

Early Life Adversity is Associated with Differential miRNA Expression in Older African American Women at Risk for Cardiovascular Disease

Karen L. Saban, PhD, RN, APRN, FAHA, FAAN¹; Michael Zilliox, PhD²; Dina Tell, PhD¹; Herbert Mathews, PhD²; and Linda Witek Janusek, PhD, RN, FAAN¹
¹Loyola University Chicago, School of Nursing, Maywood, IL, USA; ²Loyola University Stritch School of Medicine, Maywood, IL, USA

Background

Early life adversity (ELA), such as childhood maltreatment, has been linked to negative health consequences during adulthood. Evidence demonstrates that African American (AA) women experience higher levels of ELA and have higher prevalence of cardiovascular disease (CVD). Studies in animal models have suggested that miRNAs may play an important role in the mechanism linking ELA to inflammatory disease, such as CVD. However little is known about which miRNAs are associated with ELA in AA women.

Objective

The purpose of this study was to examine whole blood miRNAs in association with high and low levels of ELA in older African American women at risk for CVD.

Methods

A cross sectional sample of AA women (N=18) (mean age=50.54 SD=11.03) participated in the study. Participants completed the Childhood Trauma Questionnaire (CTQ) to assess early life adversity. Whole blood was collected in Paxgene tubes and stored at -80C until batch analyzed. cDNA libraries were generated using the TruSeq Small RNA library prep kit and sequenced on the Illumina MiSeq to render 50 base pair single end reads. The reads were mapped to GRCh38 using Bowtie2 (v. 2.2.1), counts were generated with HTSeq (v. 0.6.1p1) and differential expression was calculated using DESeq2 (v. 1.14.1). A p value of <.01 was considered significant.

Results

Table 1: Mean Values for Childhood Trauma Questionnaire

CTQ Subscale	Current sample (N=18) Mean age 50.54±11.0	Breast Cancer Sample (N=40) Mean age 55.6 ±9.4 <small>Janusek et al. (2013). Childhood adversity increases vulnerability for behavioral symptoms and immune dysregulation in women with breast cancer. Brain Behav Immun. 30 (suppl): S149-S162</small>	African American Men Sample (N=34) Mean age 20 ±2 <small>Janusek et al. (2014) Unpublished data</small>
Emotional Neglect	8.67 ±4.55	9.2±4.9	10.2 ±4.5
Physical Neglect	7.44 ±2.06	6.6±2.6	7.8±3.5
Emotional Abuse	7.22 ±3.99	8.9±4.9	7.6±3.6
Physical Abuse	7.29 ±2.37	6.9±4.3	8.3±3.1
Sexual Abuse	7.53±3.76	6.8±3.4	6.5±3.9

Table 2: Upregulated MiRNA

MiRNA	Base Mean	Fold Change	P value
hsa_miR-548-3p*	0.765	5.826	0.01
hsa_miR-3161	0.914	4.753	0.04
hsa-miR-301a-5p	1.297	2.843	0.08
hsa-miR-3120-3p	1.955	2.707	0.05
hsa-miR-6514-3p	7.978	1.717	0.06
hsa-miR-339-3p	101.589	1.567	0.04
hsa-miR-3124-5p	11.471	1.545	0.09

*p≤.01

Table 3: Downregulated MiRNA

MiRNA	Base Mean	Fold Change	P value
hsa-miR-4639-3p*	0.668	6.180	0.01
hsa-miR-6737-3p*	0.735	5.382	0.01
hsa-miR-4757-5p	0.521	4.643	0.06
hsa-miR-500b-5p	1.256	3.638	0.02
hsa-miR-6804-3p*	2.457	3.454	0.006
hsa-miR-6780a-5p	1.191	2.970	0.08
hsa-miR-4669	1.461	2.812	0.08
hsa-miR-365b-3p	2.185	2.812	0.02
hsa-miR-664b-3p	3.057	2.427	0.05
hsa-miR-144-3p	1.995	2.203	0.08
hsa-miR-6721-5p	3.025	2.084	0.07
hsa-miR-6764-5p	3.197	2.066	0.04

*p≤.01

Results

Participants who reported higher levels of ELA (CTQ ≥35) as compared to those with low levels (CTQ score <35) had differentially expressed miRNAs. Specifically, those reporting greater levels of ELA had a higher level of hsa-miR-548-3p (5.84 fold) and lower levels of hsa-miR 4639-3p (6.18 fold), hsa-miR 6737-3p (5.38 fold), and has-miR-6804-3p.

Conclusion and Implications

Identifying specific miRNAs that are associated with ELA will contribute to a better understanding of how ELA leads to negative health consequences in adulthood.



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