RESIDENT RESEARCH DAY

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MICRORNA BENCH RESEARCH

- Initially one review article
- One text book chapter
- Original research

ARE MICRORNAS TRUE SENSORS OF AGEING AND CELLULAR SENESCENCE?

- Published in Ageing Research Reviews
- Later used in Progress in Molecular Biology and Translational Science Volume 146
- Gave a primer on miRNA
- Reviewed research on a wide range on miRNA that had been found to be involved in various age-related processes and pathologies

MIRNAS

- Transcribed in the nucleus by RNA Pol II
- Processed by Drosha protein then transported to cytoplasm where maturation is completed by Dicer protein
- Function by binding to 3' UTR of mRNAs
  - This signals to prevent translation
  - Tags for destruction vs sequestration based on complementarity

SELECTED MIRNAS

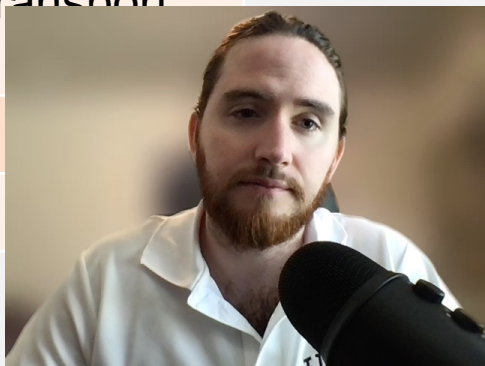
- MiR-34a - promotes senescence in hepatocellular carcinoma cells
- MiR-210, miR-376a*, miR-486-5p, miR-494, and miR-542-5p – involved in mitochondria autophagy
- MiR-192, miR-194, and miR-215 – induced by p53
- MiR-504 and miR-125b - target mRNA expressed by p53 gene
- MiR-21 – biomarker for aging-related inflammation and cardiovascular disease
- About 100 miRNAs were included in a large table

ORIGINAL RESEARCH

- Examination of differential expression of miRNA in mouse brain at different ages
- Probed for selected miRNAs using RT-PCR
- 6 selected: mmu-miR-17-5p, mmu-miR-22a-3p, mmu-miR-29a-3p, mmu-miR-133a-3p, mmu-miR-181a-5p, and 101a-3p.
- Brain of 6 and 12-month-old C57BL/6 wild-type mice probed, with future plans for 18 and 24-month-old mice

SELECTED MIRNAS

miRNA	Chromosome	Targeted cellular processes
miR-17-5a	14	Regulation of proliferation and differentiation of mouse neural precursor cells
miR-22a-3p	11	Decreases mitochondrial efficiency by targeting electron transport chain ATPase mRNA
miR-29a-3p	6	Suppresses tumors by activating p53, possible biomarker for Parkinsons
miR-101a-3p	4	Decreases mitochondrial efficiency by targeting electron transport chain ATPase mRNA
miR-133a-5p	18	Upregulated in acute myocardial infarction
miR-181a-5p	2	Absence causes degeneration of cerebellar Purkinje cells



RESULTS

miRNA	Average CT values of 6-month old mice	Average ΔCT values of 6-month old mice	Average CT values of 12-month-old mice	Average ΔCT values of 12-month-old mice	Fold change compared to 6 months ($2^{-\Delta\Delta CT}$)
miR-17-5p	28.78	9.53	24.69	8.68	**1.79**
miR-22a-3p	23.90	4.64	20.45	5.60	**0.51**
miR-29a-3p	23.89	4.47	14.16	0.15	**20.02**
miR-101a-3p	27.89	8.39	20.83	6.04	**5.08**
miR-133a-3p	17.65	2.57	20.53	5.69	**0.003**
miR-181a-5p	24.23	4.98	16.37	1.52	**10.99**

RESULTS

- Differential expression was seen in each miRNA studied between the two age groups
- The levels of miR-17-5p, miR-29a-3p, miR-101a-3p and 181a-5p were found to be increased in 12-month-old mice relative to 6-month-old mice.
- Expressions of miR-22a-3p and miR-133a-3p were found to be decreased in 12-month-old mice relative to 6-month-old mice.

FUTURE

- Ultimate goal: discover miRNA that may act as a biomarker for neurodegenerative diseases
  - Alzheimer's
  - Parkinson's
- Better understand the process of normal and abnormal aging and cellular senescence

THANK YOU