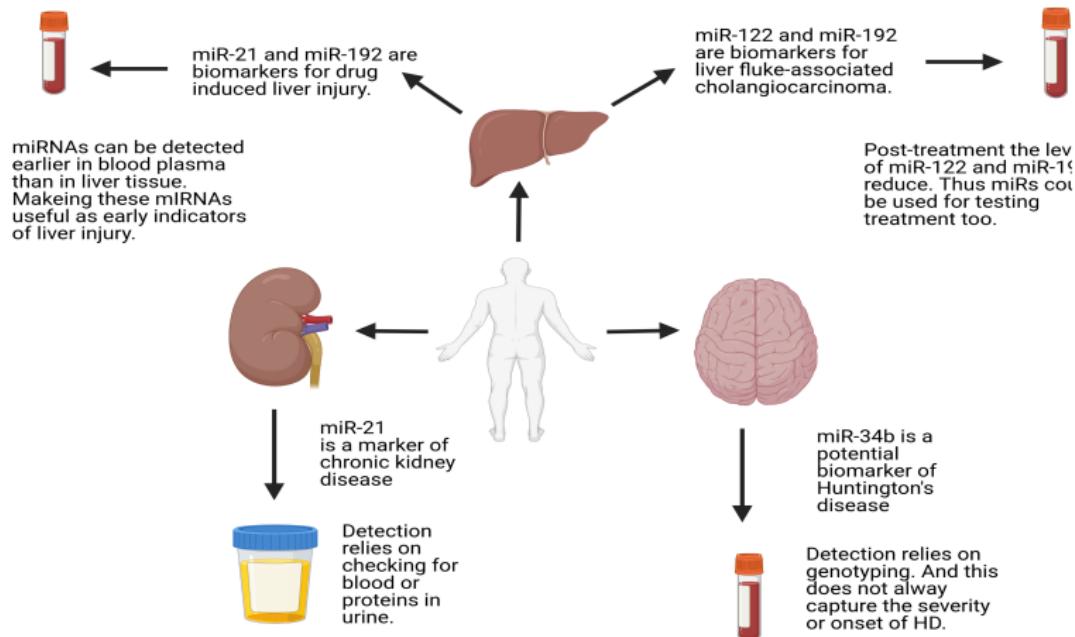
These biofluids include: blood, saliva, amniotic fluid, blood and urine. (ect)

miRNAs can be secreted out of cells several ways:

- ① Secreted with high density lipids
- ② Complexed with Ago2 (miRISC complex) (90% of extracellular miRs)
- ③ Encapsulated within exosomes
- ④ Packaged in microvesicles
- ⑤ Released with apoptotic bodies

# Using microRNAs as biomarkers a clinical setting

miRNAs have a huge potential to become non-invasive biomarkers for difficult to analyse conditions.



## Limitations of microRNAs

A single miRNA can target multiple mRNAs, and a single mRNA can be targeted by multiple miRNAs.

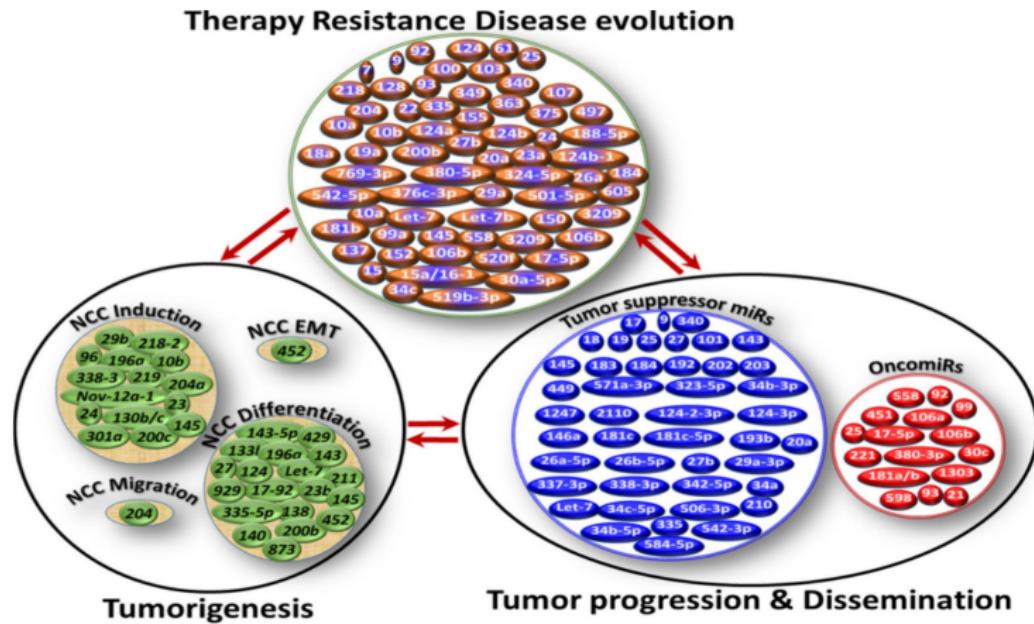
> 18,000 miRNA-mRNA interactions found in HEK293 cells [7].

