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Aging causes an aortic biomechanical dysfunction phenotype by targeting the expression of members of the ERK pathway

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INTRODUCTION

The extracellular signal-regulated kinase (ERK) pathway is a well known regulator of vascular smooth muscle cell proliferation, but it is less well known that it also serves as an inhibitor of the actin-binding protein, caldesmon, which regulates vascular tone.

AIM

The aim of this study was to examine whether ERK activation is necessary for normal function of the aorta and if this activation is regulated by aging.

METHOD

- Thoracic aortas were isolated from young (3 month old) and aged (24-28 month old) male mice euthanized with isofluorane.
- Biomechanical experiments were performed to test the contractility of aortic tissues.
- MicroRNAs were transfected into A7r5 cells to study their effects on ERK activation and expression of focal adhesion proteins.
- Protein expression was analyzed by western blot and mRNA expression was analyzed by reverse transcription and qPCR.

RESULTS

Figure 1: PE-induced contraction is reduced in the thoracic aortas from aged mice.

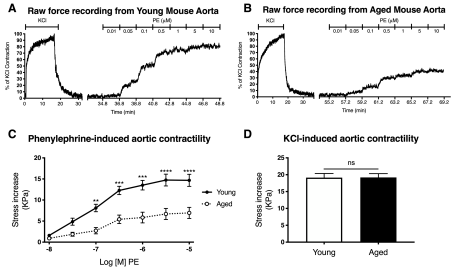


Figure 2: Aging reduces phenylephrine-induced ERK and CaD activation, which may contribute to smooth muscle contractile dysfunction.

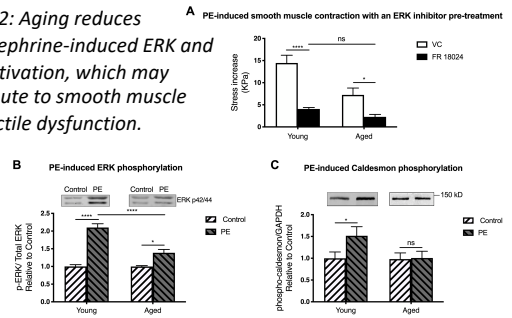


Figure 3: Overexpression of miR-34a and miR-137 downregulate focal adhesion proteins in cultured A7r5 smooth muscle cells.

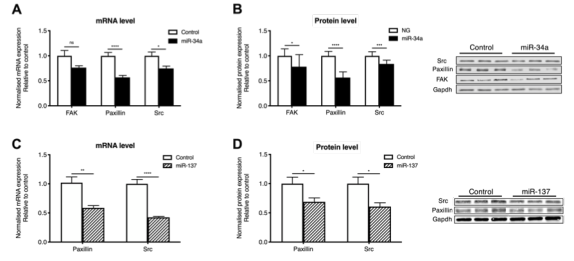


Figure 4: miR-34a and -137 overexpression attenuate agonist-induced ERK activation in cultured A7r5 smooth muscle cells.

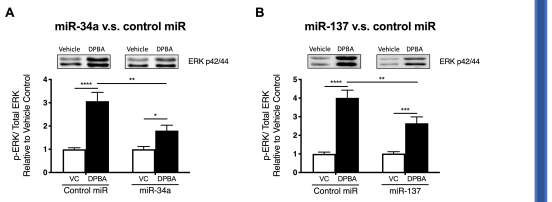


Figure 5: Src and paxillin play critical roles in agonist-induced ERK activation in aortic smooth muscle cells as scaffolding proteins.

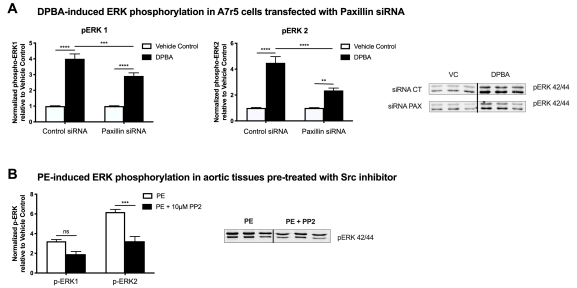
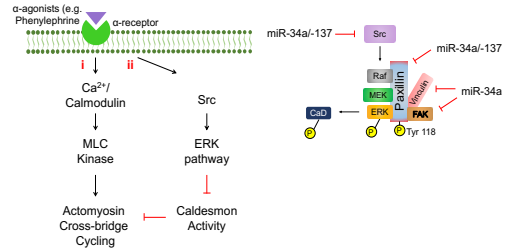


Figure 6: Summary diagram/Graphical Abstract.



CONCLUSIONS

Increases in miR-34a and -137 with aging downregulate the expression of the protein scaffolds, src and paxillin, leading to impaired ERK signalling and aortic contractile dysfunction, describing a potential novel area for therapeutic investigation.

REFERENCES

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