A NOVEL MICRORNA AND ITS POTENTIAL APPLICATION IN THE CLINICAL DIAGNOSIS OF HYPERTENSION

LABORATORY MEDICINE

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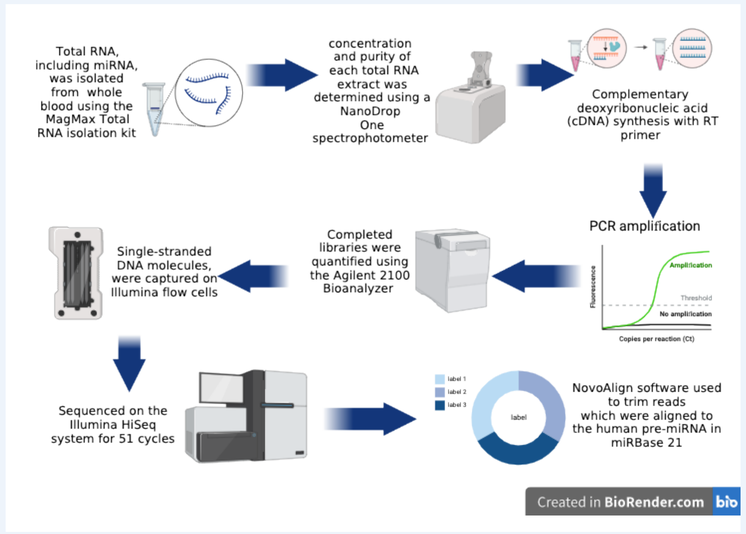
INTRODUCTION

The prevalence of hypertension (HTN) is on the rise in Africa, and molecular mechanisms involved in its development may be leveraged as potential therapeutic targets. MicroRNAs (miRNAs), which regulate various biological processes through gene expression regulation, may have an important role in blood pressure (BP) regulation, and their altered expression is associated with disease. The continuous description of novel miRNAs in different population groups around the world continues to add to the pool of existing miRNAs that can be targeted for diagnostic and therapeutic purposes in disease

METHODS

- Next-generation sequencing (NGS) technology was used to profile the entire miRNA population in blood samples from 48 participants placed into different groups based on their BP (hypertension) status.
- The NGS findings were validated in an independent sample of 881 participants using quantitative reverse transcription polymerase chain reaction technology (RT-qPCR).
- The relationships between expression of the novel miRNAs and systolic and diastolic blood pressure (SBP, DBP), as well as mean arterial pressure (MAP) were also investigated.



OBJECTIVE

This study aimed to describe novel miRNAs in a normotensive and hypertensive African population and relate their expression to clinical blood pressure parameters and hypertension status.

RESULTS

- The study was made up of 598 (67.9%) female and 283 (32.1%) male participants with a mean age of 42.6 years.
- NGS analysis revealed differential expression of two novel miRNAs (Table 1).
- The expression of hsa-miR-novel-chr1_36178 significantly differed according to sex (p = 0.002), with greater expression in males compared to females.
- BP parameters (SBP, DBP and MAP) did not show any significant difference by sex ($p \geq$ 0.085).

Table 1: Description of significantly differentially expressed novel microRNAs discovered by next generation sequencing

Mature ID	Pre-miRNA accession ID	Mature seed sequence	Mature length	Mature sequence
hsa-miR-novel-chr1_36178	MYNO2414	UCC AGC	17	CUC CAG CCU GGG CAACA
hsa-miR-novel-hr15_18383	MYNO1379	GCU CCC	22	UGC UCC CCC UCC CUU CCU GGGA

Table 2: Spearman correlations for blood pressure parameters and novel miRNA expression

	miR-MYNO2414 (2^-ΔCt)		miR-MYNO1379 (2^-ΔCt)	
	r	p-value	r	p-value
miR-MYNO2414 (2^-ΔCt)	1.000		0.477	<0.001
miR-MYNO1379 (2^-ΔCt)	0.477	<0.001	1.000	
SBP (mmHg)	0.064	0.060	0.026	0.453
DBP (mmHg)	0.082	0.016	0.048	0.162
MAP	0.076	0.024	0.045	0.195

- Age and sex adjusted OR were calculated to quantify the strength of the relationship between miRNA expression and screen-detected HTN, using the normotensives as a reference. The expression of hsa-miR-novel-chr1_36178 and hsa-miR-novel-chr15_18383 was significantly associated with screen-detected HTN, i.e they had a 36% and 31% higher odds compared to normatensive individuals, respectively (p = 0.016).
- As for the dose-response analysis, a significant association between the expression of hsa-miR-novel-chr1_36178 and the presence of screen-detected HTN was seen only when the miRNA was expressed at the highest level (Q5), OR = 2.13 (95% CI 1.32–3.45), (p = 0.002).
- In contrast, there was no dose-dependant association between the expression of hsa-miR-novel-chr15_18383 and the presence of screen-detected HTN, even at Q5 levels.

CONCLUSION

In conclusion, miR-novel-chr1_36178 showed significant dysregulation in hypertensives and its expression at higher levels, was related to SBP, DBP and MAP. As such, it warrants further study to understand its dose-dependant relationship with BP parameters and the possible role it plays in the pathogenesis of HTN. As it is a previously unreported miRNA, it has to be further characterised to understand its physiology, target networks and pathways in the body. This may shed more light on how its expression impacts BP regulation.

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