> 34,000 miRNA-mRNA interactions in hepatoma cells [8].

This complexity makes studying miRNAs difficult and potentially unpopular.

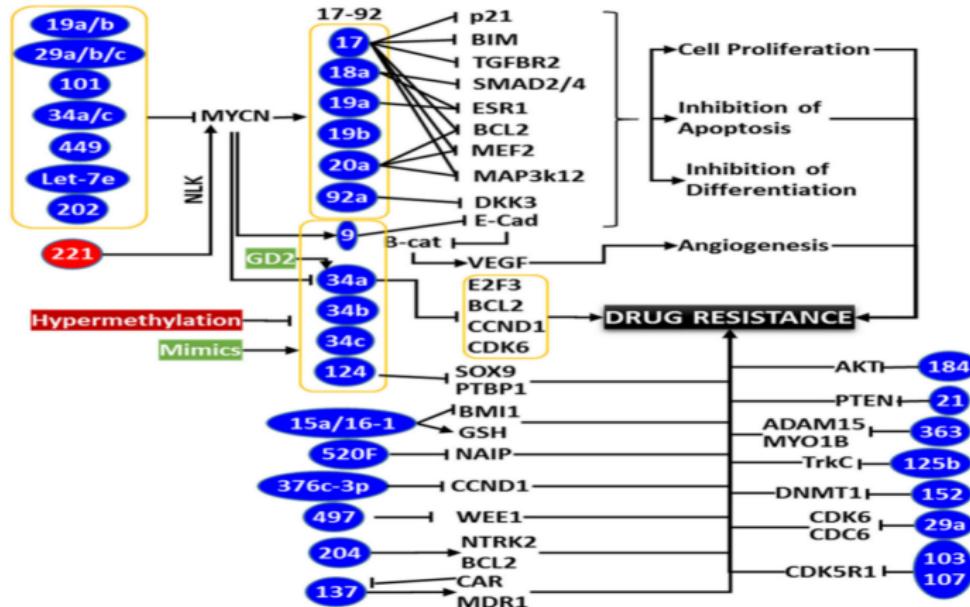
miR-192 being found in blood plasma could indicate liver injury or fluke-associated cholangiocarcinoma. Relying on miRNAs alone could be problematic.

# Neuroblastoma case study: Where have they gotten to in 18 years



Pros and cons?

# Neuroblastoma case study: miRNAs mechanistically known to be involved in NB

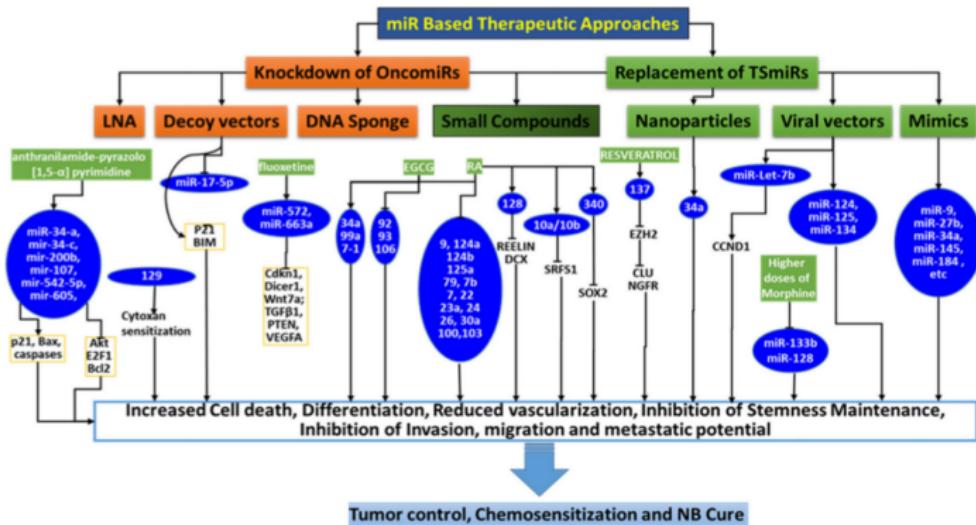


Pros and cons?

# Neuroblastoma case study: miRNA based therapies

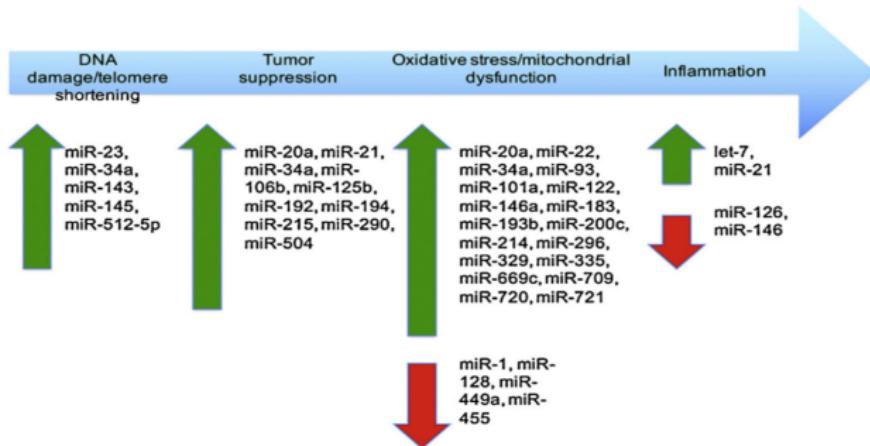
Aravindan et al.

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Pros and cons?

# Current prospects of microRNAs as ageing biomarkers



Pros and cons?

# Discussion points

Are microRNAs better biomarkers than proteins?

## Discussion points

If we do not understand what the proteins are doing in ageing, is it relevant to investigate the microRNAs?

## Discussion points

Within NB research microRNAs have been classified into: tumour suppressor miRs, oncomiRs and metastamiRs. Will ageing research reach a stage where we can class microRNAs into groups?

"InflamiRs" has already been coined. Likely others will be too.

"ScenomiRs"?

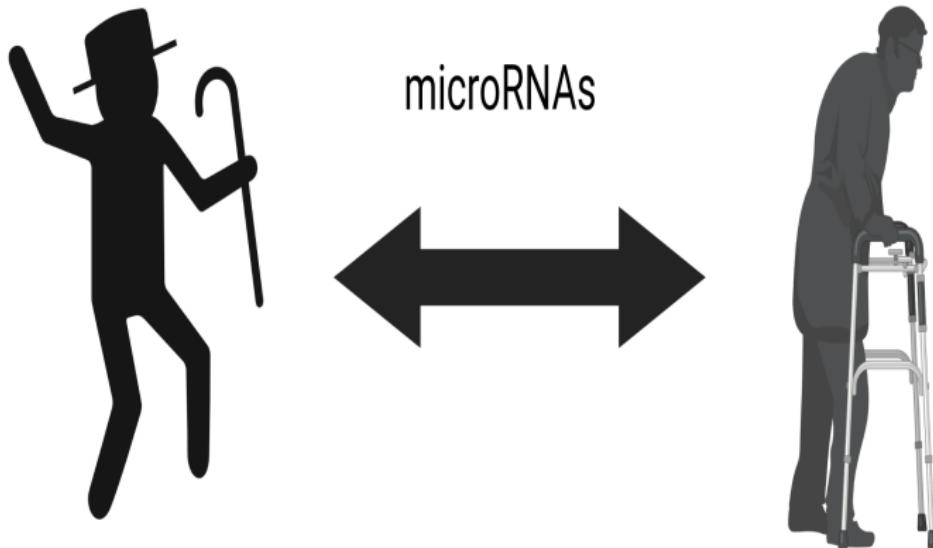
"GeromiRs"?

## Discussion points

If you had loads of funding, how would you investigate microRNAs as potential biomarkers of ageing?

# An interesting idea....

If ageing is a disease, can we classify severity of ageing by using miRNAs as an input?



# Thanks

Everyone for participating.

# References

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